Invited Speaker Abstracts

ESP16-1159
ESPID PLENARY 1 - NUTRITION & INFECTIOUS DISEASES

MECHANISMS OF VIRAL VIRULENCE IN RESPONSE TO HUMAN NUTRITION
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Host nutrition has long been known to influence the host's ability to respond to a viral infection. In addition to affecting host responses, the virus itself can also be affected by the nutritional status of the host. A host deficiency in selenium leads to a normally benign coxsackievirus B3 (CVB3) to become highly virulent due to the acquisition of specific mutations in the viral genome. Although nutrient deficiencies are often associated with increased viral virulence, what about over nutrition? Currently, we are experiencing a global epidemic of obesity. Although obesity is associated with metabolic syndrome, leading to increased risk for cardiac disease and type 2 diabetes, obesity has also been recognized as an independent risk factor for severe complications from infection with influenza virus. In the US, 36% of adults and 17% of children are obese, providing a large number of high risk individuals exposed to yearly influenza epidemics. Using a diet-induced murine model of obesity, obese mice were found to experience a high rate of mortality when infected with influenza virus which was associated with increased lung inflammation, poor generation, maintenance and function of memory T cells, reduced Treg activity, and diminished influenza specific antibody. In a human study of influenza vaccination, when stimulated with influenza virus in vitro, T cells from vaccinated obese individuals displayed less activation and functional markers when compared with healthy weight individuals. Thus, both over and under nutrition can profoundly influence the host response to viral infection.

ESP16-1168
ESPID PLENARY 1 - NUTRITION & INFECTIOUS DISEASES

HOST-PARASITE INTERACTIONS IN RELATION TO NUTRITIONAL STATUS AND THE IMPLICATIONS FOR THE WIDER SCIENTIFIC COMMUNITY

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"Child and Adolescent Development: a perspective on the relevance of nutrition and infection from the forthcoming edition of Disease Control Priorities".

Donald Bundy is responsible for Neglected Topical Diseases at the Bill and Melinda Gates Foundation in Seattle, USA, and the DCP3 Child and Adolescent Development Volume Lead Editor.

This presentation will explore why nutrition and infection need to be addressed together to improve health and development outcomes, especially in the poorest communities. To provide a global health policy context, this discussion will be presented in light of the draft conclusions from the latest edition of Disease Control Priorities (DCP3). The DCP3 Child and Adolescent Development Volume, publishing December 2016, explores a new vision of child development based on accumulating evidence of benefits that accrue from targeted interventions across the lifecourse. This volume includes evidence of costs, return on investment, and implications for trade-offs for interventions that have demonstrated impact on cognition, health or physical growth.

This volume outlines an investment case for the implementation of effective, costed, scalable interventions appropriate for low resource settings. These interventions are prioritized and organized into three essential packages: preschool, school-age, and adolescents. These packages are being developed in the context of defining and expanding Universal Health Care.

The volume is a resource for policy makers to set priorities and make evidence-based decisions to help vulnerable populations reach their developmental potential. The key messages are being validated through global consultations in China, India, the Middle East, and the continent of Africa. ESPID will further enrich these messages.

ESP16-1149
ESPID PLENARY 2 - IMMUNOLOGY & INFECTION - UNDERSTANDING THE HOST RESPONSE

ACTIVATION OF THE INNATE IMMUNE SYSTEM AND ITS IMPLICATIONS FOR TREATMENT IN INFECTIOUS DISEASES

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The New Forward Genetics

Random germline mutagenesis with N-ethyl-N-nitrosourea (ENU) has produced breakthrough understanding in immunology, but in the past was a slow process, limited by the process of mapping and finding causative mutations. Only a few mutations could be tracked down in a year's time, and some of them proved to affect well known genes. We have developed a means of identifying causative mutations within approximately one hour of the time phenotypic data are recorded. The discovery of gene function is now limited only by the rate at which mutations can be produced and screened. Approximately 1,000 mutations can be tested weekly for phenotypic effect in more than 150 screens. As of present writing 88,733 mutations altering coding sense and splice junctions have been tested for phenotypic effects in one or more of these screens (most of them for most of 48,000 G3 mice). Cumulative damage to the genome is tracked, permitting close estimates of saturation. So far, approximately 25% of all genes have been mutated to phenovariance, with mutant alleles tested three times or more in the homozygous state for phenotypic anomalies. Where dominant loss of function alleles are concerned, approximately 39% of all genes have been tested with mutant alleles examined three times or more for phenotypic effects in the heterozygous state. As an extensive allelic series develops at most loci, confidence grows concerning the relationship between genotype and phenotype, and even rather subtle associations can be detected. Many novel protein requirements for immunological function have been identified.

ESP16-1167
ESPID SYMPOSIUM 1 - GENOMICS: GENETIC SUSCEPTIBILITY TO INFECTIOUS DISEASES

AN OVERVIEW OF GENETIC SUSCEPTIBILITY TO VIRAL INFECTIONS

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Severe, unusual or recurrent viral infections of childhood are increasingly recognized as being due to an underlying genetic primary immunodeficiency. With recent advances in genomics and sequencing technology, there has been a surge in the discovery of single gene disorders identified as underlying childhood infectious diseases. Among these are a number of genes predominantly associated with viral infections of childhood, which will be discussed in this talk with a specific focus on the human herpesviruses. Some of these immunodeficiencies are specific to a particular viral infection whereas others predispose to multiple viral, bacterial or fungal infections. The discovery of these genes has greatly enhanced our understanding of protective immunity to pathogens, allowing us to gain new insights into the specific and non-specific immune mechanisms controlling viral infection.

ESP16-1116
ESPID SYMPOSIUM 1 - GENOMICS: GENETIC SUSCEPTIBILITY TO INFECTIOUS DISEASES

UNRAVELLING THE GENETICS OF MENINGOCOCCAL DISEASE: THE FACTOR H STORY REVISITED

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Genetic variants within *Complement factor H (CFH)* and *CFH-related protein (CFHR)* genes have been associated with susceptibility to a range of human diseases. FH acts as a negative regulator of the alternative complement pathway and its circulating plasma levels have been inversely correlated with susceptibility to infectious and autoimmune diseases, leading to hypothesize the existence of a putative regulatory region within *CFH-CFHR* controlling Factor H (FH) expression. However, due to the sequence complexity of this area its discovery has remained elusive.

Using a capture-targeted approach followed by deep sequencing we have characterized the extremely complex *CFH-CFHR1-5* area and fine mapped the association signal of susceptibility to meningococcal disease (MD) to a functional region. During my talk I will discuss our strategy, integrating cell differentiation and genome-editing experiments to identify the functional elements controlling FH expression levels. Our data demonstrate that FH is the ultimate complement protein associated with MD susceptibility and that its expression levels are controlled through a cis-regulatory variant providing a novel molecular mechanism relevant to other human diseases.

ESP16-1164
ESPID SYMPOSIUM 1 - GENOMICS: GENETIC SUSCEPTIBILITY TO INFECTIOUS DISEASES

AN OVERVIEW OF GENETIC SUSCEPTIBILITY TO FUNGAL INFECTIONS

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In the past decade, studies of primairy immunodeficiencies have hugely promoted our understanding of immunological pathways involved in human antifungal immunity. This knowledge helped to elucidate mechanisms that play a crucial role in antifungal host defense, and offered unique opportunities to link clinical phenotypes to immunological function. We have learned that the IL-17 pathway is fundamental for mucosal antifungal host defense, while neutrophil function, IFNg and GM-CSF are essential to prevent invasive fungal infection. Of course, our present knowledge is still limited, and there are a large number of fungal infections in which the environmental and genetic background is yet to be deciphered.

ESP16-1165
ESPID SYMPOSIUM 2 - DIAGNOSTICS: IMPROVING INFECTIOUS DISEASES DIAGNOSTIC TOOLS

ADVANCES IN PATHOGEN DETECTION

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Rapid molecular detection of pathogens is increasingly replacing culture-based testing, and has the potential to fundamentally change our approach to empiric treatment of many childhood infectious diseases. Nucleic acid amplification testing, most commonly using variations of real-time PCR, is rapid, sensitive and allows multiplex detection of a range of potential pathogens. Single-molecule nucleic acid detection without amplification is now also feasible using novel detection technologies. However the application of these methods at the point-of-care is limited by the need for relatively costly instrumentation. In contrast, sensitive detection of pathogen cellular components, metabolites or host biomarkers is possible using point-of-care assay formats, such as lateral flow assays. There are a number of constraints to these approaches, including limited ability to further characterize pathogens (for antimicrobial susceptibility testing or genotyping) and the clinical interpretation of detectable microbial nucleic acid is not always straightforward. The cost-effectiveness and clinical utility of many new tests has been poorly studied. Whole pathogen genome sequencing is increasingly being explored as a public health intervention, particularly for slow-growing organisms. Using specific examples, this presentation will focus on recent advances in each of these areas and highlight the need for a rational approach to assay selection and cautious and evidence-based interpretation of findings.

ESP16-1154
ESPID SYMPOSIUM 3 - THERAPEUTICS: USING ANTIMICROBIALS INTELLIGENTLY

TOPICAL ANTIBIOTICS WORK!

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To safeguard future antibiotic use, concerted efforts are underway to improve usage of antibiotics. Next to reducing unnecessary antibiotic prescribing, one proposed action to minimise the chance of antimicrobial resistance (AMR) development is to prevent antibiotic exposure of the 10^12 bacteria that colonise the human intestinal tract. In situations where antibiotic treatment is needed, one such approach could be to reduce the use of systemic antibiotics by substituting locally applied (topical) antibiotics.

In children with ear discharge associated with ventilation tubes (grommets), the grommet provides an unique opportunity to instil topical antibiotics directly into the middle ear where they can act and fight the infection; this route of administration avoids children being exposed to systemic adverse effects and has the potential to reduce the risk of AMR. In this lecture, results of a recent trial comparing the clinical and cost-effectiveness of three commonly applied treatment strategies in children with ear discharge associated with grommets, i.e. initial observation, oral and topical antibiotics, will be presented.

Furthermore, evidence on the use of (topical) antibiotics in children with acute otitis media presenting with ear discharge due to a spontaneous eardrum perforation and promising ongoing research on trans-tympanic delivery of antibiotics (that is without an eardrum perforation or grommet) will be briefly discussed.

ESP16-1148
ESPID/ECDC/WHO JOINT SESSION 4 - VACCINES: THE RETURN OF OLD VACCINE PREVENTABLE ENEMIES

POLIO IN THE EUROPEAN REGION – RECENT EXPERIENCES

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WHO European Region was certified polio-free in 2002. However, until global polio eradication is achieved, there remains a risk of wild poliovirus (WPV) reintroduction from endemic areas and of emergence of circulating vaccine-derived polioviruses (cVDPV) in areas with suboptimal OPV coverage. Recently, three poliovirus emergencies occurred in the European Region: WPV1 reintroductions in Tajikistan (2010) and Israel (2013), and cVDPV1 outbreak in Ukraine (since 2015).

The presentation will focus on the current outbreak in Ukraine resulting from the emergence of highly divergent cVDPV1. In August, 2015, WHO confirmed cVDPV1 in two unrelated acute flaccid paralysis cases in Ukraine. The isolates were 20 and 26 nucleotide divergent from prototype Sabin strain (with 18 identical mutations) consistent with their common origin and ~2-year-evolution.

Since 2010, Ukraine has been ranked at high risk of poliovirus spread because of low vaccination coverage (decline from 91% in 2008 to 15% by mid-2015). Contributing factors to the decline in coverage which created favorable conditions for cVDPV emergence, included: impact of the failed 2008 measles-rubella vaccination campaign, low vaccine acceptance among population and healthcare workers, anti-vaccine media environment, insufficient funding, inefficient vaccine procurement practices, and the economic and political crisis.

Outbreak response OPV immunization during October 2015-February 2016 resulted in 64.7% and 75.1% coverage for rounds 1 and 2 (target age, <6 years), and 80.3% for round 3 (target age, <10 years). The measures to strengthen surveillance have been implemented. No additional cVDPVs have been identified by March 31. WHO will re-assess the outbreak status in April, 2016.

ESP16-1150
ESPID/ECDC/WHO JOINT SESSION 4 - VACCINES: THE RETURN OF OLD VACCINE PREVENTABLE ENEMIES

MEASLES IN EUROPE – A MOVING TARGET

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Measles is targeted for elimination by Member States of the WHO European Region. However, elimination targets set for 2007, 2010 and most recently 2015 have not been achieved. Despite an 88% reduction in cases in EU/EEA Member States between 2010 and 2015, more than half of the EU/EEA Member States reported more cases than the target of less than one case per million population per year in 2015. In 2014, the Regional Verification Commission of the WHO Office for the European Region classified eight EU/EEA Member States as still having endemic transmission and seven as inconclusive due to unsatisfactory surveillance or coverage data, while no data were available from one Member State.

While a great variety of activities have increased MMR vaccine uptake in some countries, the majority of EU/EEA MS have not reached the goal of 95% coverage with two doses. Epidemiology of measles is changing, with more cases being observed in older age groups. Reasons for low uptake greatly vary in Europe and tailored immunisation strategies are necessary. Sharing experiences of what works well individually for each “hard-to-reach” group and closer collaboration between countries are necessary to achieve elimination of measles and rubella in the near future in Europe. Additional commitment from the technical, clinical and political side to achieve and maintain the goal is necessary. The only way of reaching the target will be to achieve 95% vaccine coverage with two doses of MMR by closing immunity gaps and creating trust and confidence in all vulnerable groups.

ESP16-1162
ESPID SYMPOSIUM 5 - RECENT EMERGENCIES: EBOLA AND ZIKA

PREVENTING EBOLA - THE RING VACCINATION STUDY

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The Ebola Virus Disease (EVD) outbreak in West Africa is by far the largest ever recorded. A safe and effective vaccine against EVD may help end the ongoing epidemic in West Africa and control future outbreaks. A variety of candidates are currently being evaluated in Phase I, II and III trials.

Evaluating vaccine efficacy during outbreaks is challenging. To observe a sufficient number of events, trials may need to vaccinate very large numbers of people in populations believed to be at risk. Ebola virus spreads from person to person through direct physical contact with body fluids of symptomatic EVD patients.

Here we describe a novel trial design - ring vaccination where a patient newly diagnosed with EVD becomes the index case around whom a socially and geographically defined ring of his or her contacts and the contacts of these contacts is formed. This ring is then randomized to either immediate or deferred vaccination with the candidate vaccine. As the ring can also be viewed as a cluster and because randomization occurs at the level of the ring, the extensive literature on the design, analysis and reporting of cluster randomized trials can be readily adopted. We illustrate the approach by summarizing the protocol and results of a ring vaccination trial against EVD in Guinea, West Africa. This strategy may increase trial power, reduce the required sample size, and simplify trial logistics as compared to standard vaccine trial designs and can be useful for performing vaccine trials during outbreaks.

ESP16-1184
ESPID SYMPOSIUM 5 - RECENT EMERGENCIES: EBOLA AND ZIKA

NEUROLOGICAL AND AUTOIMMUNE COMPLICATIONS OF ZIKA VIRUS INFECTION

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NEUROLOGICAL AND AUTOIMMUNE COMPLICATIONS OF ZIKA VIRUS INFECTION

Zika virus (ZIKV) is an emerging arthropod-borne virus that belongs to the genus Flavivirus, and transmitted primarily by *Aedes spp*. mosquitoes. In May 2015, the Ministry of Health of Brazil confirmed autochthonous transmission of ZIKV associated with an outbreak of “dengue-like syndrome” cases. The ZIKV outbreak continued to evolve, spreading geographically very rapidly in the Americas.

Severe presentations of the disease or deaths associated to ZIKV infection were not reported before the outbreaks in French Polynesia and Brazil. However, the results of a recent study in a large series of patients from French Polynesia who developed Guillain-Barré syndrome (GBS) following ZIKV infection, suggested that ZIKV should be included in the list of potential infectious pathogens that can trigger the development of GBS. In Brazil, hospital-based surveillance data revealed a significant increase in the number of GBS and other neurological and auto-immune complications, including acute disseminated encephalomyelitis, reported during the recent outbreak in several states from the northeastern region.

The most striking finding during the ZIKV outbreak in Brazil, however, is the cumulative evidence establishing a link between ZIKV infection during pregnancy and fetal and placental abnormalities, including fetal death, congenital neurologic and ocular disease, intrauterine growth restriction, and placental insufficiency. The neurologic malformations were characterized predominantly by microcephaly, cerebral calcifications, lissencephaly with agenesis of the corpus callosum, pachygyria, hydrocephalus and cerebellar dysplasia. Arthrogryposis, microphthalmia, funduscopic alterations in the macular region also were described in infants with suspected congenital ZIKV infection.

Marco Sáfadi, Brazil

ESP16-1151
ESPID SYMPOSIUM 6 - DIAGNOSTICS: NEW TECHNOLOGIES

CLINICAL SIGNS AND POINT OF CARE TESTING IN FEBRILE CHILDREN

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The challenge in the febrile child is to recognize the serious bacterial infection (SBI) from the majority of self-limiting illnesses. Estimates of SBI in Emergency departments (ED's) in Europe vary from 7-13% and of meningitis/sepsis from 0,4-1%. Several factors like parental report, parental worries, previous history, past experience, physical examination and gut feeling influence the threshold of risk estimates of professionals. The predictive value of alarming signs and symptoms (the NICE traffic light system) appears to be moderate. Clinical prediction rules combine several clinical signs and symptoms to predict serious infections. The performance of the most important clinical prediction rules varies from moderate to good (AUC 0.60-0.88). The biomarkers CRP and PCT has incremental value to clinical signs and symptoms to improve risk estimates for SBI, but the added value of a second biomarker was limited. PCT appears to be a better marker in infants less than 3 months.

The CRP is available as point of care test, but the implementation at the ED's in Europe is still limited. Several reasons are mentioned : high costs, risk of unnecessary testing and the predictive value of test outcome depends on setting (low prevalence vs high prevalence of SBI). The combination of clinical decision rules and biomarkers support decisionmaking in the febrile child.

ESP16-1160
ESPID SYMPOSIUM 6 - DIAGNOSTICS: NEW TECHNOLOGIES

USING BIOMARKERS TO GUIDE MANAGEMENT IN THE EMERGENCY DEPARTMENT

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Using biomarkers to guide management in the emergency department

In young children presenting to pediatric emergency departments with fever without source (FWS), the challenge is to rapidly differentiate those suffering from serious bacterial infections (SBI) from those with self-limited viral infections. The management is thus based on a probabilistic reasoning approach where the objective is to define a diagnostic probability above /below a threshold to decide initiating/withholding antibiotic treatment. Initiation of the diagnosis is based on the history, symptoms and clinical signs. However, many comprehensive clinical scores have shown poor diagnostic performances to detect SBI in febrile infants, and refinement using laboratory tests is needed. Several host biomarkers, such as C-reactive protein (CRP) and procalcitonin (PCT), increase during bacterial infections, and have displayed better diagnostic properties than clinical scores or WBC count in children with FWS. A score, called LabScore, associating CRP, PCT and urinary dipstick showed a positive and negative likelihood ratio of 4.92 (95%CI; 3.26 – 7.43) and 0.07 (0.02 to 0.27) to rule in or rule out SBI, respectively. More recently, a diagnostic test including viral and bacterial-induced host proteins (CRP, IP-10 and TRAIL) seemed to be superior than CRP or PCT alone. In conclusion, in absence of sensitive and specific clinical signs of SBI in young children with FWS, host biomarkers are helpful in clinical decision rules for the prescription of appropriate antibiotic treatment.

ESP16-1166
ESPID SYMPOSIUM 7 - THERAPEUTICS: PHARMACOKINETIC & DYNAMIC MODELLING IN ACTION

PHARMACOMETRIC MODELS AND IN SILICO STUDIES
M. PFISTER[1]
[1], *Switzerland*

PHARMACOMETRIC MODELS AND IN SILICO STUDIES

Neonates and infants represent a heterogeneous population, for which growth and maturation factors affect drug pharmacokinetics and pharmacodynamics (PK/PD). Pharmacometric models can quantify effects of these factors on drug exposure and characterize drug related biomarkers and clinical responses. These models can also account for an immature immune system and the contribution of non-ontogeny-related factors like sepsis and/or inflammation.

Pharmacometric modeling and simulation approaches can be applied to streamline development of new medicines and optimize utilization of existing medicines in pediatrics. We found a considerable inter-center variability of antibiotic use in Swiss NICUs. We observed 8 different dosing regimens for amoxicillin across these centers. There was an inconsistency with respect to the amount of dose, dosing interval, and factors such as postnatal age used to calculate individual doses. In silico studies with demographics from > 1000 neonates from the Antibiotic Resistance and Prescribing in European Children (ARPEC) dataset reveal that these different dosing strategies result in 2-3 fold differences in individual doses and drug exposures*.

National and international harmonization of dosing antibiotics in neonates and infants is critical and requires following steps (1) compare dosing strategies in NICUs and international guidelines, (2) characterize effect of various dosing strategies on individual dose and drug exposure, (3) perform model-based simulations to optimize design of prospective studies and to standardize dose regimens in pediatrics.

* *ARPEC data are used under the kind permission of Prof. Herman Goossens and Ann Versporten, University of Antwerp and the ARPEC project group*

ESP16-1158
ESPID SYMPOSIUM 7 - THERAPEUTICS: PHARMACOKINETIC & DYNAMIC MODELLING IN ACTION

A PRACTICAL GUIDE TO GETTING THE DOSE RIGHT

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In the treatment of infections in pediatric patients, the heterogeneous nature of patients combined with limited evidence on how to manage these patients often leads to a high variability of applied drug regimens and regular off-label drug use. Failure to anticipate and monitor for changes in the pharmacokinetics of a drug can contribute to clinical failures or adverse drug events.

Furthermore, pediatric patients with life threatening infections often experience multi-organ failure. These patients require aggressive therapeutic interventions that will impact the pharmacokinetics of antimicrobial drugs. Vice versa, antimicrobial drugs are not without side-effects likely causing a further deterioration of specific organ functions. Applying effective drug regimens for these patients with the selection of the most appropriate drug and to optimize the exposure of these drug, requires understanding of the pharmacokinetics.

In this session I will discuss the general principles of PK of antimicrobial drugs and how age and critical illness can influence the specific pharmacokinetic phases (absorption, distribution, metabolism and elimination). Subsequently, I will focus on the new strategies to tailor the individuals' exposure through the assessment of a patient serum or plasma concentration and subsequently adaptation of the dosing regimen (therapeutic drug monitoring (TDM)). Also I will demonstrate that TDM is not about producing a number that needs prompt action but that it is the complete clinical setting and the relation to measures of outcome that is required to make a solid recommendation.

All these points discussed will hopefully help in a practical guide to get the dose right.

ESP16-1152
ESPID SYMPOSIUM 8 - VACCINES: EPIDEMIOLOGICAL MODELLING OF VACCINE PROGRAMMES - DO THE PREDICTIONS PREDICT?

WOULD SHARING HPV VACCINE EQUALLY BETWEEN BOYS AND GIRLS MAINTAIN POPULATION IMMUNITY BETTER?

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Human papillomavirus (HPV) vaccination of adolescent females has been introduced in most high-income countries and an increasing number of low and middle income countries. Conversely, only a few countries have extended vaccination to males. Gender-neutral vaccination has not been shown to be cost-effective in many settings because most heterosexual males will be protected through indirect protection from their vaccinated female sexual partners if female vaccine uptake is sufficiently high. A range of other arguments have been advanced to support gender-neutral vaccination, including equal protection for men-who-have-sex-with-men, resilience against coverage reduction due to loss of vaccine confidence and achievement of elimination or eradication aims. At the same time, cost savings that could potentially be generated by reducing the number of doses needed for vaccination have been advanced as a way to enhance the affordability of gender-neutral vaccination. Mathematical modelling offers a framework to explore the long-term impact of novel vaccination strategies such as dose sharing between females and males.

ESP16-1156
ESPID SYMPOSIUM 8 - VACCINES: EPIDEMIOLOGICAL MODELLING OF VACCINE PROGRAMMES - DO THE PREDICTIONS PREDICT?

UNIVERSAL CHILDHOOD VARICELLA VACCINE - MODELLING AND ETHICAL CONSTRUCTS

P. BEUTELS[1]
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After primary varicella-zoster virus (VZV) infection, VZV may reactivate to give rise to herpes zoster (HZ). In previously VZV infected individuals, the risk of HZ can temporarily reduce upon natural re-exposure to VZV. This “exogenous boosting” hypothesis implies that universal childhood VZV vaccination would increase the risk of HZ in adults by reducing re-exposure “opportunities” to childhood chickenpox. Although controversial, exogenous boosting exists, but not in all individuals and in all circumstances where VZV re- exposure occurs. Different mathematical modelling constructs predict various magnitudes for this undesirable effect of VZV vaccination, with large implicit uncertainty.

Model-based cost-utility analyses with Quality Adjusted Life Years (QALYs) as health outcome are rooted in “utilitarianism”. If exogenous boosting is ignored, such analyses typically find that universal childhood VZV vaccination is an efficient use of resources. But if exogenous boosting is accounted for, it is considered cost-ineffective in a utilitarian sense, as it is projected to lose more QALYs than it gains over time spans of 20 to 60 years. Despite a discrepancy in strength of evidence – a definite beneficial, lasting impact on chickenpox versus a transient HZ rise of uncertain magnitude – this has helped postponing the introduction of childhood VZV vaccination in many countries.

Contractualism provides a fundamentally different ethical construct than utilitarianism. The moral justifiability of decisions is then not determined by quantifying outcomes, but by principles and rules, resulting from a hypothetical ‘social contract’. Using contractualism, it is argued that universal childhood VZV vaccination is justifiable under the exogenous boosting hypothesis.

ESP16-1115
ESPID PLENARY 3 - INFECTION & IMMUNITY - NEW PERSPECTIVES IN VIROLOGY

PROTECTING AGAINST THE CHANGELING DEMON AND THE TROLL OF TRANSPLANTATION

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PROTECTING AGAINST THE CHANGELING DEMON AND THE TROLL OF TRANSPLANTATION

Stanley A Plotkin, University of Pennsylvania

The human cytomegalovirus is the most prevalent congenital infection, causing abnormalities at birth but also sequelae that are not apparent until later in life, affecting what appears to be a normal newborn. Thus, HCMV has been called "The Changeling Demon". In addition, HCMV is the most common cause of disease after solid organ or hematogenous stem cell transplantation, also earning the sobriquet of "The Troll of Transplantation". Although antivirals have their place in prevention of both forms of disease, there has long been a need for a vaccine, and development of one has proceeded sporadically over many years. Fortunately, at this point there are multiple candidate vaccines being tested, including live attenuated, replication-defective, multiple vectors, subunit, virus-like particles, peptides, nucleic acid and others. However, decisions as to how to license a vaccine and how to use it are complex because of the epidemiology of HCMV and the varying endpoints for demonstration of efficacy.

ESP16-1153
ESPID SYMPOSIUM 9 - GLOBAL IMPACT: BETTER UNDERSTANDING RESPIRATORY INFECTIONS

DIAGNOSIS AND PATHOPHYSIOLOGY OF BIOFILM INFECTIONS IN CYSTIC FIBROSIS

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Pseudomonas aeruginosa biofilm infections in the united airways of of cystic fibrosis patients

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ABSTRACT. Cystic fibrosis (CF) patients suffer from recurrent and chronic sinus- and lung infections due to the basic defect of the CFTR protein, which is a chloride channel. This leads to decreased volume of the paraciliary fluid in the airways and impaired mucus detachment which interfere with the mucociliary transport and the consequence is therefore defective host defense against bacterial infections. *P. aeruginosa* is causing the most important chronic lung infection in CF and it was the first biofilm infection which was described in human beings and the most well studied biofilm infection. The inflammatory response - dominated by polymorphonuclear leukocytes - to the chronic infection is the main cause of the lung tissue damage. The antibody response against the sinus biofilm infections is mainly s-IgA which reduce the inflammation, whereas IgG dominates against the lung biofilm infection and aggrevates the inflammation. The antibody response is used diagnostically. The current treatment is early aggressive eradication therapy of intermittent *P. aeruginosa* colonization to prevent chronic biofilm infection which is treated by chronic suppressive 'maintenance' therapy to maintain the lung function for decades. Both systemic and inhaled antibiotics are used.

ESP16-1161
ESPID SYMPOSIUM 9 - GLOBAL IMPACT: BETTER UNDERSTANDING RESPIRATORY INFECTIONS

RSV - NEW THERAPEUTIC HORIZONS BRING CLINICAL CHALLENGES

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Respiratory syncytial virus is the most common infection of the lower respiratory tract in early childhood with poorly efficient prevention therapies and no effective treatments. The health and economic burden of RSV lower respiratory tract infection is significant. In development is a range of preventative and treatment therapeutics for RSV that is receiving impressive investment. Vaccines (44 preclinical, 11 Phase I, 3 Phase II and 2 Phase III trials), immunoglobulins (6 preclinical, 3 Phase 1-III) and antivirals (7 preclinical, 5 Phase I/II) are in pharmaceutical development. Promising early results suggest that novel products may come to market within 5 years. Novovax maternal immunisation programme completing Phase II with Phase I trials for children age 6-60 months. Monoclonal antibody (REGN-2222 Phase III) and extended life monoclonal (MEDI-8897 – completed Phase I/IIa) are being tested in preterm infants, whilst nebulised nanobody (ALX0171) is completing a Phase I/IIa trial in infants. Antiviral therapeutics (ALS-8176 and GS-5806) in adult challenge models are effective in reducing viral load. ALS-8176 is in Phase I for infants to identify an effective treatment dosing. The pace of development has exposed gaps in our understanding of RSV disease: what is the impact of RSV on healthy infants and what is the economic case for vaccine therapeutics in the general infant population,? How do we rapidly identify RSV to provide therapeutics to those infected in the community and secondary care? To demonstrate efficacy, improved capability to consistently measure meaningful clinical outcomes and/or biomarkers of disease severity will be required.

ESP16-1163
ESPID SYMPOSIUM 10 - VACCINES: VACCINE SAFETY - ACHIEVEMENTS, CHALLENGES/ THE BRIGHTON COLLABORATION

ENHANCING VACCINE SAFETY CAPACITY GLOBALLY: A LIFECYCLE PERSPECTIVE

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Major vaccine safety controversies have arisen in several countries beginning in the last decades of 20th century. Such periodic vaccine safety controversies are unlikely to go away in the near future as more national immunization programs mature with near elimination of target vaccine-preventable diseases that result in relative greater prominence of adverse events following immunizations, both true reactions and temporally coincidental events. There are several ways in which vaccine safety capacity can be improved to potentially mitigate the impact of future vaccine safety controversies. This talk aims to take a "lifecycle" approach, examining some potential pre- and post-licensure opportunities to improve vaccine safety, in both developed (specifically U.S. and Europe) and low- and middle-income countries.

ESP16-1157
ESPID SYMPOSIUM 10 - VACCINES: VACCINE SAFETY - ACHIEVEMENTS, CHALLENGES/ THE BRIGHTON COLLABORATION

HIGHLIGHTS & LESSONS FROM THE FIRST 17 YEARS OF THE BRIGHTON COLLABORATION

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Vaccines are now distributed faster and to wider populations than ever before. Reliable safety information must be available rapidly on a similar scale so that vaccine recipients and decision makers can evaluate vaccine benefits and risks accurately. The Brighton Collaboration is committed to addressing this need.

The Brighton Collaboration is a growing global network over 3600 individual professionals and partnering organizations from all stakeholder groups with a shared mission: To enhance the science of vaccine research, by providing standardized, validated objective methods for monitoring safety profiles and benefit-risk ratios of vaccines.

Conceptualized in 1999 and launched in 2000, the initial focus was on the development of a shared language case definitions. Today, the work is carried out in five focus areas: setting standards, clinical assessment, data sharing, capacity building, public confidence. Today, the Brighton Collaboration is unique in its capacity to rapidly leverage highly specific expertise and data sources for building consensus on harmonized methods and investigating vaccine safety concerns.

The Brighton Collaboration Foundation is a public charity registered in Switzerland, fostering the network's activities and serving its partners. It has supported network partners to create over 50 case definitions for adverse events, 3 guidelines for vaccine safety studies, 4 template protocols, a series of tools for data collection, sharing and analysis. It has supported the conduct of vaccine safety and public confidence studies and created workshops and training modules. It has created working processes and infrastructures for rapid consultation and knowledge transfer among professionals concerned with vaccine safety.

ESP16-1155
ESPID/ECDC/WHO JOINT SESSION 12- VACCINES: COMMUNICATION, HESITANCY AND SOCIAL MEDIA

VACCINE HESITANCY – THE EMERGENCE OF GLOBAL MISUNDERSTANDING

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Vaccine hesitancy has been defined in 2014 by the WHO SAGE working group on Vaccine Hesitancy as a "*delay in acceptance or refusal of vaccination despite availability of vaccination services. (…) It is influenced by factors such as complacency, convenience, and confidence*". It occurs on the continuum between high and no vaccine demand, and relates to heterogeneous groups with varying degrees of indecision about vaccination. Although only recently defined, vaccine hesitancy is as old as vaccination itself and individuals have raised concerns ever since the discovery of the first smallpox vaccine. Recent studies have shown the extent of hesitancy in Europe and have found that individuals are mostly concerned about vaccine safety, insufficient testing and low vaccine effectiveness, as well as beliefs that vaccine-preventable diseases are not severe or threatening. Recent developments in communication technologies such as social media have facilitated the spread of concerns across population groups, countries, and regions. The most effective strategies addressing vaccine hesitancy will therefore be those that are context-, population- and vaccine-specific and that take into account the role of new communication technologies and the potential for rumours and concerns to cross borders. This presentation will discuss the different definitions of vaccine hesitancy, determinants of low confidence in vaccination in European Member States, the role of social media in spreading rumours, and strategies available to address this issue and close immunisation gap.

ESP16-1169
ESPID RESEARCH MASTER CLASS

THE EFFECT OF SNP IN GENES RESPONSIBLE FOR INFLAMMATORY RESPONSE ON SEVERITY OF BACTERIAL MENINGITIS IN CHILDREN

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Background:

Single nucleotide polymorphism gives variability in individual immunologic response. These genetic variations underlie differences in our susceptibility to disease.

Research question:

The aim of the study is an analysis of single nucleotide polymorphisms in genes involved in the inflammatory response on susceptibility, severity and outcome of bacterial meningitis in children.

Methods:

The study group consists of children (n=50), survivors from bacterial meningitis. A control group is formed from adults with no history of meningitis in childhood.

Based on patients medical records and test performed during hospitalization following data will be analysed:

1. Risk factors for developing the disease (age, body mass, family and social background, comorbidities, vaccinations).

2. Severity of neuroinfection (symptoms duration, CRP, PCT, WBC, blood culture, cerebrospinal fluid culture).

3. Early and late sequele (neurological examination, hearing test).

In both groups of patients genomic DNA will be isolated from whole blood by Gentra Puregene Blood Kit (Qiagen) following the manufacturer’s instructions. Analysis of 14 polymorphisms in 7 genes (TIRAP S180L, NFKBIL2, SFTPD, SFTPA1, IL 10, MBL2, TLR 9) will be determined by HRM (High Resolution Melting) analysis, using Type-it HRM PCR Kit (Qiagen).

Results and Conclusions:

The results will give insight into genetic basis of immune response and its correlations with increased susceptibility to severe meningitis. Genetic studies can identify a risk group more

prone to invasive bacetrial neuroinfections. Such data might be more effective in *encouraging* patients to accept *vaccinations* The results will be helpful in finding new therapies.

ESP16-1170
ESPID RESEARCH MASTER CLASS

ANTIBIOTIC RESISTANCE PATTERNS AND PREVALENCE OF VIRULENCE DETERMINANTS AMONG ENTEROCOCCUS FAECALIS CAUSING COMMUNITY ACQUIRED URINARY TRACT INFECTIONS

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Research Question: Recently, *Enterococcus* species is considered as the second most common cause of UTIs. In the case of UTIs, the roles of virulence factors are not clear yet. On the other hand some of the community acquired Urinary tract infection (CA-UTIs) is endogenous. The aim the current study was to investigate of antibiotic resistance patterns and the incidence of virulence determinants among endogenus *E. faecalis* isolated from fecal and urine samples of patients with endogenous CA-UTIs.

Methods: During August 2014 to April 2015 urine and fecal samples were obtained from outpatients UTI which had been referred to the two teaching hospitals, Tehran, Iran. Antimicrobial susceptibility of these strains was assessed by the disk diffusion and Etest according to CLSI guide line. *esp, efba, asa, ace, cyl* and *gelE* virulence genes were detected by conventional PCR. RAPD-PCR will be used for confirmation of endogenous CA-UTIs.

Results: 63.4% of isolated *E. faecalis* from feces and urine specimens similar antibiotic sensitivity patterns. PCR results showed *efba* as the most frequent virulence gene among these strains, 97.1%, while *ace* 95.7%, *gelE* 94.3%, *esp* 75.7%, *asa1* 54.3% and *cyl* 52.8% genes showed lower frequencies, respectively. This project is on progress and the results of RAPD-PCR is not ready now.

Conclusion: The endogenous CA-UTIs are the important problem in communities. If we can inhibit transmission of *E. faecalis* from faeces to urine tract and make UTIs, we might prevent CA-UTIs.

ESP16-1171
ESPID RESEARCH MASTER CLASS

PRESENCE OF ANTIBIOTIC RESISTANCE GENES IN PNEUMOCOCCI ISOLATED FROM NEPALESE CHILDREN IN THE CONTEXT OF CARRIAGE AND DISEASE

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Research Question: With a focus on temporal changes and differences between healthy and diseased contexts, the purpose of this study is to determine the presence of antibiotic resistance genes in pneumococci isolated from Nepalese children.

Methods: Pneumococcal nasopharyngeal carriage isolates were collected from healthy community carriers (in three distinct time periods: 2009, 2012, and 2014) and children admitted to hospital with clinician diagnosed pneumonia in 2014. Invasive pneumococcal disease (IPD) isolates were collected from sterile site cultures between 2005-2014. Extracted DNA underwent whole-genome-sequencing. Genes conferring antibiotic resistance were identified using short-read-sequence-typing (SRST2) against the ARG-ANNOT database.

Results: 287 genes conferring antibiotic resistance in 171 isolates were identified. The majority of detected genes related to tetracycline (55.4%) and macrolide (44.5%) resistance. The prevalence of isolates with at least one resistance gene in the healthy carriage cohorts was 25/108 (23.1%) in 2009, 35/86 (40.7%) in 2012, and 56/134 (40.3%) in 2014. Antibiotic resistance genes were identified in 116/328 (35.4%), 34/70 (48.6%), and 21/70 (30%) of healthy carriage, carriage during pneumonia, and IPD contexts respectively. Interestingly serotype 1 represents 38/70 (54.3%) of IPD isolates but only 4/21 (19%) of resistance genes detected, all of which conferred chloramphenicol resistance. No other chloramphenicol resistance genes were detected across the entire study.

Conclusions: There was a significant increase in prevalence of antibiotic resistance genes from healthy carriers in 2009 compared with both the 2012 and 2014 healthy carriage cohorts. Identification of phenotypic resistance patterns will provide further insight into differences in resistance genes detected across time and context.

ESP16-1172
ESPID RESEARCH MASTER CLASS

RESPIRATORY MUCOSAL MODEL: LOCAL IMMUNOLOGICAL RESPONSES TO COLONIZATION AND INFECTION WITH BORDETELLA PERTUSSIS

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Purpose: to investigate local immunological responses of normal human bronchial epithelial cells after *Bordetella pertussis* exposure. More specifically, to study the different immunological patterns of normal human bronchial epithelial cells (NHBE) after adherence, colonization, and infection with *B. pertussis.*

Context of study: to align an *in vitro* respiratory mucosal model for *B. pertussis* with the *in vivo* human challenge model for *B. pertussis* planned at the NIHR Wellcome Trust Clinical Research Facility in Southampton for 2016.

Methods

Primary set-up: Use of well-differentiated human airway epithelial cell cultures maintained at an air-liquid interface (ALI).

Primary experiments: Building of high-quality and reproducible ALI with NHBE; dose-finding for colonization and exposure of NHBE to Bordetella pertussis.

Secondary experiments: Use of human epithelial cells from participants of human challenge model, extend model to both a lower and an upper respiratory tract mucosal model, addition of other immunological and non-immunological human cell types, use of different (mutated) Bordetella pertussis strains, use of microfluidics system.

Methods for measurement: First phase emphasis on quality testing and reproducibility. Second phase (to be decided): chemo- and cytokines, transcript- and proteomics with e.g. ELISA, Luminex, FACS and qPCR.

Results and Conclusion: The main study aims to start recruitment in summer 2016 therefore no results will be presented at ESPID 2016.

ESP16-1173
ESPID RESEARCH MASTER CLASS

PROGNOSTIC VALUE OF SERUM PROCALCITONIN LEVELS UPON ADMISSION OF CHILDREN HOSPITALIZED WITH COMMUNITY-ACQUIRED PNEUMONIA

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Research question: Procalcitonin (PCT) is an inflammatory biomarker that has been studied in children with community-acquired pneumonia(CAP) as a biologic predictor of bacterial infection. We aimed to evaluate the prognostic value of serum PCT levels on admission in relation to therapeutic response to aqueous penicillin G, stratified by aetiology, among children hospitalized with CAP.

Methods: Children under-5-years-old hospitalized with CAP were evaluated in a 21-month period. On admission, clinical and radiological data were collected as well as nasopharyngeal aspirates and blood to investigate 19 aetiological agents and serum PCT levels. Evolution and outcome were registered in standardized forms. Children with pleural effusion on admission were excluded.

Results: The study group comprised 89 patients. The median (interquartile range) age was 18(11-27) months and 53(60%) were boys. Viral (49.4%), typical bacterial (38.2%) and atypical bacterial (12.4%) infections were diagnosed. Overall, 25.8% were pneumococcal infections. In total, 75 (84.3%) children became afebrile within 48hr of treatment. Median serum PCT (ng/ml) levels on admission was higher in 14 children who remained febrile after 48hr of treatment (2.1[0.8–3.7] *versus* 0.6[0.1-2.2];P=0.025). In these children, pneumococcal infections were more common (71.4% versus 17.3%;P<0.001). PCT levels on admission were higher in children with pneumococcal pneumonia (2[0.7–4.2] *versus* 0.5[0.08–2.1];P=0.002). The ROC curve found that 0.25ng/ml of serum PCT had a high negative predictive value (93% [95%CI:80%–99%) for pneumococcal infection. All children that remained febrile after 48hr of treatment had PCT >0.25ng/ml on admission.

Conclusions: Serum PCT level >0.25ng/ml predicted delayed clinical response to antibiotic therapy and pneumococcal aetiology.

ESP16-1174
ESPID RESEARCH MASTER CLASS

MOLECULAR EPIDEMIOLOGY AND CLINICAL PRESENTATION OF RESPIRATORY SYNCYTIAL VIRUS INFECTION AMONGST HOSPITALIZED CHILDREN IN HEIDELBERG/GERMANY

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Research question: The aim of this research project is to understand the interrelation between molecular epidemiology and clinical features of respiratory syncytial virus (RSV) infection amongst hospitalized children (<5 years) in Heidelberg/Germany.

Methods: We are investigating RSV as well as influenza causing acute respiratory tract infection (ARTI), analyse patterns of circulating RSV subtypes/genotypes and determine their impact on the disease severity using a standardized score across consecutive winter seasons between 2015 and 2020. Nasopharyngeal swabs are obtained from hospitalized children (<5 years) who present with clinical symptoms of ARTI at the Paediatric Department of the University Hospital Heidelberg/Germany. All nasopharyngeal swabs are analysed for RSV and Influenza using real time PCR. For RSV positive samples, sequence analysis of the second variable region of the RSV G gene is performed to obtain circulating sub-/genotypes.

Results: Previous data showed a high number of RSV positive children in this cohort (55.8% in 2012/13). Phylogenetic analysis revealed that the majority of RSV-A strains clustered with strains of the novel ON1 genotype with a 72-nucleotide duplication first described in Canada in 2010. However, we have started to systematically collect clinical data in 2014/15 and we therefore would like to present first data obtained during the winter season 2015/2016 at the ERMC 2016.

Conclusion: Mapping the spread of novel genotypes using data from different seasons can reveal transmission dynamics and the fitness of the viral strains. Further surveillance of circulating genotypes in combination with corresponding clinical data is needed to understand their full implications.

ESP16-1175
ESPID RESEARCH MASTER CLASS

DIAGNOSIS OF HOSPITAL ACQUIRED INFECTIONS IN CRITICALLY ILL PATIENTS: COMPARISON OF MOLECULAR TEST AND BLOOD CULTURES

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Introduction

Nosocomial infections are a prevalent cause of death in critically ill children.

The microbiological diagnosis is challenging due to routine cultures only detect up to 25% of the bacteremia.

Several studies have suggested that molecular tests could be a faster and effective tool for detection of bacterial infections. However, there is a lack of studies comparing molecular tests with conventional cultures in hospital acquired infections (HAI).

Research questions:

1. Could the molecular method be more sensitive and accurate for early bacteremia/ diagnosis compared to routine culture in critically ill pediatric patients?

2. Would it be particularly useful for identification of bacterial pathogens in patients pretreated with antimicrobials?

Methods

Assess the diagnostic performance 16s PCR compared with conventional diagnostic work up, in suspected bloodstream infection in PICU patients.

- STUDY DESIGN: Prospective case-control study
- PRIMARY OUTCOME:
    - Proportion of children with high suspicion of HAI in whom 16S PCR has been positive compared to those patients in whom only blood cultures has been positive and the strength of association between detection of positive 16s PCR in HAI cases compared to controls.
    - Proportion of children pretreated with antimicrobials and high suspicion of HAI in whom 16S PCR has been positive compare to those patients in whom only blood cultures has been positive
    - Evaluate Sensitivity, specificity, NPV and PPV of the 16s PCR.

- SECONDARY OUTCOME:
    - Time reduction (days) of antimicrobials.

Results and conclusion: work in progress.

ESP16-1176
ESPID RESEARCH MASTER CLASS

TUBERCULIN SKIN TEST IN HIV-EXPOSED UNINFECTED INFANTS VACCINATED WITH BCG IN THE FIRST MONTH OF LIFE

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Research question: There is not enough data to establish the best cut off to determine tuberculosis (TB) infection in HIV-exposed and uninfected (HEU) children vaccinated with BCG early in life. This study aims to establish the average TST induration size in HEU infants in order to confirm or not the 10mm cut off suggested by the Brazilian guidelines.

Methods: HEU children less than 24 months of age vaccinated with BCG in the first month of life and without known contact with adults with pulmonary TB or chronic cough were selected. After written informed consent, 0.1 mL PPD RT-23 was administered by a qualified professional on the anterior forearm and measurement of induration was read after 72 hours with a millimeter ruler.

Results: The study is still in progress, however, among the 24 patients already invited, 8 agreed to participate and 2 of them did not return after 72 hours. Two out of 6 (33.3%) were male and mean age was 13.2 months (range, 7.9.-19.0). TST induration was zero mm in all patients included.

The factors that possibly influenced adherence to the study and TST result include: necessity to return in 72 hours, age at TST, time interval since BCG and vertical exposure to HIV.

Conclusion: Preliminary results suggest that BCG might not interfere with the response to TST among HEU infants. The main practical difficulty for the progression of the study was the necessity of children to return in 72 hours for evaluation.

ESP16-1177
ESPID RESEARCH MASTER CLASS

PIPERACILLIN PHARMACOKINETICS IN HOSPITALISED CHILDREN

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Research question:

Piperacillin is commonly used in children but there are limited pharmacokinetic (PK) data to support current paediatric dosing regimens. NAPPA is a multicentre paediatric antimicrobial PK study employing opportunistic sampling strategies in routine care. This interim analysis aimed to investigate piperacillin PK in the first cohort of participants.

Methods:

Eligible children, administered intravenous piperacillin/tazobactam as standard-of-care, were enrolled. Following informed consent, study blood samples were obtained with routine blood tests or at recommended times. All plasma samples were frozen and analysed in retrospect using HPLC/MS/MS. A population-PK model was fitted simultaneously to the measured drug concentration-time data using non-linear mixed-effects modelling software (NONMEM v7.3, Icon plc). The log-likelihood ratio was used to discriminate between nested structural models.

Results:

For this interim analysis 41 evaluable samples were available from 17 study participants (age range: 1 month to 11.8 years). Using NONMEM v7.3, one- , two- and three-compartment models were compared. A 2-compartment model was most suitable, giving these final PK parameter estimates: 0.96 L/h for clearance (CL) and 0.27 L for the central volume of distribution (Vd), 0.98 L/h for intercompartmental CL and 0.88 L for the peripheral volume.

Conclusion:

Based on these interim data, a paediatric piperacillin PK model was developed. A 2-compartment structural model provided the best fit. Future analysis will incorporate allometric scaling and glomerular filtration maturation, and covariate analysis. The final dataset will be used for model-based simulations to evaluate different paediatric dosing regimens, in order to improve the evidence underpinning future dosing recommendations.

ESP16-1178
ESPID RESEARCH MASTER CLASS

VALIDATION OF THE ONCE-DAILY ISONIAZID DOSE AT 10 MG/KG IN INFANTS UNDER 6 MONTHS OF AGE

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Research question: The World Health Organization (WHO) recently issued revised first-line anti-tuberculosis (TB) drug dosage recommendations for children. Isoniazid (INH) daily dose was increased from 5 to 10-15 mg per kg of body weight; the 10 mg/kg once-daily INH dose has been recently validated in infants aged >3mo. However, no dosing recommendation can be made in children <3mo due to the lack of specific data.

Methods: Multicentric national cross-sectional post-authorization observational study. We aim to document the pharmacokinetics of INH in neonates (n=8, Group A) and infants 1-3mo (n=8, Group B), as compared to a control group of infants aged 3-6mo (n=16, Group C). The effect of clinical covariates, including age, gender, nutritional status, type of TB infection, concomitant treatment with other anti-TB drugs and the NAT2 acetylator status will be investigated. Samples will be taken at 3 time-points following dosing (+1-3-6 or +2-4-8 hours). The maximum drug concentration (Cmax; main objective: Cmax over 3 mg/L, as per adult PK/PD studies) in serum, the time to Cmax (tmax) and the area under the concentration-time curve (AUC) will be calculated.

Results: 14 infants have been included to date (4 and 10 in groups B and C), and samples from 6 patients have been analyzed: the exposure to INH in terms of Cmax (clearly >3 mg/L in all cases) and AUC is high as compared to adult data. INH half-lives are relatively long in these young children.

Conclusion: Low recruitment rates, specially among neonates, are the main problem encountered to date. In infants <6mo, the INH dose increase is effective from a pharmacokinetic point of view.

ESP16-1179
ESPID RESEARCH MASTER CLASS

PHARMACOKINETIC, PHARMACODYNAMIC AND IMMUNOMODULATORY STUDIES OF COLISTIN IN CHILDREN

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Research question Currently there is a paucity of PK data regarding colistin administration in children. Little is known as well regarding the *in vitro* PD and immunomodulatory activity of colistin against bacterial biofilms caused by organisms resistant to conventional antimicrobial agents. The objectives of this project are: a) to elucidate the pharmacokinetics of colistin in pediatric patients; b) to investigate the *in vitro* pharmacodynamic and immunomodulatory activity of colistin against biofilms of resistant to conventional agents *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* isolates.

Methods A sequential-group dose escalation study is conducted in children 1mo-14yrs requiring treatment with colistin. Serum colistin concentrations are determined by UPLC combined with MS/MS method. PD effects of colistin against biofilms are investigated by treatment of biofilms *in vitro* with various colistin concentrations alone or in combination with other antimicrobial agents. Its immunomodulatory effects will be investigated by pretreatment of biofilms with sub-inhibitory concentrations of colistin and subsequent addition of human polymorphonuclear leukocytes or monocytes.

Results Serum samples from 16 children are currently obtained and determination of colistin concentrations is in progress. The PD effects of colistin against *K. pneumoniae* and *P. aeruginosa* isolates are currently investigated, showing increased resistance of biofilms compared to planktonic cells.

Conclusion Our work plan for next year includes the enrollment of more children for PK study and the immunomodulatory studies with monocytes.

ESP16-1180
ESPID RESEARCH MASTER CLASS

HAS VACCINATION WITH THE PCV-10 VACCINE REDUCED ANTIBIOTIC RESISTANCE RATES IN CHILDREN ATTENDING DAY CARE CENTRES?

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Research question: Has the PCV-10 vaccination that was initiated in Iceland in 2011 affected the rate of penicillin non-susceptible pneumococci in isolates collected from healthy children attending day care centres (DCCs)?

Methods: The study is an ongoing, repeated cross-sectional study conducted in the greater Reykjavik area, Iceland where nasopharyngeal swabs are collected from children attending 15 DCCs in March every year from 2009 to 2015. Susceptibility testing is performed using disc diffusion tests and E-tests according to the EUCAST methods and criteria. To attain comparable age distribution only children <3 year of age were compared. The Non-Vaccine Eligible cohort (NVEC, born 2010 and earlier) was compared with the Vaccine Eligible Cohorts (VEC, born 2011 and later). To exclude possible herd effect bias within the DCC, NVECs sampled in 2013 and later were excluded.

Results: There were no significant differences in average age (2.39 vs 2.44), total carriage (70.5% in both groups) or sex (53.9% vs 56.8% males) between the NVEC and VEC respectively. In the NVEC 13.8% (65/470) of the isolates were PNSP and in the VEC 9.1% (21/231) were PNSP (NS, p:0.086). When stratifying according to the MIC of the two groups, 77% of the isolates in the NVEC had MIC values 1.5-3, while 76% of isolates in the VEC were of MIC value: 0.094-0.38.

Conclusion: Although the decrease in number of PNSP isolates was not significant when comparing VEC and NVEC, the number of isolates with higher MIC values was significantly reduced in the VEC.

ESP16-1181
ESPID RESEARCH MASTER CLASS

INFLUENZA VIRUS INFECTIONS DURING THE FIRST TWO YEARS OF LIFE IN A PARTIALLY VACCINATED CHILD COHORT

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Research question

Influenza vaccine was included in the Finnish national immunization programme in 2007 for children 6 to 35 months of age, but the vaccination coverage has been variable. We investigated the incidence of influenza in a cohort of young children in 2008-2011.

Methods

We followed 923 children from birth to 2 years of age for respiratory tract infections. A nasal swab sample for influenza A and B virus PCR was taken whenever a child got symptoms of an acute respiratory infection during influenza season. Samples were collected either at the study clinic or at home by parents. Vaccination data were retrieved from the health registries.

Results

Vaccination coverage of children aged 6 to 35 months at the beginning of the season was 21 to 47% against seasonal influenza and 86% against the 2009 pandemic virus. During 3 influenza seasons, 2113 nasal swabs were taken. By 2 years of age, 58 of 867 children (6.7%) had a symptomatic influenza infection. Sixteen cases were pandemic influenza A/H1N1 infections, 14 were seasonal influenza A/H2N3, and 28 were influenza B cases. Five percent of children with influenza were hospitalized, 45% had an outpatient visit and 55% had no physician visit. Effectiveness of the adjuvanted vaccine against the 2009 pandemic influenza was 98% (95% confidence interval 86-100%).

Conclusion

Incidence of influenza was low in this partially vaccinated child cohort and cases were mostly non-severe. Vaccine against the pandemic influenza was highly effective. Next we will study the serologic responses towards influenza viruses and vaccinations.

ESP16-1182
ESPID RESEARCH MASTER CLASS

A LONGITUDINAL STUDY OF NEISSERIA CARRIAGE IN A WELL-CHARACTERIZED COHORT OF TERM INFANTS

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Research question

The DORMICe (Development of Respiratory Microbiota in Children) study is an ongoing exploration of how bacterial populations develop in the upper respiratory tract over time in infants. We seek to understand the normal succession of Neisseria carriage, and the effects of external influences such as feeds and vaccinations.

Methods

Throat swab samples have been taken from 220 enrolled infants at 6 weeks, 1.5, 3, 4.5, 6, 12, 18 and 24 months. Bacterial populations present in samples were analysed by 16s analysis using the Roche 454 platform. Further to this information, extensive clinical metadata has been collected and a methodology trialled for high-throughput *Neisseria* speciation.

Results

Based on the 16s analysis, we know that 85% of the infants in our study have carried *Neisseria* at some point, and 75.91% have carried *Neisseria* in one or more occasions. Increased *Neisseria* carriage was also found to be associated with infants having a sibling and being on formula feeds ($p = 0.006$ and $p < 0.001$ respectively) up to the 6 month timepoint. Successful identification of *Neisseria* carriage now enables us to study the effects of vaccine on general carriage, with ongoing work concerning the species identification then allowing us to determine species specific effects.

Conclusion

Neisseria carriage is heavily influenced by external factors in the first few months of life, with further analysis determining whether these factors remain consistent over early years. Following establishment of species level identifications the analysis will be extended to determine factors influencing carriage of the more potentially harmful *Neisseria* species.

ESP16-1183
ESPID RESEARCH MASTER CLASS

THE IMPACT OF ROTAVIRUS VACCINATION ON HOSPITALIZATIONS DUE TO ACUTE GASTROENTERITIS IN ESTONIA

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Research question: How rotavirus vaccination changes the pattern of patients and causative agents of hospitalized patients with acute gastroenteritis?

Methods: This study is conducted from 01.02.2015 to 31.05.2016 in seven biggest Estonian hospitals. All children aged 0-18 years hospitalized with acute gastroenteritis (AGE) are eligible for the study. After written informed consent is obtained demographical data, vaccination history, severity of disease according to Vesikari and Clark severity scale, and aetiology of AGE is recorded in electronic database. Stool samples are collected and tested for rotavirus, norovirus G1, G2, astrovirus, adenovirus and sapovirus. Rotavirus (RV) positive samples are further genotyped.

The study design is based on the recommendations of the Brighton Collaboration Diarrhoea Working Group in order to provide standardized collection and assessment of information as well as allow comparability of data with other countries and with study done in the pre-vaccine era.

Results: In first season we recruited 1070 children, collected stool samples, extracted DNA and RNA and started statistical analysis of data. During the first vaccine season hospitalized rotavirus gastroenteritis (RVGE) cases were older than in pre-vaccine era reflecting most likely the decline of cases among immunized children. No changes in severity of RVGE is seen between two periods but poor correlation between severity scoring systems should be noted.

Conclusion: This large study covers about 80% of paediatric RVGE hospitalizations in Estonia and allows drawing conclusions about AGE aetiology, trends in RVGE hospitalizations after initiation of RV vaccination program, and determining further prophylactic measures needed.

Plenary Abstracts

ESP16-0188
ESPID PLENARY 1 - NUTRITION & INFECTIOUS DISEASES

IMPACT ON ACUTE ILLNESS PRESENTATIONS AND GROWTH OF PHYSICIAN-PRESCRIBED LIPID-BASED MULTIPLE MICRONUTRIENT SUPPLEMENTS: A RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL IN GAMBIAN CHILDREN

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Background

Multiple micronutrients (MMN) are commonly prescribed to children in primary health care clinics in sub-Saharan Africa though evidence for their effectiveness and international clinical guidelines are lacking. We assessed the efficacy of lipid-based MMNs in children presenting to a rural clinic in The Gambia.

Methods

We undertook a double-blind randomised controlled trial of lipid-based MMNs in children presenting with acute illness. Participants were randomly assigned to receive 12wk MMN (MMN-12), 6wk MMN followed by 6wk placebo (MMN-6) or 12wk placebo (base lipid paste; MMN-0) provided in daily portions. Parents/guardians and all investigators were blinded to supplement allocation. Primary outcomes were repeat clinic presentations and growth over six months. Intention-to-treat analysis included all participants correctly enrolled.

Results

1101 children (age 6–60m) were enrolled between 12/12/2009 and 03/06/ 2011 (MMN-0: n=361, MMN-6: n=362, MMN-12: n=362). MMN supplementation was associated with a small increase in height-for-age z-scores 24wk after recruitment (effect size for MMN groups combined: 0·084 SD/24wks, 95%CI: 0·005, 0·168; p=0·037). Repeat clinic presentations within 6m were not significantly affected (incidence per child week: MMN-0: 0·09 (n=740/6m), MMN-6: 0·09 (n=789/6m), MMN-12: 0·09 (n=782/6m) with no supplement-related adverse events. In *post hoc* analysis, clinic visits significantly increased by 43% over the first 3wk of MMN versus placebo (adjusted rate ratio 1·43; 95%CI: 1·07, 1·92; p=0·016), with respiratory presentations increasing by 52% (adjusted rate ratio 1·52; 95%CI: 1·01, 2·30; p=0·046).

Conclusions

Prescribing micronutrients to unwell children presenting for primary care in rural Gambia had a very small effect on growth and did not reduce the frequency of repeat clinic visits. Evidence for an early increase in repeat visits (possibly mediated by iron in the MMN) indicates a need for caution and the establishment of evidence-based guidelines.

Clinical Trial Registration (Please input N/A if not registered)

ISRCTN73571031.

ESP16-0566
ESPID PLENARY 1 - NUTRITION & INFECTIOUS DISEASES

MICAFUNGIN ALTERS THE AMINO ACID, NUCLEIC ACID, AND CENTRAL CARBON METABOLOMIC PROPERTIES OF CANDIDA ALBICANS AT SUBINHIBITORY CONCENTRATIONS: NOVEL INSIGHTS INTO MECHANISMS OF ACTION

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Background

Candidiasis is an important infection complicating the course of malnourished children worldwide. Micafungin was the first echinocandin approved for the use of treatment of invasive candidiasis in children, including preterm neonates. However, little is known about the mechanistic effects of micafungin on the metabolic profile of Candida. We performed LC/MS-based metabolomics profiling of the response of Candida cells to increasing doses of micafungin to determine the metabolic response of Candida to micafungin sub-inhibitory injury.

Methods

We cultured Candida albicans cells to the mid-logarithmic phase in liquid media and then inoculated replicates onto nitrocellulose filters under vacuum filtration. Isolates were cultured to mid-logarithmic phase of growth on the same agar and micafungin 0-0.25 µg/ml was added. At mid-logarithmic phase of growth, replicates were metabolically quenched by immersion into 40% acetonitrile, 40% methanol, 20% water on dry ice. Intracellular metabolites extracted by mechanical lysis were analyzed by LC/MS. Changes in pool sizes of individual metabolites were analyzed by Students' T-test adjusted for multiple hypothesis testing by Benjamini-Hochberg correction. Metabolites were ascribed to pathways by comparison against the KEGG metabolic pathways database.

Results

We reproducibly detected 495 metabolites whose identities could be confirmed by either comparison against a pure standard or comparison against a library of accurate mass-retention-time pairs (mass-matching). Among them, 103 had significantly altered mean abundance in response to increasing micafungin concentrations. Pool sizes of aminoacid, glutathione and nucleic acid metabolism were significantly increased by 0.5-3.4 fold ($p \leq 0.05$). By comparison, intermediates of central-carbon-metabolism were decreased by 0.4-1 fold ($p \leq 0.05$).

Conclusions

Micafungin induces a re-routing of metabolic pathways promoting a protein repair biosynthetic response. These results may shed light into new mechanisms of action of echinocandins.

Acknowledgment
This study was supported by an ESPID Fellowship Award to AK and an SECIM Award (NIH Grant #U24 DK097209) to TJW Clinical Trial Registration

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0548
ESPID PLENARY 2 - IMMUNOLOGY & INFECTION - UNDERSTANDING THE HOST RESPONSE

GENETIC INSIGHT INTO THE PERSISTENCE OF VACCINE-INDUCED IMMUNITY FOLLOWING CHILDHOOD IMMUNISATION

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Background

The World Health Organisation estimates childhood immunisations prevent 2.5 million deaths annually. However, considerable interindividual variability in the magnitude and persistence of immunity following vaccination is observed. Heterogeneous vaccine-induced immunity in childhood is particularly concerning, as infants generally have lower magnitude immune responses that wane more rapidly than adults. Maintenance of protective vaccine-specific serum antibody is essential for continuity of protection against rapidly invading pathogens, such as encapsulated bacteria. Genetic factors are likely to be determinants of the vaccine response, and identification of the genes controlling persistence of response may help in design of improved vaccines.

Methods

Here we report the first genome-wide association study of the persistence of immunity after immunisation with three routine childhood vaccines: capsular group C meningococcal (MenC), *Haemophilus influenzae* type b (Hib), and tetanus toxoid (TT) vaccines. We conducted a two-stage study, performing genome-wide genotyping on an initial cohort of 2000 European children, with replication data in a further 2000individuals.

Results

We describe novel, genome-wide significant associations ($p<5 \times 10^{-8}$) between variants in a locuscontaining a family of signal-regulatory proteins (SIRPs) involved in immune regulation and MenC immunity. In particular, a variant linked with the expression of *SIRPG*, the protein of which is involved in antigen-specific T-cell proliferation, was found to be associated with the persistence of functional antibody directed to MenC. Furthermore, we described significant associations between variants within the human leukocyte antigen (HLA) locus and the persistence of TT-specific immunity, the most statistically significant of which was associated with the expression of *HLA-DRB1* and *HLA-DRB5*.

Conclusions

These findings provide new insights into the determinants of persistence of immunity following childhood vaccinations.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0943
ESPID PLENARY 2 - IMMUNOLOGY & INFECTION - UNDERSTANDING THE HOST RESPONSE

DIAGNOSIS OF KAWASAKI DISEASE USING BLOOD GENE EXPRESSION SIGNATURES

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Background

There is currently no diagnostic test for Kawasaki disease (KD). As diagnosis is based on clinical features that are shared with other infectious and inflammatory diseases, diagnosis and treatment of KD is often delayed or missed, resulting in increased risk of coronary artery aneurysms. We explored the use of transcriptional signatures to distinguish KD from other conditions in children.

Methods

We established a case-control cohort of children with infectious and inflammatory conditions (78 KD cases, 84 other inflammatory disease cases, 242 cases with bacterial or viral infections) and 55 healthy controls. Whole blood was collected into PAXgene RNA tubes for gene expression analysis using Illumina HT-12 BeadChip arrays. Using novel variable selection analyses, minimal transcript sets distinguishing KD from other conditions were identified in the 'training set' (80% of the discovery cohort) and validated on the 'test set' (20% of the discovery cohort). We applied the signatures to a validation cohort of 130 febrile children and 102 KD patients.

Results

A 59-transcript signature distinguished KD from other infectious and inflammatory conditions, with a sensitivity of 87.5%, specificity of 90.8% and ROC-AUC of 93.9% in the validation cohort. Accuracy of diagnosis paralleled clinical certainty (ROC-AUC 92.0%, 94.1%, 73.5% for Definite KD, Highly Probable KD, and Possible KD respectively). A simplified disease risk score (DRS) 5-transcript signature showed a sensitivity of 87.5%, specificity of 83.8% and ROC-AUC of 90.8% in the validation cohort, with accuracy also following clinical certainty.

Conclusions

Gene expression signatures distinguished KD from other febrile conditions. Sensitivity and specificity of the signatures decreased with uncertainty of clinical diagnosis. A test based on the DRS signature may enable earlier diagnosis of KD and allow more timely treatment.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0764
ESPID PLENARY 3 - INFECTION & IMMUNITY - NEW PERSPECTIVES IN VIROLOGY

EARLY ANTIRETROVIRAL THERAPY PRESERVES THYMIC OUTPUT IN CHILDREN INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS: EVIDENCE FROM THE CHILDREN WITH HIV EARLY ANTIRETROVIRAL THERAPY (CHER) TRIAL

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Background

The rate of HIV-induced CD4 loss and ART-stimulated restoration is determined by rates of T-cell death, proliferation and thymic production of new T-cells. Thymic output may have particular importance in immune-reconstitution and immunological health of HIV-infected children.

Methods

Thymic output was estimated using a mathematical model combining naïve CD4 T-cells levels and proliferation rates with DNA PCR quantification of T-cell receptor excision circles from purified naïve CD4 T-cells. Cryopreserved PBMCs from 454 healthy HIV-uninfected children (0.04-12 years) delineated normal thymic output. The effect of HIV and ART on thymic output was explored with 825 cryopreserved PBMCs from 299 children of the Children with HIV Early Antiretroviral Therapy (CHER) trial (0.1-8 years). Here, HIV-infected infants <12 weeks (CD4% >25%) were randomised to early-limited ART for 40 or 96 weeks, or deferred ART. For Infants on deferred ART or during ART-interruption, ART was started/re-started for clinical progression (CDC severe stage B/C disease) or CD4% <25%.

Results

HIV-uninfected children demonstrated peak thymic output between 6-12 months, declining until 2 years with subsequent plateau. Thymic output of HIV-infected children while on ART was similar to HIV-uninfected children, whereas time not on ART resulted in diminished thymic output (p-values <0.05, Figure 1). In all children, higher age-adjusted CD4 counts z-scores

were related to increased thymic output (cor=0.39, 95%CI[0.34-0.44], p<0.0001).

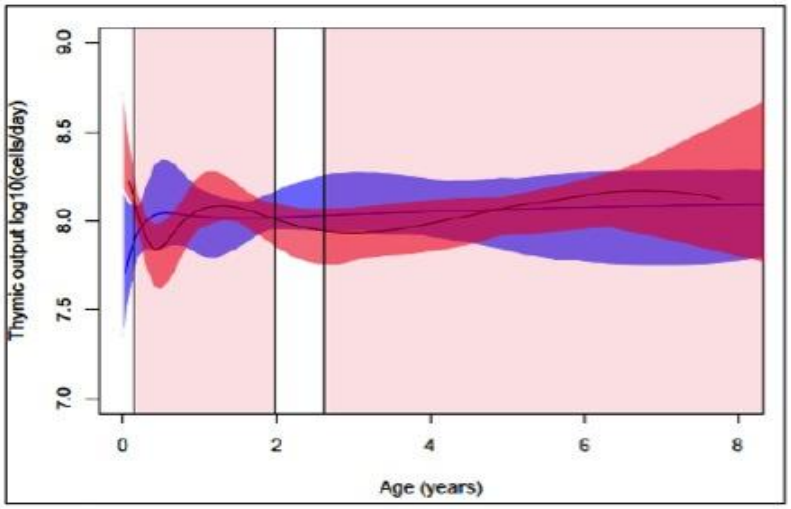

Figure 1: Non-linear regression of thymic output from healthy HIV-uninfected children versus HIV-infected children on ART. Healthy HIV-uninfected children are indicated by the blue line, with 95% confidence intervals reflected by the surrounding blue borders (n=435). HIV-infected children on ART are delineated by the red line with 95% confidence intervals reflected by the surrounding red borders (n=321 samples from 107/144 (74%) of children from ART-96W which is the arm of CHER that started ART at median 7 weeks of age, continued ART for 96 weeks, followed by ART-interruption for median 34 weeks (IQR 0-152). The pink shaded areas indicate time on ART for ART-96W. The shape of the non-linear regression curves differ significantly at 0.08-0.15, 0.29-0.58, 1.27-1.42 and 2.21-3.17 years of age (p-values <0.05).

Conclusions

HIV-infected children who were not on ART resulted in lower thymic output than uninfected children**,** however with early ART, thymic output was comparable to that seen in healthy children. Our data shows that in this age group, thymic output is a key determinant of CD4 counts and provides a mechanism whereby early ART can promote CD4 cell reconstitution and long-term immunological health.

Clinical Trial Registration (Please input N/A if not registered)

CHER trial registration ClinicalTrials.gov.NCT00102960.

ESP16-0827
ESPID PLENARY 3 - INFECTION & IMMUNITY - NEW PERSPECTIVES IN VIROLOGY

ZIKA VÍRUS AND GESTATION: FIRST CASES DETECTED IN SERGIPE

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Title of Case(s)

ZIKA VÍRUS AND GESTATION: FIRST CASES DETECTED IN SERGIPE

Background

Congenital infections are important cause of problems for both mothers and newborns(NB), and may have distinct outcomes for them. Viral diseases infecting mother and consequently their concept is long date known, but very few is reported about arbovirosis. Zika virus was recently introduced (2014) in Brazil and is now concomitantly circulating in the country with Dengue and Chikungunya. The association of Zika virus infection with congenital malformation is being by the first time investigated. We here report the first cases of Microcephalia associated with the presence of Zika virus infection in Sergipe.

Case Presentation Summary

There were 75 cases suspected of Zika vírus infection at the reference maternity of Sergipe State, Brazil. The 21 cases here described were the first who fullfilled the criteria for Zika virus congenital infection without any other congenital infection being detected (Syphilis, Rubella, Citomegalovirus, Toxoplamosis). Six cases are from Aracaju´s metropolitan area (4 Aracaju; 2 NS do Socorro) and all others from different regions of Sergipe state. The majority were females (14) and were born at term (19). Only six mothers had identified symptoms compatible to Zika vírus during gestation (4 first semester and 2 second semester). Birth weigh average was 2645.3g (1684-3352g, one with missing information) and head cicunference average was 29.5cm (26-32 cm, no missings), with only two born prematurely. All NB had no clinical problems (Apgar scores >7 at 5 minutes in all) and were discharged with their mothers.

Learning Points/Discussion

Zika vírus congenital infection may be an important clinical situation and its causality still is to be fully confirmed, but a strong association is under ocurrence in Sergipe, as in other places in Latin America.

Parallel Abstracts

ESP16-0818
ESPID SYMPOSIUM 2 - DIAGNOSTICS: IMPROVING INFECTIOUS DISEASES DIAGNOSTIC TOOLS

BACTERIAL AND VIRAL INFECTION IN CHILDREN IS DISTINGUISHED BY A TWO-TRANSCRIPT HOST BLOOD RNA EXPRESSION SIGNATURE

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Background

Accurate identification of the children with severe bacterial infection amongst the large number presenting with self-limiting febrile illness remains a major problem for healthcare providers. We investigated use of host blood RNA expression to distinguish bacterial from viral infection in febrile children.

Methods

A case-control paediatric cohort was established comprising of children with definite bacterial and viral infection (discovery and validation), and children in whom bacterial infection was neither confirmed nor ruled out following investigation. Illumina gene expression arrays were used to evaluate whole blood RNA. We identified a minimal transcript set that discriminated bacterial from viral infection in the discovery group. The minimal transcript set was tested in a validation group, and in publicly available data.

Results

Using a discovery cohort of 240 children, we identified a minimal 38-transcript signature distinguishing bacterial from viral infection. This was tested in the validation group (130 children) and in patients with indeterminate aetiology. We applied a novel computational method for transcript selection (Disease Risk Score) to derive a 2-transcript signature that

distinguished bacterial from viral infection with 100% sensitivity and 96% specificity in the validation group. In the patients with uncertain aetiology, 37 out of 79 patients that had been treated with antibiotics were classified as having viral infection.

Conclusions

We have identified a 2-transcript signature that accurately discriminates bacterial and viral infection. This signature predicted that almost half of children with uncertain diagnosis, but treated with antibiotics, had a viral signature. Our signature has potential for development as a diagnostic test that could help reduce unnecessary antibiotic use in febrile children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0435
ESPID SYMPOSIUM 2 - DIAGNOSTICS: IMPROVING INFECTIOUS DISEASES DIAGNOSTIC TOOLS

PROSPECTIVE VALIDATION OF LIPOCALIN-2 AS A PREDICTOR OF BACTERIAL INFECTION IN CHILDREN: A HOSPITAL-BASED STUDY.

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Background

Acute febrile illness is one the most frequent causes of consultation in general pediatric practice. The identification of children who are likely to benefit from antibiotic use is critical to effectively manage severe bacterial infection (SBI).

Methods

A prospective cohort study was designed to evaluate the diagnostic performance of plasma lipocalin-2 (LCN2) and C-reactive protein (CRP) to predict severe bacterial infection (SBI) in 221 children admitted to hospital. The diagnostic performance of LCN2 was estimated by the area under the receiver operating characteristic curve (AUROC) and compared to the performance of CRP.

Results

LCN2 and CRP predicted bloodstream infection with an area under the receiver operating characteristic curve (AUROC) of 0.80 (95% CI: 0.67-0.92) and 0.78 (95% CI: 0.61-0.95), respectively. When the analysis was repeated including patients with prior antibiotic use or with co-morbidities, the AUROC of LCN2 decreased to 0.68 (95% CI: 0.51-0.84) but the diagnostic value of CRP remained high (AUROC 0.76 [95% CI: 0.61-0.92]). In younger children (age<12 months, N=90), LCN2 was significantly superior to CRP (AUROC: 0.81 vs AUROC: 0.51, P<0.01).

Conclusions

LCN2 is a sensitive and specific predictor of bacteremia in the pediatric population and superior to CRP in infants. Prior antibiotic use and comorbidities decrease the diagnostic performance of LCN2. LCN2 alone or in combination with CRP can improve clinical management and antimicrobial stewardship.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0585
ESPID SYMPOSIUM 3 - THERAPEUTICS: USING ANTIMICROBIALS INTELLIGENTLY

ANTIBIOTIC PRESCRIPTION IN FEBRILE CHILDREN: IMPACT OF CLINICAL PROFILE AND CULTURAL BACKGROUND. A EUROPEAN OBSERVATIONAL STUDY IN EMERGENCY CARE.

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Background

Fever is the most frequent reason for a child to attend pediatric emergency care (ED). The majority suffers from self-limiting illness; bacterial infections comprise pneumonia and urinary tract infections mostly. We have a high antibiotic prescription rate in febrile children; often broad-spectrum. Aim: evaluating antibiotic prescription in febrile children at EDs focusing on variability among countries and clinical symptoms.

Methods

Design: Prospective observational multicenter study between October 2014-February 2016. Population: Febrile children aged 1 month-16 years visiting the pediatric ED. Outcomes: antibiotic prescription rate (primary); antibiotic type, geographical background, clinical symptoms (secondary). Data collection: each center registered clinical data and treatment (one randomly selected day per month, during 12 consecutive months).

Results

Preliminary results are based on 4546 children from 28 hospitals, 11 European countries. Median age was 2.5 years (25^{th}–75^{th} percentile 1.1–5.0); 2485 (55%) male. Working diagnosis was definite bacterial in 202 children (4%) and probable bacterial in 1189 (26%). Infections were located in upper airway most frequently (n=2756, 61%); followed by lower aiway (n=584, 13%) and enteric (n=495, 11%). The majority was managed ambulatory (n=4155, 91%). Antibiotics were prescribed in 1431 (32%), with (amino)penicillin and amoxicillin-clavulanic acid (both 37%) most frequent; cephalosporins in 15%. Antibiotic use and ratio of narrow/broad antibiotics was related to countries varying from 20-61%; antibiotic use was related to hospitalization and clinical symptoms.

Conclusions

In a multicenter study among 28 European paediatric EDs, a minority of febrile children is at risk for bacterial infections. Antibiotics were prescribed in 32%, with (amino)penicillin and amoxicillin-clavulanic-acid most frequently. There are substantial differences in antibiotic use in febrile children among different European countries and their clinical spectrum. International best practices need to be identified for management of acute febrile children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0438
ESPID SYMPOSIUM 3 - THERAPEUTICS: USING ANTIMICROBIALS INTELLIGENTLY

MEROPENEM VS STANDARD OF CARE ANTIBIOTICS (SOC) FOR LATE ONSET NEONATAL SEPSIS (LOS): A RANDOMIZED CONTROLLED TRIAL NEOMERO-1

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Background

Meropenem is often used for treatment of LOS but is not licensed for it. We aimed to compare the efficacy and safety of meropenem to SOC in infants aged <90 days with LOS.

Methods

NEOMERO-1 was a multinational, open-label, phase-3 superiority trial. Infants with suspected LOS were randomised to receive meropenem or predefined SOC (ampicillin+gentamicin or cefotaxime+gentamicin) for 11±3 days. The primary outcome was treatment success (survival, no modification of allocated therapy [AT], resolution/improvement of clinical and laboratory markers with no need of additional antibiotics and presumed/confirmed eradication of baseline pathogens) at test-of-cure visit (TOC) 2±1 days after the end of therapy (EOT). At follow-up (FU) visit on Day 28 hearing function and brain imaging were recorded. Stool samples were collected at baseline, EOT and FU for detection of carbapenem-resistant Gram-negative organisms (CRGNO).

Results

Of 271 patients in full analysis set 267 had LOS (74% <37wks), 136 received meropenem and 131 SOC (35% ampicillin+gentamicin). 140 (52%) cases were culture-confirmed; *Staphylococcus epidermidis* (33%), *Enterobacter* spp. (16%) and *Klebsiella pneumoniae* (9%) were the most common. The primary outcome is depicted in Table. Adverse events (AE) occurred in 72% and serious AEs in 17% of patients with a similar distribution between treatment arms. At FU, abnormal hearing was recorded in 15% and 29%, abnormal brain imaging in 25% and 27% and relapse/new infection in 18% and 17% in meropenem and SOC arms, respectively. CRGNO were acquired by 4/94 (4%) patients in meropenem and 12/101

(12%) in SOC (p=0.05) during the study.

Table. Primary outcome	Full analysis set		Culture-confirmed LOS	
	Meropenem N = 136 (%)	SOC N = 135 (%)	Meropenem N = 63 (%)	SOC N = 77 (%)
Treatment success at TOC	44 (32)*	31 (23)	17 (27)**	10 (13)
Reasons for failure				
Death	10 (7)	6 (4)	3 (5)	4 (5)
Clinical or microbiological failure	29 (21)	31 (23)	12 (19)	18 (23)
Modification of AT	78 (57)	85 (63)	43 (68)	59 (77)
- Treatment completed before Day 8	30 (38)	10 (12)	ND	ND
- Resistant microorganism isolated at baseline	3 (4)	16 (19)	ND	ND
Not allowed antibiotics given or antibiotics not started	2 (1)	10 (7)	2 (3)	4 (5)

*p=0.087; **p=0.022; ND – not done

Conclusions

The efficacy of meropenem was superior of SOC in culture-confirmed LOS but not in the FAS. Meropenem is an alternative for treatment of LOS in targeted population and does not outselect CRGNO.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrial.gov NCT01551394

ESP16-0950
ESPID SYMPOSIUM 3 - THERAPEUTICS: USING ANTIMICROBIALS INTELLIGENTLY

FEBRILE URINARY TRACT INFECTION DUE TO EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING ENTEROBACTERIACEAE IN CHILDREN: AN OBSERVATIONAL FRENCH STUDY

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Background

Our aim was to describe the characteristics and treatments of febrile urinary tract infections (F-UTI) caused by Extended spectrum betalactamase-producing *Enterobacteriaceae* (ESBL-E).

Methods

In this prospective observational study between March 2013 and December 2015, children (0 to 18 years) with ESBL-E F-UTI were enrolled in 24 pediatric departments. First and second lines of antibiotic therapies were analyzed. We used the Kaplan-Meier method to estimate the time to fever defervescence and hospitalization duration, and Log-rank test to assess equality of survivor functions.

Results

180 children with F-UTI were enrolled, the most common pathogen was *E. coli* (82%), and amikacine remained active for 90% of the strains. Urinary malformation and prior antibiotic exposure were reported in 39% and 48% of ESBL-E UTI respectively. Eighty six (46.1%) were treated initially (before the knowledge of in vitro susceptibility) by regimen active (alone or with others antibiotics) in vitro against the strain isolated: amikacine 70 (66.6%), gentamicin 14 (13.3%), ciprofloxacin 6 (6%). Forty seven (26.1%) were treated with carbapenem. The susceptibility in vitro of the initial therapeutic regimen seems do not affect the time to

defervescence (p= 0.52), and hospital stay (p= 0.08). Oral antibiotic treatment adapted against the ESBL strains responsible of the F-UTI was possible for 118 patients (60%): cotrimoxazole 55 (51 %), ciprofloxacin (if cotrimoxazole resistant) 49 (45.4%), combination of cefixime and amoxicillin-clavulanate (if cotrimoxazole and ciprofloxacin resistant) 14 (11.2 %).

Conclusions

ESBL F-UTI is an increasing problem in Europe. None single oral antibiotic is active against these strains. Except carbapenems, amikacin remains the most active compound.We found no significant difference in early outcome between children treated with in vitro effective treatment and those treated with non-effective antimicrobials.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0790
ESPID/ECDC/WHO JOINT SESSION 4 - VACCINES: THE RETURN OF OLD VACCINE PREVENTABLE ENEMIES

MAY EARLY PREGNANCY VACCINATION AGAINST PERTUSSIS BENEFIT TO PRETERM NEONATES?

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Background

Maternal immunization against pertussis is recommended between 26 and 36 gestational weeks (GW). Data on the optimal timing of maternal vaccination is yet limited.

Methods

We conducted a large prospective observational study assessing the optimal timing of maternal Tdap immunization for antibody transfer to term and preterm neonates. Geometric mean concentrations (GMC) of cord blood antibodies to recombinant pertussis toxin (rPT) and filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay.

Results

We included 374 women at term (335, 39.3 GW ± 1.3) or preterm (39, 34.5 GW ± 2.2) delivery, previously immunized with Tdap at 29.7 ± 8.0 (term) or 26 ± 5.2 (preterm) GW. An interval of 15 days between immunization and delivery was sufficient to confer higher anti-PT and FHA GMCs in both term groups (Table I). Anti-PT and FHA GMCs were significantly higher following second versus third trimester immunization in term neonates (Table I). A similar trend is observed for preterm neonates, whose recruitment is ongoing.

Conclusions

Early second-trimester maternal Tdap immunization increased neonatal antibodies not only in term but also in preterm neonates. Recommending immunization from 13 gestational weeks onwards could also improve seroprotection in this fragile population.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1081
ESPID/ECDC/WHO JOINT SESSION 4 - VACCINES: THE RETURN OF OLD VACCINE PREVENTABLE ENEMIES

CONTROL OF HIB IN CHILDREN: EPIDEMIOLOGY AND SEROPREVALENCE IN ENGLAND

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Background

The introduction of the *Haemophilus influenzae* type b (Hib) conjugate vaccine in England resulted in a rapid decline in invasive Hib disease. However, a resurgence of Hib during 2000-2002 prompted the introduction of additional control measures, including a routine 12-month booster in 2006. Here we describe the recent epidemiology of Hib among children and results from a national seroprevalence study.

Methods

Public Health England conducts enhanced national surveillance of invasive Hib disease. Clinical information was obtained for all confirmed cases <16 years during 2009-15. A national seroprevalence study was performed to determine the prevalence of Hib IgG antibodies among 807 children <10 years.

Results

Hib cases have declined since 2002 with the lowest ever incidence in children in 2015 (0.01/100,000; 1 case). Of the 29 children diagnosed during 2009-15, 17 (59%) developed meningitis and 1 died. Twenty-six were eligible for vaccination, but only three were fully immunised.
In the seroprevalence study, median anti-PRP IgG concentrations were highest among 1 year olds (4.45 µg/mL); but declined to 1.14 µg/mL at 4 years of age. Overall, 92% of children aged 6 months to 10 years had achieved short-term protective antibody threshold of ≥0.15 µg/mL, indicating short-term immunity

Conclusions

Control of Hib in England is currently the best ever achieved. However, Hib antibodies wane rapidly after the 12 months booster. Although most children remained protected against disease, antibody levels may not be high enough to prevent carriage among toddlers. Ongoing monitoring is essential to inform future vaccination policy.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0666
ESPID/ECDC/WHO JOINT SESSION 4 - VACCINES: THE RETURN OF OLD VACCINE PREVENTABLE ENEMIES

EPIDEMIOLOGY AND VACCINE EFFECTIVENESS DURING A LARGE MUMPS OUTBREAK IN WESTERN AUSTRALIA

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Background

Mumps is a vaccine-preventable infection causing parotitis, fever and malaise. Mumps outbreaks have been reported but are rare since the introduction of the measles-mumps-rubella (MMR) vaccine.

We describe epidemiologic and laboratory aspects of a large mumps outbreak which began in remote Western Australia in March 2015 and spread across an area covering more than 2.1 million km^2.

Methods

Clinically-suspect cases were laboratory-confirmed or epidemiologically linked. Case information was obtained from the statewide notifiable diseases database. To estimate MMR vaccine effectiveness (VE), cases ≤18 years of age were matched by age and location to controls using a population-based vaccination register at a ratio of 11:1. A conditional logistic regression model was fitted with MMR vaccine doses as the exposure and VE calculated using 1-(odds ratio)*100. We compared this approach to VE calculated using the screening method.

Results

Between March 2015 and January 2016, more than 477 cases were reported, of which 194 (40.1%) were ≤ 18 years old. Aboriginal-Australians were disproportionately affected, comprising 87% of all cases but just 3% of the general population. Cases were more likely than controls to be vaccinated; 93.1% vs. 89.5%. VE was estimated at —122.8% (—626.5 to 31.7) for two doses of MMR in the matched case-control analysis and —107% using the screening method. Thirty-eight mumps isolates were genotyped and all were genotype G.

Conclusions

The disproportionate burden of disease among Aboriginal Australians could be the result of increased transmission for a number of reasons including high mobility or household density, or decreased VE in this group. Our study found low VE in the paediatric outbreak cases however we were unable to restrict our analysis to Aboriginal-Australians. This highlights the need to investigate mumps vaccine immunogenicity in different populations.

ESP16-0558
ESPID SYMPOSIUM 6 - DIAGNOSTICS: NEW TECHNOLOGIES

EFFICACY AND SAFETY OF PROCALCITONIN-GUIDED DECISION MAKING IN NEONATES SUSPECTED OF EARLY ONSET SEPSIS: NEOPINS STUDY – AN INTERNATIONAL, MULTICENTRE, NON-INFERIORITY RANDOMIZED CONTROLLED INTERVENTION TRIAL

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Background

Uncertainty about the presence of neonatal early-onset sepsis (EOS) results in unnecessary and prolonged empiric antibiotic treatment. This study evaluates whether PCT-guided treatment for suspected EOS can reduce the duration of antibiotic treatment with unchanged outcome (re-infection/death in the first month of life with 2% margin for non-inferiority).

Methods

Randomized controlled intervention trial recruiting neonates (gestational age ≥ 34 weeks) suspected of EOS requiring antibiotic therapy. Patients were stratified in 4 risk-categories and randomized for duration of antibiotic treatment based on PCT-guided-decision-making or standard care. Analyses were done as intention-to-treat (ITT) as well as per protocol (PP).

Results

1770 neonates were randomized and included in the ITT analysis, 1408 in the PP analysis. The duration of antibiotic therapy was significantly shorter in the PCT-group than in the standard group (ITT: 55.0 vs. 64.4 hours, p<0.001; PP: 39.5 vs. 62.0 hours; p<0.001). Length of hospital stay was significantly (p=0.002) reduced in the PCT group with a small effect size (ITT: -3.2 hours; PP: -5.1 hours). No sepsis related deaths occurred and the rate of possible re-infection was below 1% with a risk difference of 0.1% (exact CI -5.2 to 5.3%). Non-inferiority (margin 2%) could not be statistically proven due to the low occurrence of possible relapse infections.

Conclusions

Initial risk assessment for suspected EOS and PCT-guidance on duration of empirical antibiotic therapy results in a significant reduction of duration of antibiotic therapy and length of hospital stay. The effect size is dependent on protocol adherence. The used approach seems to be safe whereas non-inferiority cannot be claimed statistically.

Clinical Trial Registration (Please input N/A if not registered)

Clinical trials.gov NCT00854932

ESP16-0235
ESPID SYMPOSIUM 6 - DIAGNOSTICS: NEW TECHNOLOGIES

ROLE OF SERUM PROCALCITONIN IN PREDICTING SIGNIFICANT INFECTIONS AND MORTALITY IN PEDIATRIC ONCOLOGY

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Background

There is paucity of data on role of inflammatory biomarkers in pediatric oncology patients. Procalcitonin (PCT) has been observed to discriminate infections.

Methods

Children on chemotherapy presenting with fever were enrolled (2007-2015). Clinical and laboratory data were recorded. Presence of pneumonia, hemodynamic instability, infective focus or prolonged fever with unknown cause was considered clinically significant infection (CSI). Microbiologically documented infection (MDI) was defined by positive microbiological tests. Association of PCT with CSI, MDI and deaths was analyzed.

Results

821 febrile episodes were evaluated in 316 children. 522 (63.6%) episodes were febrile neutropenia. CSI, MDI and deaths were seen in 336 (40.9%), 165 (20.1%) and 24 (2.9%) episodes respectively. PCT levels ranged from 0.05-560 ng/ml (median–0.38). Median PCT (interquartile range) was higher in episodes of CSI [0.80(0.34–3.17) *vs.* 0.28 (0.16–0.50), p<0.001] and in episodes of MDI [0.71(0.28–3.63) *vs.* 0.34 (0.19–0.76), p<0.001]. PCT ≥0.7ng/ml optimally predicted CSI (AUC–0.740) and MDI (AUC–0.636). Relative risk of mortality for PCT ≥5ng/ml was 7.1 (95%CI=3.2–15.1). PCT ≥0.7ng/ml had poor sensitivity (45–55%) but good specificity and NPV (70–90%). PCT ≥0.7ng/ml adequately predicted CSI (PPV-70%), but not MDI and documented bacterial infections (PPV 20–30%). Prevalence of CSI, MDI and deaths increased with PCT (p<0.001). PCT was elevated in half of documented viral and fungal infections.

Conclusions

PCT cut-off of ≥0.7ng/ml and ≥5.0ng/ml at admission predicts significant infections and mortality in pediatric oncology patients respectively. Procalcitonin at admission for fever identifies a high-risk group in these immunosuppressed children, but does not rule out significant infections altogether. Procalcitonin correlates with the severity of infection and not the type of infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0921
ESPID SYMPOSIUM 7 - THERAPEUTICS: PHARMACOKINETIC & DYNAMIC MODELLING IN ACTION

PHARMACOKINETICS OF AMIKACIN WITH OR WITHOUT AMINOPHYLLINE IN NEONATES WITH SUSPECTED SEPSIS

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Background

Amikacin is often combined with other medications for treatment of severe bacterial infections in neonates. Although concurrent administration of amikacin with aminophylline is used among preterm neonates, there is lack of information on potential interaction.Furthermore, there is a paucity of aminoglycoside pharmacokinetic (PK) data in neonates of African origin.

The objective of this study was to describe the PK of amikacin with or without co-administered aminophylline in neonates with suspected sepsis.

Methods

Neonates with suspected sepsis admitted to a neonatal intensive care unit (n = 247) and treated with amikacin (15 mg/kg loading followed by 7.5 mg/kg twice daily) with or without co-administered aminophylline (8 mg/kg loading followed by 3 mg/kg every 8 – 12 hours) were recruited. Selected admission clinical and demographic information were recorded. Serum amikacin concentration was measured at specified times after treatment initiation and data analyzed using population PK modeling.

Results

A total of 419 serum concentration data was available for 247 neonates. Mean (SD) trough amikacin concentration among term (n = 25) and preterm (n = 36) neonates were 6.23 (3.45) and 9.23 (5.68) µg/mL, respectively. A one-compartment model best fitted amikacin distribution. The population clearance (CL), and volume of distribution (V) of amikacin were related as: $CL = 0.153 (\text{birth weight}/2.5)^{1.31}$, $V = 2.94 (\text{birth weight}/2.5)^{1.18}$.Although a high between-subject variability, 58.9 and 50.7%, in CL and V, respectively, was found none of the other covariates tested improved model. The mean half-life of amikacin was 13.2 hours.

Conclusions

Birth weight was an important predictor of amikacin CL and V. There was a relatively large V and long half-life of amikacin in this cohort of neonates. Co-administration of aminophylline with amikacin showed little effect on amikacin PK.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0592
ESPID SYMPOSIUM 7 - THERAPEUTICS: PHARMACOKINETIC & DYNAMIC MODELLING IN ACTION

PHARMACOKINETIC (PK) MODELLING OF MEROPENEM IN PLASMA AND CEREBROSPINAL FLUID (CSF) IN INFANTS WITH LATE-ONSET SEPSIS (LOS) AND/OR BACTERIAL MENINGITIS

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Background

Meropenem is used off-label in the treatment of LOS and bacterial meningitis. We aimed to develop a population PK model of meropenem in both plasma and CSF, and then use it for dosing recommendations in infants aged <3 months.

Methods

Data for population PK analysis were collected from infants aged <90 days with LOS and/or meningitis. Meropenem was given at 20mg/kg (LOS) or 40mg/kg (meningitis) as a 30-minute infusion every 8, or every 12h in infants <32 weeks gestational age (GA) and <2 weeks postnatal age (PNA). Plasma/CSF concentrations were determined using UHPLC-MS/MS. PK data were modelled using non-linear mixed-effects (NONMEM 7.3). A CSF compartment was added and CSF penetration estimated as a model parameter. Monte Carlo simulations (n=1000) for different dosing regimens and 8 MIC values were used to generate the probability-of-target-attainment (PTA) curves.

Results

401 plasma samples were obtained from 167 infants, 56 of whom also had at least one CSF sample (78 samples in total). The median (IQR) GA was 33.3 (28.6-38.3) weeks, and PNA 13 (7-28) days at enrolment. The final model was a one-compartment model, where allometric weight scaling with a postmenstrual-age-driven maturation function was used *a priori*. Serum creatinine proved a significant covariate on clearance (CL); PNA was not significant. The values of meropenem CL and central volume of distribution for a typical infant were 0.50 L/h and 1.26 L, respectively; and penetration of meropenem into the CSF 12%. PTA plots are

presented in Figure 1.

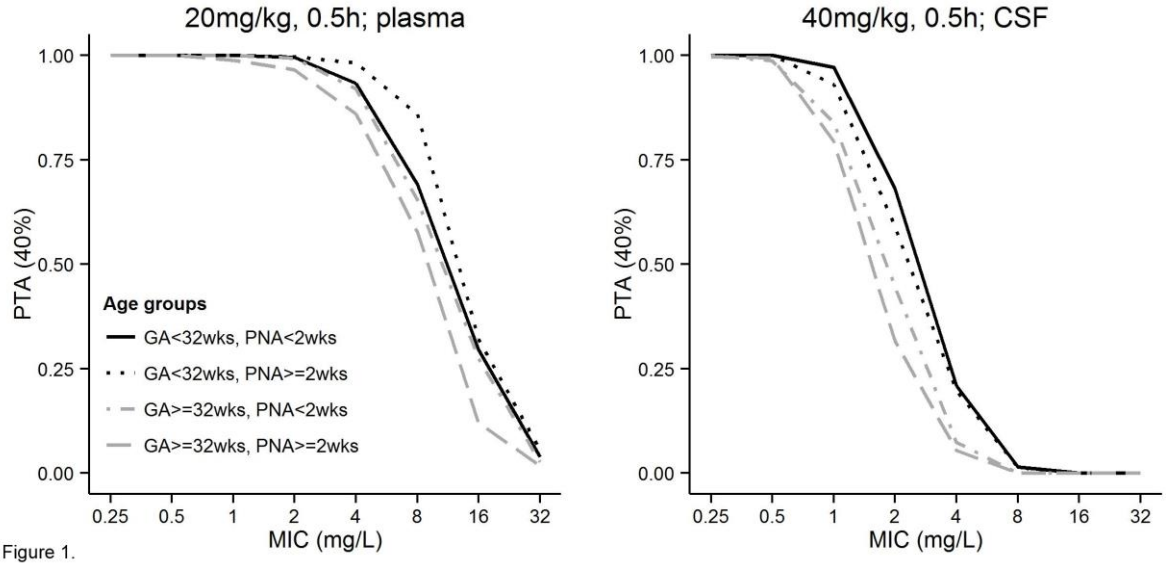

Figure 1.

Conclusions

Simulations showed that dosing regimens used in the study for LOS and meningitis in infants aged <3 months are appropriate if MIC <4mg/L (LOS) or <1mg/L (meningitis).

Clinical Trial Registration (Please input N/A if not registered)

NCT01551394

ESP16-0931
ESPID SYMPOSIUM 7 - THERAPEUTICS: PHARMACOKINETIC & DYNAMIC MODELLING IN ACTION

POPULATION PHARMACOKINETICS AND PHARMACODYNAMICS OF TEICOPLANIN IN NEONATES

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Background

There is uncertainty about teicoplanin neonatal optimal dosage regimens. The study aim was to determine the population PK of teicoplanin in neonates, evaluate currently recommended regimens and explore the exposure-effect relationships.

Methods

Anopen label PK study was conducted. Neonates from 26-44 weeks post-menstrual age were recruited (n=18). Patients received a loading dose (16 mg/kg) followed by 8 mg/kg q24h. Serum was collected at 1, 3, 6 and 24 h, and at steady state. A standard 2-compartment PK model was developed, followed by models that incorporated weight. C-reactive protein (CRP) serial concentrations were also collected as a PD input. A PK-PD model was fitted to the data. Semi-parametric simulations (n=5000) were performed using Pmetrics. The AUCs at steady state and the proportion of patients achieving the recommended drug exposures in terms of Cmin (>15 mg/L) were determined.

Results

The PK allometric model best accounted for the observed data and was chosen for further analysis. The PK parameters medians were: Clearance=0.435*(weight /70) $^{0.75}$ (L/h), Volume 0.765 (L), Kcp 1.3 (h^{-1}), Kpc 0.629 (h^{-1}). The fit of the PK-PD data was acceptable. The individual time-course of CRP was well described using the Bayesian posterior median estimates for each patient. The simulated median AUC_{96-120} was 302.3 mg*h/L, median Cmin at 120 h was 12.9 mg/L. The percentage of patients with Cmin >15 mg/L was 38.8 %.

Conclusions

Teicoplanin population PK is highly variable in neonates, being weight the best descriptor of PK variability. AUC drug exposures were effective in terms of suppressing CRP levels, however, only a low percentage of neonates were able to achieve Cmin >15 mg/L. The routine use of TDM together with improved knowledge of the teicoplanin PD is required.

Clinical Trial Registration (Please input N/A if not registered)

(EudraCT): 2012-005738-12

ESP16-0313
ESPID SYMPOSIUM 9 - GLOBAL IMPACT: BETTER UNDERSTANDING RESPIRATORY INFECTIONS

SEASONAL AND PANDEMIC INFLUENZA IN PAEDIATRIC INTENSIVE CARE UNITS IN ENGLAND AND WALES: RISK FACTORS FOR ADMISSION AND MORTALITY

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Background

Data from paediatric intensive care units (PICUs) have been used to examine risk factors for severe influenza in children and monitor severity between strains. Such analyses should be based on whole country data on all children admitted to PICUs and suitable population denominators.

Methods

We extracted data from the Paediatric Intensive Care Audit Network on influenza admissions during pre-pandemic (September 2003-March 2009), H1N1 pandemic waves 1 & 2 (April 2009-March 2010), wave 3 (April 2010-March 2011) and post-pandemic (April 2011-December 2014) periods. We calculated admission rates by age, sex and period per 100,000 child years (cy), and used logistic regression models to determine the association between demographic and clinical variables, period, and death during admission.

Results

There were 906 influenza-related PICU admissions in the study period; 112 (12.4%) children died. The highest admission rate was observed in 2010/11 (2.5/100,000 cy). Admission rates were highest among infants in all four periods, but 50.2% of admissions were in 5-18 year olds in 2009/10 (cf. <30% in other periods). Overall age-adjusted admission rates were lower in girls than boys (incidence rate ratio 0.80, 95% confidence interval (CI) 0.70, 0.92). The odds of mortality was higher in girls compared to boys (adjusted odds ratio 1.57 95% CI 1.04, 2.38), adjusted for ethnicity, period and chronic illness. The odds of mortality did not significantly differ between the four periods.

Conclusions

Infants had the highest risk of admission to PICU with influenza. Girls had a lower risk of admission but a higher odds of death once admitted. Using linked hospital in-patient data we will further assess the effect of gender, ethnicity, socio-economic status and pre-existing conditions on the risk of PICU influenza admission and subsequent outcomes.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1067
ESPID SYMPOSIUM 9 - GLOBAL IMPACT: BETTER UNDERSTANDING RESPIRATORY INFECTIONS

NASOPHARYNGEAL BACTERIAL DENSITY IS INCREASED BY VIRAL RESPIRATORY INFECTIONS WHICH MAY FACILITATE TRANSMISSION

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Background

The prevalence of the common nasopharyngeal colonisers, *S.pneumoniae*, *S.pyogenes*, *N.meningitidis*, *M.catarrhalis*, *H.influenzae* and *S.aureus* is dependent on several factors. Our aim was to explore the associations between viral infections and the prevalence and density of bacteria in the nasopharynx.

Methods

This was an observational cohort study, with ethical approval using informed consent, recruiting 161 children attending nurseries in Bristol, UK. All had monthly nasopharyngeal swabs taken and stored in STGG broth. qPCR was used for detection of respiratory viruses and six bacterial species. t-tests and logistic regression models were used for analysis.

Results

Carriage rates of *S.pneumoniae*, *M.catarrhalis* and *H.influenzae* were high (78.8%, 85.7% and 85.0%, respectively), remained stable throughout the study period and were frequently found in high density (>1000 gene copies/ml) in comparison to the other species. Respiratory viral infections and nasal discharge were both independently and consistently associated with higher bacterial density with an observed twofold increase in density for *S.pneumoniae*, *M.catarrhalis* and *H.influenzae* (p= 0.004 - 0.017). In addition, the sum of bacterial load of these six species declined with increasing age. Bacterial density varied widely within the same individual over the course of the study.

Conclusions

Respiratory viral nucleic acids were consistently associated with higher bacterial carriage rates and bacterial density in the absence of significant clinical illness. Young age was an independent predictor of high *M. catarrhalis* carriage rates and bacterialdensity of *S.pneumoniae, M.catarrhalis* and *H.influenzae*. A higher nasal discharge was independently associated with higher density of pneumococci and *H. influenzae* suggesting that these species may promote nasal discharge. Increased colonisation density and rhinitis may promote transmission of these commonly carried organisms.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0056
ESPID SYMPOSIUM 9 - GLOBAL IMPACT: BETTER UNDERSTANDING RESPIRATORY INFECTIONS

DEXAMETHASONE FOR PLEURAL INFECTION IN CHILDREN: A DOUBLE BLIND, RANDOMIZED, CLINICAL TRIAL OF EFFICACY AND SAFETY

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Background

Pleural infections lead to long hospitalizations. In this trial, we investigate whether dexamethasone decreases the time to recovery of pleural infection. Also we evaluate complications and adverse events associated with dexamethasone.

Methods

CORTEEC is a phase II, multi-center, stratified, randomized, double blind, placebo-controlled trial with 60 children. Patients were stratified into simple effusion or complicated effusion. Patients were assigned to intravenous dexamethasone or placebo.

Results

Dexamethasone was better than placebo with respect to time to recovery. The hazard ratio (HR) for recovery was 1.85 (95% confidence interval [CI], 1.08 to 3.17; P=0.024). In the multivariate Cox model, the superiority of dexamethasone was consistent, regardless of severity group (HR, 1.73; 95% CI, 1.02 to 2.9; P=0.042). The median time to recovery for patients on dexamethasone was 68 hours (2.8 days) shorter than patients on placebo. The median time to recovery for patients with simple effusion on dexamethasone was 76 hours (3.1 days) shorter than patients with simple effusion on placebo. The median time to recovery for patients with complicated effusion on dexamethasone was 14 hours (0.5 days) shorter than patients with complicated effusion on placebo. Hyperglycemia was more frequent in patients on dexamethasone (risk ratio [RR], 4; 95% CI, 1.2 to 12.5; P=0.01). Patients on dexamethasone had less severe anemia than patients on placebo (RR, 0.1; 95% CI, 0.01 to 1.2; P=0.07). No further differences were found in complications or adverse events.

Conclusions

Dexamethasone is a safe and effective adjunctive therapy for decreasing time to recovery in children with pleural infection.

Clinical Trial Registration (Please input N/A if not registered)

This trial was registered at www.clinicaltrials.gov (NCT01261546).

ESP16-0723
ESPID SYMPOSIUM 10 - VACCINES: VACCINE SAFETY - ACHIEVEMENTS, CHALLENGES/ THE BRIGHTON COLLABORATION

USING SMS TECHNOLOGY FOR REAL-TIME SURVEILLANCE OF ADVERSE EVENTS FOLLOWING IMMUNISATION

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Background

On-going, post-licensure surveillance of adverse events following immunisation (AEFI) is critical to detecting and responding to potentially serious adverse events in a timely manner. SmartVax is a novel vaccine safety monitoring tool that uses automated data extraction from existing practice management software and short message service (SMS) technology to follow-up vaccinees in real-time. We report on childhood vaccine safety surveillance using SmartVax at a medical practice in Perth, Western Australia.

Methods

Parents of all children below five years, vaccinated according to the Australian National Immunisation Schedule between November 2011 and June 2015 were sent an SMS three days post vaccine administration to enquire whether the child had experienced a suspected vaccine reaction. Affirmative replies triggered a follow up SMS requesting details of any possible reactions via a link to a survey that could be completed on a smartphone. Rates of reported AEFI including fever, headache, fatigue, rash, vomiting, diarrhoea, rigors, convulsions, and local reactions were calculated by age and vaccine type.

Results

Overall, possible vaccine reactions were reported for 239 (8.2%; 95% CI 7.2%—9.2%) of 2,898 vaccination visits. A significantly greater proportion of AEFI, mostly local reactions, occurred following administration of diphtheria-tetanus-pertussis-poliomyelitis vaccine at 4 years of age (77/441 [17.5%]; 95% CI 13.9%—21.0%) compared to the vaccinations given at 2–18 months ($p<0.001$). Across all time points, local reactions and fatigue were the most frequently reported AEFI.

Conclusions

Automated SMS-based reporting can facilitate sustainable, real-time, monitoring of adverse reactions and contribute to early identification of potential vaccine safety issues. This is critical in maintaining public confidence in the safety of vaccines.

ESP16-0470
ESPID SYMPOSIUM 10 - VACCINES: VACCINE SAFETY - ACHIEVEMENTS, CHALLENGES/ THE BRIGHTON COLLABORATION

INFLUENZA VACCINATION IN CHILDREN WITH CYSTIC FIBROSIS USING INTRANASAL LIVE ATTENUATED INFLUENZA VACCINE: EXPERIENCE FROM AN AUSTRIAN PAEDIATRIC HOSPITAL

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Background

Cystic fibrosis (CF) is a genetic disorder of mucociliary clearance affecting mainly the respiratory and digestive systems. Patients with CF are predisposed to respiratory infections, particularly influenza, which carries significant morbidity and increased bacterial colonisation. While influenza vaccination is recommended for this group, data on the use of intranasal live attenuated influenza vaccine (LAIV) are limited.

Methods

Children with CF aged 2–18 years who had not already received influenza vaccination that season were offered LAIV vaccination during the 2013/2014 and 2014/2015 seasons in an Austrian paediatric CF centre. Adverse events (AEs) and incidence of influenza-like illness (ILI) were evaluated retrospectively through telephone interviews.

Results

The number of children offered LAIV, uptake of LAIV and reasons for no vaccination are provided in the Table.

TABLE: Vaccination details for children offered LAIV in 2013/2014 and 2014/2015 influenza seasons

	2013/2014 season (n=44)	2014/2015 season (n=102)
Vaccination uptake		
LAIV	43	94
Non-vaccinated	1	8
Contraindicated (e.g. pulmonary exacerbation, wheezing)	0	5
Vaccine-refusing families	1	3
AEs with LAIV		
Mild AEs	4/43	5/94
Serious AEs (pulmonary exacerbation)	1/43	0/94
Incidence of ILI		
LAIV	0/43	4/94 (mild)
Non-vaccinated	0/1	4/8 (severe)

LAIV was well accepted by children and their parents. Total AEs following LAIV administration were reported by 5/43 and 5/94 children in the 2013/2014 and 2014/2015 seasons, respectively (Table). AEs were mostly mild; pulmonary exacerbation occurred in one child with end-stage lung disease. No children (vaccinated or unvaccinated) contracted influenza during the 2013/2014 season. In the 2014/2015 season (influenza epidemic and significant mismatch between vaccine and circulating viruses) four children vaccinated with LAIV displayed evidence of ILI; illness was mild and did not require hospitalisation. In contrast, four cases of severe ILI occurred in the eight unvaccinated children, two of whom required hospitalisation. There was no change in bacterial colonisation after LAIV.

Conclusions

LAIV is well accepted by children with CF and their parents and does not appear to be associated with severe AEs. Results also suggest a protective effect of LAIV vaccination against influenza and influenza-related outcomes.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0406
ESPID SYMPOSIUM 10 - VACCINES: VACCINE SAFETY - ACHIEVEMENTS, CHALLENGES/ THE BRIGHTON COLLABORATION

NO ASSOCIATION OF THE TEN-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV10) WITH PREVIOUSLY SUGGESTED PCV SAFETY SIGNALS

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Background

Serious adverse events like febrile seizures, breath-holding, urticarial rash (hives), hyperactive airway disease and/or asthma and Kawasaki's disease have been reported in at least one of the large clinical trials conducted using pneumococcal conjugate vaccines. PCV10 was introduced in the Finnish National Vaccination Programme (NVP) in September 2010 using a 2+1 schedule (at 3, 5 and 12 months). We investigated the incidence of these diseases using hospital discharge register in Finland.

Methods

We collected hospitals' in/outpatient discharge notifications with ICD-10 diagnoses compatible with the suggested safety signals reported from clinical trials. Incidence of first-recorded ICD-10 codes at three months of age or later were compared between children eligible for the PCV10 in the NVP in 2010 up to end of 2014 (children born 06/2010-09/2014) and a reference cohort before the NVP from 2004 through 2008 (born 06/2004-09/2008). Vaccine uptake is estimated at 92%. Incidences were compared using Poisson regression.

Results

The relative risks between PCV-eligible and reference cohorts are shown in table.

Table. Incidences of safety signals in pre- and postvaccination periods

	Incidence in the reference cohort 2004 to 2008	Incidence in the PCV10 eligible cohort 2010 to 2014	Relative (9
1. Febrile seizures (R560)	399.1	398.7	1.00
2. Breath-holding (R068)	60.3	54.7	0.91
3. Urticaria (L500, L501, L509)	184.9	285.5	1.54
4. Acute bronchitis (J20, J20.9 or J21.9)	2195.5	1986.5	0.91
5. Asthma (J45 or J46)	1054.6	873.4	0.83
6. Kawasaki's disease (M303)	16.2	11.2	0.69

Conclusions

No differences were found except for urticaria, which was more common during the vaccination era. However, the increase in urticaria was seen in many age groups in the post-

vaccination era, not only in those vaccinated. Although further analysis is warranted regarding e.g. potential temporal associations, the lack of apparent incidence-changes in these diseases provides reassuring information regarding the safety of PCVs.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0704
ESPID SYMPOSIUM 10 - VACCINES: VACCINE SAFETY - ACHIEVEMENTS, CHALLENGES/ THE BRIGHTON COLLABORATION

EXPLORING INCIDENCE RATES OF GUILLIAIN BARRÉ, CHRONIC FATIGUE AND POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME TO UNDERSTAND SAFETY PROFILE OF HPV VACCINATION AMONG ADOLESCENT GIRLS

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Background

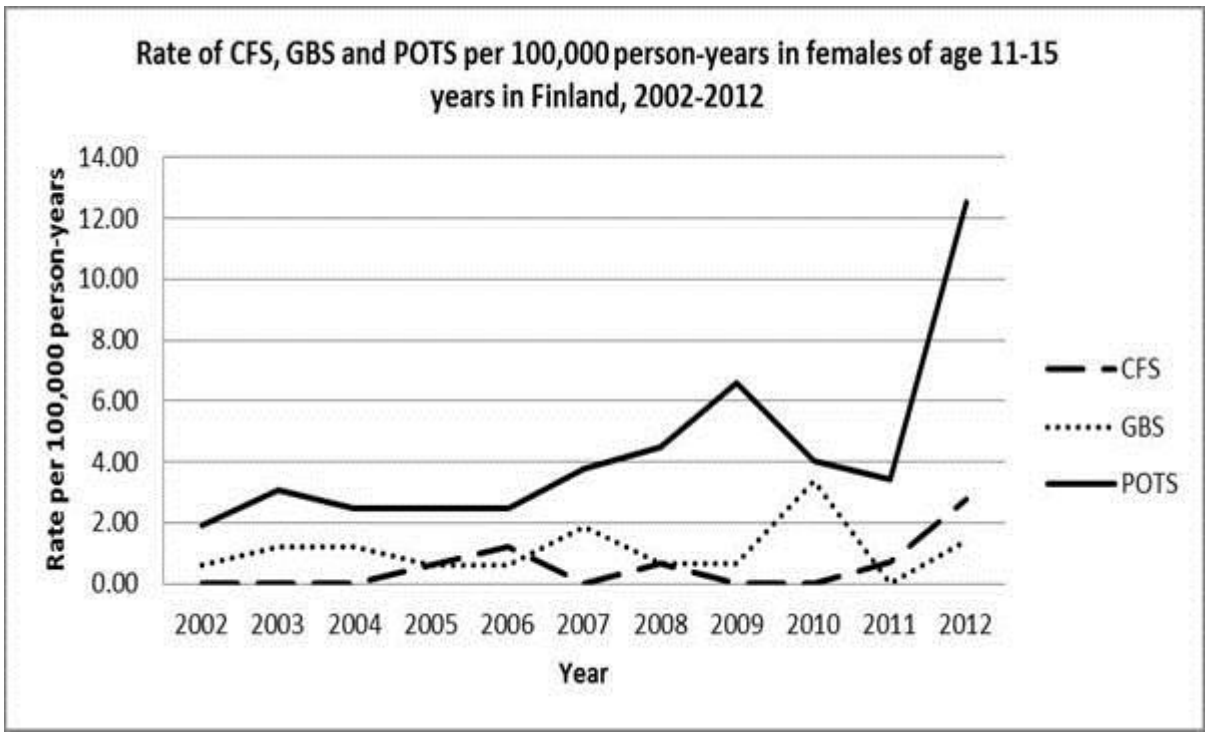
In Finland, a vaccination program against human papillomavirus (HPV) was introduced in November 2013 for girls aged 11-15 years. Allegations that HPV vaccine is causing Guilliain Barré syndrome (GBS) and non-specific diagnostic entities, such as chronic fatigue syndrome (CFS) and postural orthostatic tachycardia syndrome (POTS), continue to surface. We examined register based pre-vaccine incidence rates of CFS, GBS and POTS to provide baseline data for future HPV vaccine safety evaluations.

Methods

First diagnosis of CFS, GBS and POTS in girls aged 11-15 years were obtained from the National Hospital Discharge Register during 2002-2012. We considered the following ICD-10 codes: G93.3 for CFS; G61.0 for GBS and G90.9, G90.8, G93.3, I49.8 for POTS. We calculated incidence rates per 100,000 person-years with 95% confidence intervals (CI).

Results

In total, 9 CFS, 19 GBS and 72 POTS cases were identified. The overall incidence rate was 0.53/100,000 (95% CI; 0.27-1.01) for CFS, 1.11 (95% CI; 0.71-1.74) for GBS and 4.21 (95%CI; 3.34-5.30) for POTS. Significant relative increase in incidence rate per year with a peak in 2012 was observed in CFS (33% (95% CI; 3.0-70.3: p=0.029) and POTS (16.5% (95% CI; 7.8-25.9: p<0.05), but not seen in GBS (5.4% (95% CI; -8.4-21.3: p=0.460) (Figure).



Conclusions

Our findings provide baseline estimates of CFS, GBS and POTS incidences in Finland. However, rates based on register data should be interpreted with caution, especially for non-specific diagnostic entities for which internationally and even nationally agreed criteria are still being formed. To assess the associations with HPV vaccine, methods using vaccine register for cohort and self-controlled case series should be explored as well as factors contributing to set the diagnoses and use of codes.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0908
ESPID SYMPOSIUM 10 - VACCINES: VACCINE SAFETY - ACHIEVEMENTS, CHALLENGES/ THE BRIGHTON COLLABORATION

MEASUREMENT OF FEVER AFTER INFANT IMMUNISATIONS: COMPARISON OF INTERMITTENT AND 24 HOURS CONTINUOUS MONITORING

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Background

In clinical trials temperatures are routinely measured intermittently, potentially missing a febrile episode. The aim of this study was to compare the rates of fever identified with continuous and intermittent temperature monitoring in infants receiving their routine immunisations with or without a licensed capsular group B meningococcal (MenB) vaccine.

Methods

This was a sub-analysis of a randomised trial in which 4 month-old infants received 13-valent pneumococcal vaccine and DTaP/IPV/Hib with or without a licensed MenB vaccine. Paracetamol was not routinely administered with immunisations. Children had their post immunisation temperature measured using a wireless 24hr continuous trans-cutaneous temperature monitoring system (iButton®) applied directly to the infant's abdomen. Temperatures were also recorded per-axilla using a digital thermometer at 4, 8 and 24hrs after vaccination. Fever was defined as temperature ≥ 38ºC, while temperature <35 ºC were considered errors.

Results

Of the 185 children enrolled in the study, 11 had no iButton® records available, while 10.6 % of available time points were considered errors (<35 ºC).
Including all infants with measurements, rates of recorded fever were higher when recording was continuous (43.7%) rather than intermittent (5.2%). Regardless of measurement technique, recorded fever rates were higher for infants receiving MenB (59.1% for continuous readings, 10.3% intermittent measurement) than for those receiving routine vaccines alone (27.9% continuous, 3% intermittent). Using continuous measurement, fever was observed to develop most commonly between 4 and 8 hours following immunisation.

Conclusions

Continuous measurement of temperature may more accurately define the post –immunisation temperature profile, and can be readily used in an infant population. Intermittent measurement of fever in clinical trials may underestimate fever rates.

Clinical Trial Registration (Please input N/A if not registered)

NCT02080559

ESP16-0103
ESPID SYMPOSIUM 11- CURRENT CONTROVERSIES

COMPARISON OF CHILDREN TESTING NEGATIVE AND POSITIVE FOR EBOLA VIRUS DISEASE IN EBOLA HOLDING UNITS, SIERRA LEONE

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Background

The paediatric case definition of Ebola virus disease (EVD) is broad so many children are admitted to Ebola Holding Units(EHUs) as suspect cases who subsequently test negative. We compared features at presentation in children testing positive and negative for EVD and studiedoutcomes of those testing negative.

0 0 1 46 268 ICH 2 1 313 14.0 Normal 0 false false false EN-US JA X-NONE

Methods

All children admitted to 11 EHUs in the Western Area of Sierra Leone between 1/8/2014-31/3/2015 aged <13 years were eligible. Retrospective data were collected from paper based clinical records, cross-referenced with district-wide laboratory results, burial records, child protection records and staff interviews in the absence of documentation. Follow-up telephone calls were made to guardians post-discharge.

Results

1059 children were admitted, 309 (29%) testing positive and 750 (71%) negative for EVD, with outcomes available for 91% and 99% respectively. Children testing negative were younger (crude OR for each additional year 1.16, 95% CI 1.13-1.21) with a lower case fatality rate (12% versus 58%, p<0.001) (Table 1). Features at presentation associated with positive

status were a history of positive contact (OR 13.4, 95% CI 9.1-19.6), conjunctivitis, abdominal pain, joint and muscle pain. Difficulty breathing and skin rash were negative predictors (Table 1). Adjusted analysis of features related to EVD positive status ongoing. 160 guardians admitted to care for children testing negative were contacted post discharge. None of these caregivers nor their children were readmitted with EVD (sensitivity analysis ongoing).

Table 1: Descriptive and univariable analysis of all children who attended an Ebola holding unit (EHU)

		n (%)	EVD negative n (%)	EVD positive n (%)	Crude Odds Ratio (OR)
Total	All children	1059 (100)	750 (71)	309 (29)	-
Gender	Female	537 (51)	373 (69)	164 (31)	1
	Male	522 (49)	377 (72)	145 (28)	0.87 (0.67 - 1.14)
Age	Mean (SD)	4.85 (3.89)	4.18 (3.71)	6.49 (3.82)	1.16 (1.13 – 1.21)
	Median (IQR)	4 (1.25 – 8.0)	3 (1 – 7)	6 (3 – 10)	*OR per +1 yr*
Age (grouped)	5 - <12 years	482 (46)	291 (60)	191 (40)	1
	0 - <5 years	570 (54)	452 (79)	118 (21)	0.40 (0.30 - 0.52)
	Missing	5 (0)	5 (100)	0 (0)	-
Positive contact	No	491 (46)	445 (91)	46 (9)	1
	Yes	288 (27)	121 (42)	167 (58)	13.35 (9.10 - 19.59)
	Missing	280 (26)	184 (66)	96 (34)	-
Days symptoms to EHU admission	Mean (SD)	7.89 (56.98)	7.64 (60.72)	3.5 (2.94)	1.06 (1.02 – 1.10)
	Median (IQR)	2 (1 – 4)	2 (1 – 4)	3 (2 – 4)	*OR per +1 day*
Fever	No	49 (5)	40 (82)	9 (18)	1
	Yes	770 (73)	558 (72)	212 (28)	1.69 (0.81 - 3.54)
	Missing	240 (23)	152 (63)	88 (37)	-
Fatigue/weakness	No	22 (2)	17 (77)	5 (23)	1
	Yes	587 (55)	412 (70)	175 (30)	1.44 (0.52 - 3.98)
	Missing	450 (42)	321 (71)	129 (29)	-
Vomiting/nausea	No	318 (30)	224 (70)	94 (30)	1
	Yes	493 (47)	366 (74)	127 (26)	0.83 (0.60 - 1.13)
	Missing	248 (23)	160 (65)	88 (35)	-
Diarrhoea	No	431 (41)	315 (73)	116 (27)	1
	Yes	364 (34)	265 (73)	99 (27)	1.01 (0.74 - 1.39)
	Missing	264 (25)	170 (64)	94 (36)	-
Conjunctivitis	No	540 (51)	413 (76)	127 (24)	1
	Yes	157 (15)	78 (50)	79 (50)	3.29 (2.27 - 4.77)
	Missing	362 (34)	259 (72)	103 (28)	-
Anorexia	No	165 (16)	115 (70)	50 (30)	1
	Yes	646 (61)	477 (74)	169 (26)	0.81 (0.56 - 1.19)
	Missing	248 (23)	158 (64)	90 (36)	-
Abdominal pain	No	340 (32)	252 (74)	88 (26)	1
	Yes	280 (26)	166 (59)	114 (41)	1.97 (1.40 - 2.76)
	Missing	439 (41)	332 (76)	107 (24)	-
Muscle pain	No	384 (36)	269 (70)	115 (30)	1
	Yes	219 (21)	134 (61)	85 (39)	1.48 (1.05 - 2.10)
	Missing	456 (43)	347 (76)	109 (24)	-
Joint pain	No	392 (37)	281 (72)	111 (28)	1
	Yes	203 (19)	113 (56)	90 (44)	2.02 (1.42 - 2.87)
	Missing	464 (44)	356 (77)	108 (23)	-
Headache	No	241 (23)	154 (64)	87 (36)	1
	Yes	383 (36)	269 (70)	114 (30)	0.75 (0.53 - 1.06)
	Missing	435 (41)	327 (75)	108 (25)	-
Difficulty breathing	No	561 (53)	386 (69)	175 (31)	1
	Yes	208 (20)	178 (86)	30 (14)	0.37 (0.24 - 0.57)

Conclusions

Clinically identifying EVD in children is extremely challenging. Sensitive and specific point of care tests for EVD in children are crucial to expedite appropriate treatment and minimise EVD exposure in those uninfected. Furthermore, in a well designed high risk zone with handwashing advice, the risks of nosocomial transmission of EVD may be low.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0848
ESPID SYMPOSIUM 11- CURRENT CONTROVERSIES

TO LP OR NOT TO LP: SAFETY OF LUMBAR PUNCTURE IN COMATOSE CHILDREN WITH CLINCIAL FEATURES OF CEREBRAL MALARIA

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Background

In resource-limited settings concerns over the risk of cerebral herniation following lumbar puncture (LP) may lead to omission of the procedure, resulting in suboptimal management. This is a particular concern in patients with cerebral malaria (CM) in whom increased brain volume is strongly associated with a fatal outcome. Whether LP is independently associated with death in CM has not previously been assessed.

Methods

Retrospective cohort study in Malawian children with clinical features of CM. Allocation to LP was non-random and was associated with severity of illness. Propensity score based analyses were used to adjust for this bias and assess the independent association between LP and mortality.

Results

Data were available for 966 children: 746 (77%) underwent LP and 220 (23%) did not. Unadjusted mortality rates were lower in children who underwent LP (15% versus 26% in no-LP group) but intergroup differences in covariates implied bias in LP allocation. After propensity score adjustment all covariates were balanced and in all analyses LP was associated with either no change or a reduction in mortality rate: the average risk reduction was 4.7% at 12 hours (95% confidence interval 0.9% to 8.4%, p=0.02) and 1.3% during hospital admission (95% confidence interval -4.6% to 7.3%, p=0.56). Undergoing LP did not change the risk of mortality in sub-analyses of children with severe brain swelling on MRI or in those with papilledema.

Table 1: Baseline characteristics of the children before and after propensity score matching. Characteristics where the standardized difference is greater than 0.1 (10%) are in italics.

	Before Propensity Score Matching					After Propensity Score matching				
	No LP (N=220)		LP done (N=748)		Standardised difference	No LP (N=988)		LP done (=988)		Standardised difference
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Date of admission - month	May 2004	n/a	Apr 2005	n/a	0.04	May 2005	n/a	Dec 2005	n/a	0.02
Age - months	41.3	30.8	45.0	28.5	*0.12*	43.4	30.9	44.7	28.8	0.04
Female gender - proportion	0.49	0.50	0.54	0.50	0.09	0.49	0.50	0.55	0.50	0.09
Blantyre coma score	1.26	0.75	1.33	0.70	*0.10*	1.37	0.73	1.31	0.69	0.09
Papilledema present - proportion	0.34	0.47	0.15	0.36	*0.43*	0.18	0.38	0.21	0.41	0.07
Acidotic breathing present - proportion	0.34	0.48	0.36	0.48	0.04	0.34	0.48	0.35	0.48	0.03
Respiratory Rate - breaths / minute	47.7	13.6	46.2	12.9	*0.11*	46.7	13.6	46.3	12.9	0.04
CV exam normal - proportion	0.93	0.26	0.97	0.17	*0.19*	0.95	0.21	0.96	0.19	0.05
Pulse- within normal range for age*	1.55	0.53	1.58	0.54	*0.11*	1.57	0.51	1.57	0.54	0.01
Systolic blood pressure-within normal range for age*	1.03	0.25	1.01	0.19	0.07	1.01	0.21	1.01	0.18	0.01
Weight-for-height z score	-1.16	1.38	-1.06	1.35	0.07	-1.09	1.25	-1.07	1.36	0.02
Admission Glucose - mmol/L	6.50	3.76	6.84	3.91	0.09	6.59	3.53	6.81	3.82	0.06
Hematocrit - %	22.2	8.85	23.4	8.02	*0.16*	23.3	8.88	23.2	8.0	0.01
Retinopathy- % positive	70.8	0.46	61.1	0.49	*0.18*	62.5	0.49	63.7	0.48	0.02
Parasite count-logarithm	4.06	1.78	4.04	1.85	0.01	3.90	1.81	4.02	1.85	0.07

*0=below reference range, 1=within reference range, 2=above reference range

Conclusions

In clinically stable children with suspected CM, LP does not increase the risk of mortality, even in those with objective signs of raised intracranial pressure.

Clinical Trial Registration (Please input N/A if not registered)

Meet the Professor Abstracts

ESP16-0836
MEET THE PROFESSOR 1 - MANAGEMENT OF SEVERE VIRAL INFECTIONS IN IMMUNOCOMPROMISED PATIENTS - NEW ANTIVIRALS

NEW ANTIVIRAL THERAPY OF DRUG-RESISTENT PRIMARY CMV INFECTION IN A D+/R- KIDNEY TRANSPLANT PATIENT

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Title of Case(s)

NEW ANTIVIRAL THERAPY OF DRUG-RESISTENT PRIMARY CMV INFECTION IN A D+/R- KIDNEY TRANSPLANT PATIENT

Background

CMV infection is an important cause of clinical disease and complications after solid organ transplantation (SOT). Donor/recipient CMV serostatus and the intensity of the immunosuppressive regime are important risk factors for serious primary infection or reactivation of CMV. Therapeutic options can be limited by development of drug resistance and nephrotoxicity of some antiviral agents. Currently, new antiviral drugs with novel mechanisms of action are investigated in phase III trials, including brincidofovir (CMX001) and letermovir (AIC246).

Case Presentation Summary

A four-year-old boy with end-stage renal disease due to congenital nephrotic syndrome developed primary CMV infection after living donation of a seropositive kidney by his mother (D+/R- mismatch). CMV viremia was first detected after therapy of acute rejection with intravenous pulse methyl-prednisolone few days after transplantation. The primary disease mainly presented as CMV nephritis causing nephrotic syndrome and indirectly cytokine-mediated acute graft rejection. First-line treatment with intravenous Ganciclovir led to a UL97 kinase and later UL54 polymerase related drug resistance and CMV viral load rose again. Second-line therapy with intravenous Foscarnet had to be stopped due to nephrotoxicity. Ultimately, compassionate use of oral brincidofovir (CMX001; Chimerix, Durham, NC/USA) was commenced, very well tolerated and viral load declined again. The prodrug Brincidofovir is conjugated to a lipid and therefore releases cidofovir intracellularly without nephrotoxic adverse effects and benefit of oral administration. Accompanying reduction of immunosuppressive therapy enabled specific T-cell response and stopped CMV replication. Later transient CMV reactivation revealed wild type virus.

Learning Points/Discussion

New antivirals such as Brincidofovir with novel mechanisms of action have a great potential to significantly reduce morbidity and mortality in high-risk patients with severe disease and limited therapeutic options.

ESP16-0276
MEET THE PROFESSOR 2 - THE CHILD WITH FEVER RETURNING FROM HOT/SOUTHERN COUNTRIES /TOP TIPS FOR PAEDIATRIC TRAVEL MEDICINE

SEVERE EOSINOPHILIA IN A CHILD FROM ETHIOPIA WITH A NEGLECTED TROPICAL DISEASE

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Title of Case(s)

Severe eosinophilia in a child from Ethiopia with a neglected tropical disease

Background

Neglected tropical diseases (NTD) cause enormous human sorrow and death. One example is Schistosomiasis, caused by trematodes of the genus Schistosoma that live in freshwater snails. We present a child with dysenteric diarrhea, fever and severe eosinophilia from Ethiopia with Schistosomiasis.

Case Presentation Summary

A 5 year old boy from Ethiopia, who had been living in Spain for 3 months, was adopted and came from Addis Abeba with fever, pruritus and dysenteric diarrhea.

On initial assessment he was pallid, painful abdomen with hepatomegaly (4 cm), the rest of the examination was unremarkable.

Laboratory showed 15,700 leucocytes, neutrophils 9%, lymphocytes 30%, eosinophils 59% (total count 9250), hypochromic microcytic anemia with hemoglobin 10,4 g/dl, VCM 69,5 fL, HCM 21 pg. IgE 3870 (normal <230 U / ml). Liver function was normal.

Thorax Rx was normal. Abdominal echography showed hepatomegaly, periportal lymphadenopathies (2,5 cm), slightly splenomegaly and perivesicular collection.

Three stool tests were negative; strongyloides, salmonella, toxocara, ameba, VIH and leishmania serology were negative. *Schistosoma mansoni* IgG was positive (10:64).

He started Prazicuantel and began with fever, urticaria and bronchospasm. A thorax Rx was made because of the suspicious of a parasite migration, but it was normal and he recovered with bronchodilators and corticoids.

Learning Points/Discussion

NTDs denote a group of diseases that cause significant morbidity and mortality worldwide. According to WHO, more than 1 billion people is affected.

The diagnosis include a microscopic examination that can be negative in acute schistosomiasis like our patient, serology is useful with a sensibility up to 90%.

Although Schistosomiasis is uncommon in Europe, it should be considered as a diagnosis for any patient with fever, eosinophilia and hepatosplenomegaly coming from an endemic area.

ESP16-0124
MEET THE PROFESSOR 2 - THE CHILD WITH FEVER RETURNING FROM HOT/SOUTHERN COUNTRIES /TOP TIPS FOR PAEDIATRIC TRAVEL MEDICINE

VACCINATION STATUS IN CHILDREN WITH CULTURE PROVEN TYPHOID FEVER

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Background

Typhoid fever is endemic in Northern India including the state of Punjab.It is often overdiagnosed and unnecessary antibiotics continued for long.As a result more and more cases of typhoid/paratyphoid fever are showing multidrug resistance. This study was done to know the vaccination status in children ,diagnosed as typhoid/paratyphoid fever based on blood culture positivity.

Methods

In this study all the consecutive children admitted to the pediatrics department ,Dayanand medical college and hospital,Ludhiana,Punjab and diagnosed as cases of Typhoid fever on blood culture ,were included.A detailed history,clinical examination and relevant investigations were done in all these cases.A special emphasis was laid on knowing vaccination status against typhoid in these children.

Results

A total of 110 cases with blood culture positive for Typhoid/Paratyphoid fever were admitted during this time period.Fever was seen in all the 110 cases(100 %),followed by vomiting in 38 (37.6 %),pain abdomen in 31(30.6 %) cases.Hepatomegaly was present in 68 patients (67.3 %%),splenomegaly in 65 patients(64.3 %).Serum LDH was raised in 100 patients((98 %).Widal test was done in 87 patients out of which it was positive in 44 (65.5%).Typhoid vaccination was already done in 20 patients(19.8%).

Conclusions

Typhoid fever is endemic in children of Punjab.Besides blood culture positivity,raised serum LDH,Positive Widal test and soft splenomegaly clinch the diagnosis in most of the patients.Inclusion of typhoid vaccine in the national immunization schedule will help in decreasing the incidence of this disease

ESP16-0135
MEET THE PROFESSOR 2 - THE CHILD WITH FEVER RETURNING FROM HOT/SOUTHERN COUNTRIES /TOP TIPS FOR PAEDIATRIC TRAVEL MEDICINE

DENGUE FEVER IN A 12-YEAR-OLD POLISH GIRL. A CASE REPORT.

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Title of Case(s)

DENGUE FEVER IN A 12-YEAR-OLD POLISH GIRL. A CASE REPORT.

Background

Dengue fever is a mosquito-borne viral disease which is endemic in tropical and subtropical regions. It is an emerging infection in returning travelers. We describe the clinical and laboratory findings of imported dengue fever in a teenager.

Case Presentation Summary

A 12-year-old girl returning from a trip to Sri Lanka was admitted to the hospital with a history of fever (up to 40C) of 3-day duration with concomitant headache with retro-orbital pain, arthralgia, myalgia, nausea and abdominal pain. She had been treated by GP with cefuroxime p.o. for 3 days for tonsillitis. Her medical history was unremarkable, immunizations were up-to-date. She had not taken antimalarial chemoprophylaxis and had been exposed to mosquito bites. On admission she was dehydrated. Findings on examination included a macular rash on the trunk, petechiae on the lower limbs and a palpable liver. The laboratory tests revealed: leucopenia (3,0x10^3/mm3), thrombocytopenia (98G/l) and left shift (31% of band neutrophils). Rapid diagnostic test(Bio-Rad) for malaria was negative. The ultrasound examination showed hepatosplenomegaly. The hemodynamic parameters were stable. Normalization of the temperature was observed since the first day after admission. History of an international travel and the clinical findings suggested the diagnosis of dengue, confirmed with ELISA test- IgM(+) and IgG(+). The girl was treated symptomatically, recovered without complications.

Learning Points/Discussion

As there is no specific treatment for dengue, therapy is basically supportive and consists of early recognition of complications and appropriate fluid management. Travelers returning from endemic regions presenting with acute febrile illness should be screened for dengue.

ESP16-0232
MEET THE PROFESSOR 3 - HIV IN THE 21ST CENTURY - CURRENT ISSUES/CHALLENGES

HBV SERONCOVERSION RATE IN HIV-VERTICALLY-INFECTED PEDIATRIC PATIENTS

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Background

A complete vaccination against HBV leads to protection in 98% of healthy patients, vs 23-56% of HIV-infected patients. Among these, a booster dose produces an anamnestic response in only 33-46%. This could be more evident in vertically-HIV-infected patients, since the virus interferes longer and more with the immune system. The aim of this study was to evaluate the prevalence of protective HBsAb among vertically-HIV-infected patients and the seroconversion rate after a booster dose .

Methods

Forty-nine patients (median age 18 years, range 13,5-24,5; 53% male), vertically-HIV-infected, vaccinate against HBV virus during the first year of age and showing HBsAb levels <10 mUI/ml, received a booster dose of intramuscular HVB vaccine. HBV Ab titre, HIV RNA, CD4+ count are measured at the time of the booster dose (T0) and 4 weeks ± 7 days after the dose (T1). Tobit regression estimated the relationship between the seroconvertion rate and the CD4 count at T0 a T1, and between the seroconversion rate and the CD4 nadir.

Results

Only 26 (27%) of enrolled patients had HBsAb titer >10mIU/mL. All patients showed HIV viral load <37 cp/mL both at T0 and T1. The seroconvertion rate was 49% after 4 weeks from the booster dose and was significantly associated with the CD4 count (absolute number and percentage) at T0 (p 0.014 and p 0.050) and with the CD4 (absolute number) at the nadir (p 0.050).

Conclusions

Despite the HAART and an optimal viro-immunological profile at the moment of the booster dose, most of patients did not develop an appropriate immune response. HBV seroconversion rate is lower in vertically HIV infected pediatric patients and CD4 count is showed to be the major prognostic factor of the immune response.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0277
MEET THE PROFESSOR 3 - HIV IN THE 21ST CENTURY - CURRENT ISSUES/CHALLENGES

LATE-PRESENTING HIV-INFECTED PREGNANT WOMEN – AN INCREASING RISK FOR MOTHER-TO-CHILD TRANSMISSION?

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Title of Case(s)

HIV infection by in utero transmission

Background

Due to early antenatal screening and treatment, mother-to-child transmission of HIV is rare in Germany. In 2014, 25 cases were reported, of which 16 children were born in a foreign country. However, with rising number of refugees, antenatal care becomes more challenging due to late-presenting HIV-infected pregnant women not on treatment (after 28 weeks of gestation).

Case Presentation Summary

From 2010 to 2012, only one of all pregnant women with HIV infection, who gave birth in our hospital, started antiretroviral therapy after 28 weeks of gestation. Between 2013 and 2015, 10 children were born to women who presented with untreated HIV infection in late pregnancy (13% of all HIV-infected pregnant women) at our hospital alone. Nine of the 10 women were refugees from Sub-Saharan Africa. In one case, mother-to-child transmission occurred. This woman presented with 35 weeks of gestation after having been in Germany for two weeks. HIV infection with a viral load of 58,607 copies/ml and latent syphilis of unknown duration were diagnosed. She was treated with raltegravir, tenofovir plus emtricitabine orally and 3 doses of benzathine penicillin G intramuscularly. Complete viral load suppression was achieved by the time of delivery. The neonate was diagnosed with HIV infection by in utero transmission with a maximum viral load of 150,000 copies/ml. The newborn was treated with abacavir, lamivudine, zidovudine and nevirapine orally. Congenital syphilis infection was not proven.

Learning Points/Discussion

With rising number of refugees, we face more HIV infections diagnosed and treated in late pregnancy. The risk for mother-to-child transmission increases during the last weeks of pregnancy and with certain coinfections such as syphilis. Antenatal care as early as possible is necessary to prevent transmission.

ESP16-0600
MEET THE PROFESSOR 4 - NEONATAL INFECTIONS

ENDOGENOUS ENDOPHTHALMITIS IN A PRETERM INFANT: A RARE COMPLICATION OF ENTEROBACTER SEPSIS

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Title of Case(s)

ENDOGENOUS ENDOPHTHALMITIS IN A PRETERM INFANT: A RARE COMPLICATION OF ENTEROBACTER SEPSIS

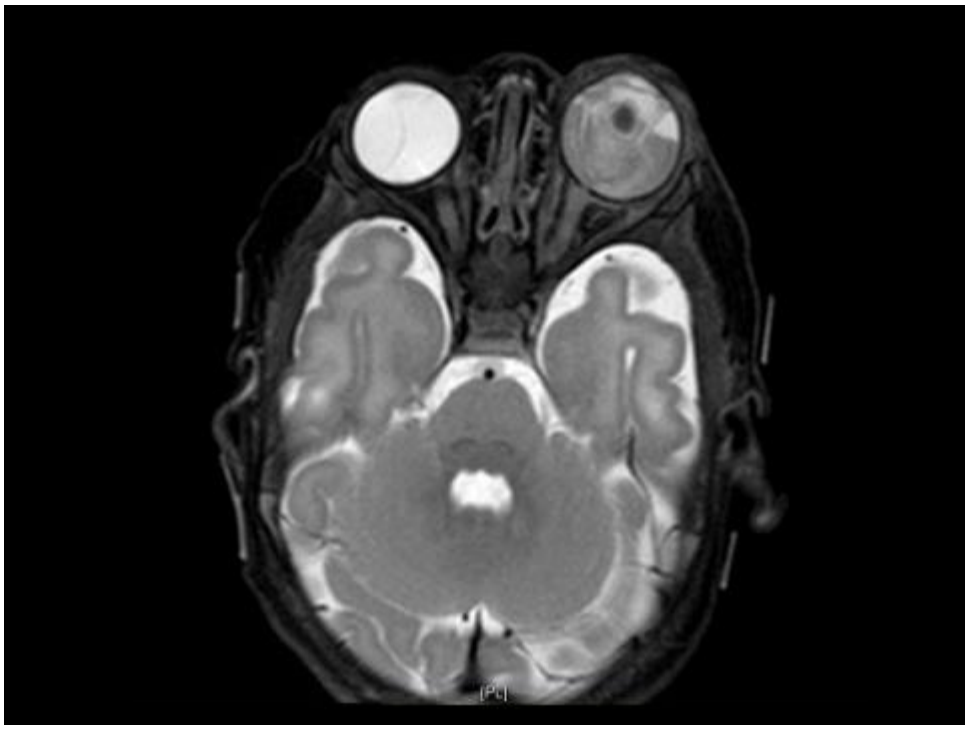
Background

Endogenous endophthalmitis is a rare but potentially blinding complication of neonatal sepsis. We report the case of a preterm infant who developed Enterobacter septicemia first and later endophthalmitis. To our knowledge, it has so far not been reported in neonates.

Case Presentation Summary

A 25-weeks preterm was investigated for late onset sepsis on day-18 of life. Her blood and urine cultures grew Enterobacter cloacae but CSF culture was negative. Meropenem was started, as per sensitivity and given for 21 days. Repeat blood and CSF cultures after 3 weeks were negative. Serial ROP examinations were performed as per protocol.

She presented to us on day-87 of life with worsening ROP from stage-I-II to stage-III in left eye in since last 2 weeks with left eyelid swelling, clouding and mucoid discharge for last 5 days. Her complete eye examination revealed left endophthalmitis with retinal detachment. We investigated for sepsis. Vitreous aspirate grew Enterobacter cloacae while CSF, blood and urine cultures were negative. Empiric antibiotics were started and later switched to Meropenem as per of sensitivity.



MRI Brain on day of life 90, confirmed left endophthalmitis, lens dislocation and retinal detachment. USG on day-93 of life showed periglobe abscess vs rupture of the posterior part of globe. On day-95 of life, Enucleation was done. Pus collected during surgery grew again Enterobacter cloacae. Artificial eye was kept on day of life 97 and she was discharged with plan to continue Meropenem for 6-weeks.

Learning Points/Discussion

Enterobacter sepsis in preterm infants warrants strict follow up with eye examinations to identify early signs of Endophthalmitis and its prompt referral to higher center will help in saving vision and reducing mortality

ESP16-1101
MEET THE PROFESSOR 4 - NEONATAL INFECTIONS

RESPIRATORY VIRUS OUTBREAKS IN A NEONATAL INTENSIVE CARE UNIT IN BRAZIL – RESULTS FROM AN ACTIVE SURVEILLENCE PROGRAM

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Title of Case(s)

Respiratory Virus Outbreaks in a Neonatal Intensive Care Unit in Brazil – results from an active surveillence program

Background

Patients admitted to the neonatal intensive care unit (NICU) are at high risk of nosocomial infection. The screening tests for bacterial infections are well stablished. However, viral infections remain a challenge in diagnosis and treatment.

Case Presentation Summary

In may 2013, a premature new born was clinically diagnosed with a viral pneumonia in the NICU. In the following days other patients started with respiratory symptoms. We tested with PCR for 14 viruses all the babies. By that time 58% of the 17 newborns were infected with RSV. Nucleotide sequencing of the isolates was done to determine relatedness. The RSV outbreak was detected and the containment programs were instituted.

With the objective to diagnose, determine the most effective interventions and describe risk factors as well as the outcomes, we established an active surveillance program, in which every time a patient presented respiratory symptoms compatible with a viral disease, a sample was collected and the whole process was initiated.

The surveillance program started on may 2013. The data was collected from may 2013 until December 2015. During this period 640 newborns were admitted to the NICU. A total of 41 babies were infected in 5 different outbreaks: 3 for RSV (novel subtypes ON-1 e NA2), 1 for parainfluenza and 1 for rhinovirus. There was 1 death related directly with the viral infection**Learning Points/Discussion**

Standard procedures were effective in controlling the outbreaks once they were identified. However the availability of diagnostic methods (nested PCR) vital in the management of the outbreaks. Non-developed coutries do not have easy access to molecular biology diagnostic methods, leading to underdiagnosis and poorer outcomes.

ESP16-0670
MEET THE PROFESSOR 4 - NEONATAL INFECTIONS

IS NECROTIZING ENTEROCOLITIS A CHRONIC DISEASE

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Background

Necrotizing enterocolitis (NEC) affects up to 7% of very low birth weight (VLBW) infants and may be complicated by intestinal failure (IF). Blood stream infections (BSI) are common among NEC patients. The microbiology and outcomes (increased risk for death) related to NEC-associated BSI, post-NEC BSI, and Non-NEC BSI in VLBW neonates were compared. Development or presence of IF was analyzed.

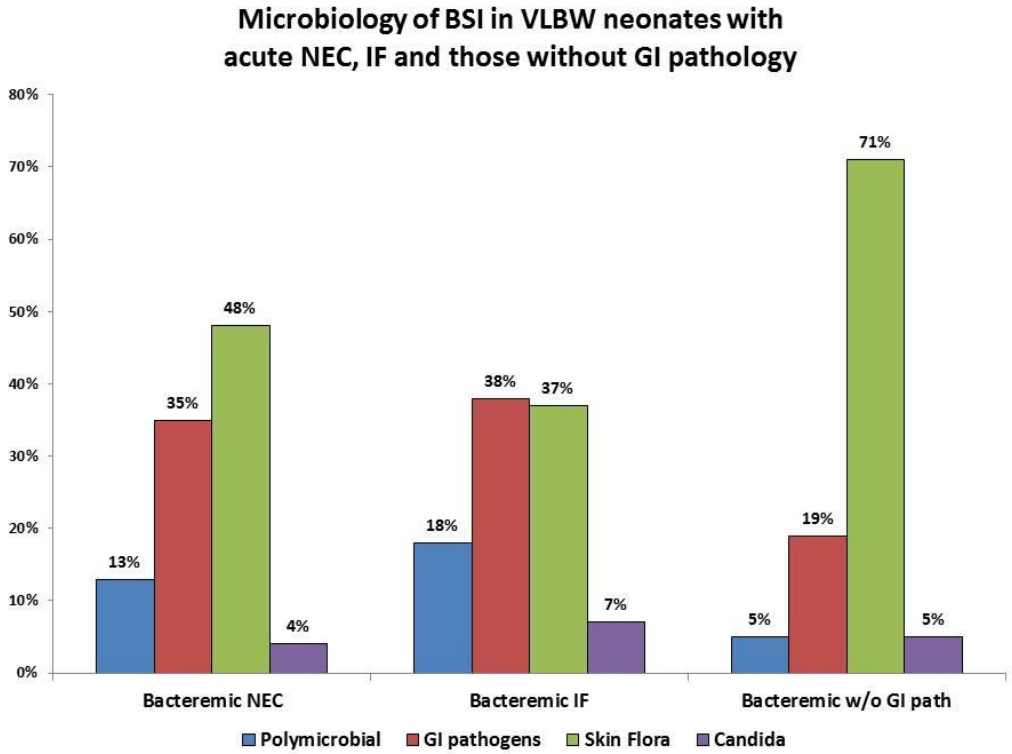
Methods

A retrospective data analysis of neonates with late-onset BSI and NEC from the NICU at CHOC Children's Hospital, in Orange, CA from June 2005 to December 2013 was conducted. The various types of pathogens present in BSI events, the timing of BSI events and NEC diagnosis, the presence or development of IF and mortality of these VLBW infants were analyzed.

Results

Of 177 neonates with BSIs,75**(**43%) had NEC of which 23 (30%) had NEC-associated BSI (6 (26%) died and 14/17 survivors (82%) developed IF); among 56 post NEC IF, 4 (7%) died. Of 102 neonates without NEC 19 (19%) died.

Microbiology of NEC (gastrointestinal (GI) flora and polymicrobial) acutely (48%) or during IF (56%) is similar, yet different than the microbiology of bacteremic neonates without GI pathology (skin flora 71%). See table.



Conclusions

NEC-associated BSI is a severe complication of prematurity resulting in 26% mortality and 82% long term complications (IF) compared to 16% BSI mortality. High frequency and common microbiology of acute NEC-associated BSI and IF-associated BSI suggests an ongoing inflammatory GI process suggesting NEC is a chronic GI pathology. NEC may be a biphasic illness where the acute phase carries a high mortality and the chronic phase a high risk of BSI with similar microbiology but without the associated mortality, both phases different from BSI in VLBW without NEC.

ESP16-1087
MEET THE PROFESSOR 4 - NEONATAL INFECTIONS

ASSESSMENT OF HEALTHCARE DELIVERY IN THE EARLY MANAGEMENT OF BACTERIAL MENINGITIS IN UK YOUNG INFANTS

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Background

Bacterial meningitis is a medical emergency and remains a significant cause of mortality and morbidity in young infants. Prompt recognition, appropriate initial management and follow up is essential.

Methods

Between September 2010 and June 2013, we undertook, a national study to assess in detail the current management in order to identify gaps and therefore propose ways to improve outcome.

Results

Of the 97 cases recruited across England and Wales, 66 (68%) were admitted from home and 31 (32%) were already in hospital prior to the onset. Fever was noted at the time of presentation in 40/66 (61%) of cases from home and 8/31 (26%) of in-patient cases.

Amongst cases admitted from home 47/62 (76%) presented to hospital within 24 hours of onset of features. The median time from onset of symptoms to first help was 4.8 hours (IQR: 2-10), triage to first dose of antibiotics was 2 hours (1.0-3.3), significantly shorter in infants who had fever or seizures at presentation 1.7hours (IQR: 1-3) compared to those who did not 4.2 hours (IQR: 1.8-6.3), p=0.02. Follow up duration was <2 years in 26/65 (40%).

For cases in hospital already, the median time from onset to first dose of antibiotics was 2.6 hours (1.3-9.8). LP was performed after antibiotics in 27/31 (87%). Follow up duration was <2 years in 5/31(16%).

Conclusions

There are some notable variations in the management of bacterial meningitis in young UK infants. Absence of fever in nearly half of the cases is very important and seems to contribute to the delay in the initiation of appropriate antibiotics. An educational programme to highlight

the existing gaps and inform clinicians on best practice is required alongside prevention strategies.

ESP16-0759
MEET THE PROFESSOR 7 - WHEN ARE INFECTIONS RECURRENT?

TUBERCULOSIS: IS THIS A DISEASE PROGRESSION OR RELAPSING INFECTION?

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Title of Case(s)

TUBERCULOSIS: IS THIS A DISEASE PROGRESSION OR RELAPSING INFECTION?

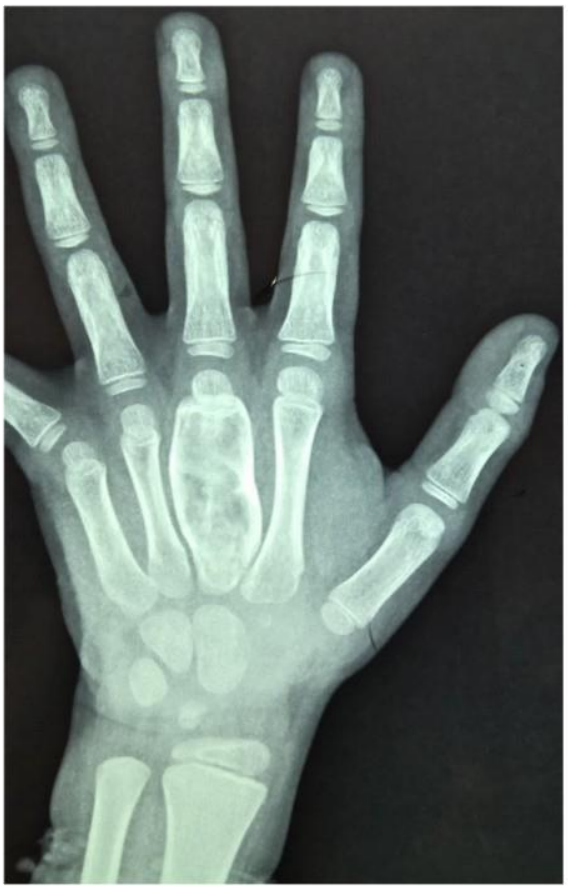
Background

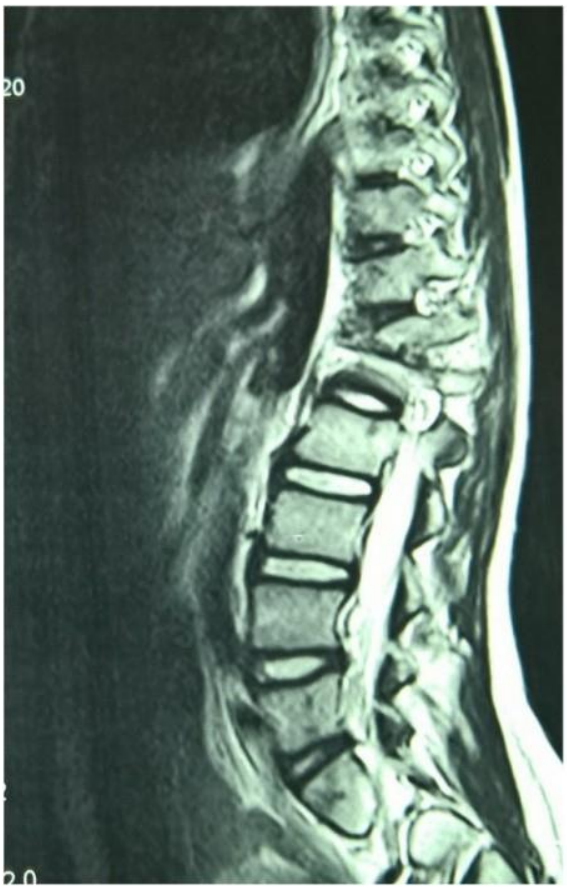
Tuberculosis is an ancient enemy. Although TB deaths have declined due to effective antibiotics and improvement of living conditions, it still remains a scourge in developing nation like ours. India accounts for 23% of world's TB incidence and 21% of world TB deaths. Diagnosis of TB remains a challenge in children. Treatment is complicated with changing regimen, dosages and emergence of drug resistance. Underlying predisposition if any often goes unrecognised.

Case Presentation Summary

9 year boy was admitted in our hospital in March, 2015, diagnosed as tubercular meningitis with dactylitis. He was started on daily anti-tubercular therapy (ATT) with steroids for initial 4 weeks. He was on regular follow up with good compliance to therapy. In November 2015, he complained intermittent back pain during a follow-up visit, when examination revealed gibbus. He was re-admitted for evaluation. Imaging revealed spondylolisthesis of D12 –L1 vertebrae with pre-vertebral collection, suggestive of tubercular pathology. The child had completed 7 months of ATT when he presented, hence considering treatment failure, he was shifted to 5-drug ATT. CT-guided aspiration of collection revealed sero-sanguineous fluid. AFB stain, culture and geneXpert of this specimen were negative. Induced sputum samples were also negative for AFB. Reduction in gibbus size and pain was present following category-II ATT; hence child was continued on same. The consensus was to err on side of over treatment than

under-treat TB.





Learning Points/Discussion

Whether decision to start relapse/recurrence regiment was correct? What further investigation could have made sure that active disease was not missed? Should we have tested for underlying predisposition like Mendelian Susceptibility to Mycobacterial Diseases (MSMD)?

ESP16-1091
MEET THE PROFESSOR 7 - WHEN ARE INFECTIONS RECURRENT?

RECURRENT BORDIE'S ABSCESS FORMATION IN SUBACUTE OSTEOMYELITIS; AN IMMUNOLOGICAL FAILURE?

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Title of Case(s)

Recurrent Brodie's abscess formation in subacute Osteomyelitis; an immunological failure?

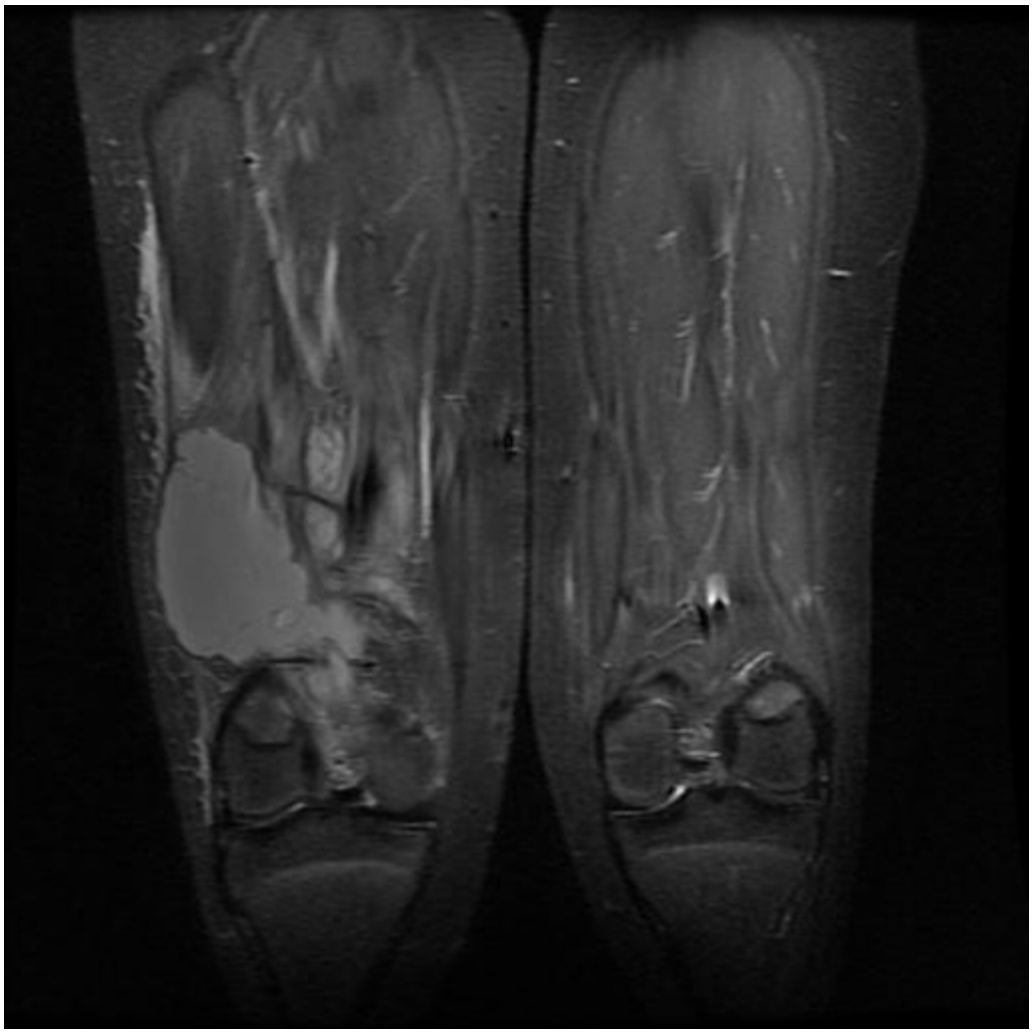
Background

Brodie's abscess is an uncommon form of subacute osteomyelitis which has atypical presenting features. We present a case of subacute osteomyelitis, with significant bone and soft tissue involvement, with a low inflammatory response and with recurrence despite surgical and antimicrobial treatment.

Case Presentation Summary

12 year old boy admitted with a painful swollen right distal thigh that developed over 3 months. An MRI suggested chronic osteomyelitis, and while awaiting aspiration his thigh rapidly increased in size and tenderness, but was afebrile and systemically well. He was taken to theatre after ultrasonography showed the abscess had increased in size, 300mls of pus was drained. Post-operatively he remained systemically well and afebrile. He was treated with intravenous Ceftriaxone. Full sensitive S. Aureus grew from the fluid drained.

6 days after the drainage, a firmness in his lateral thigh was noted. An ultrasound showed a large loculated abscess, which was drained. He was converted to intravenous Flucloxacillin and oral Rifampicin. He presented a clinical improvement, and is still under treatment.



Investigations: normal full blood counts, low inflammatory markers (highest CRP 68), unremarkable blood film. Lymphocyte subsets and immunoglobulins (including IgE) normal for age. The Nitro Blue Terazolium not pathological and further macrophage function essays are still awaited. Cultures negative for *Micobacterium* infection.**Learning Points/Discussion**

Brodie's abscess is an uncommon form of subacute osteomyelitis. This case illustrates the importance of ruling out immunodeficiency, malignancy, and atypical organisms in difficult to treat or recurrent osteomyelitis. As the patient is followed up, it will be important to monitor for further recurrence, a key feature of chronic osteomyelitis. In the long term for any bone deformities or weaknesses.

ESP16-0108
MEET THE PROFESSOR 7 - WHEN ARE INFECTIONS RECURRENT?

WE PRESENT A PATIENT WITH 4 RECURRENT BACTERIAL MENINGITIS DUE TO DIFFERENT BACILLI AS A RESULT OF A NEURENTERIC FISTULA, ESOPHAGEAL DUPLICATION AND KLIPPEL-FEIL SYNDROME.

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Title of Case(s)

RECURRENT MENINGITIS: A UNIQUE CASE REPORT

Background

We present a patient with 4 recurrent bacterial meningitis due to different gram-negative bacilli as a result of a neurenteric fistula, esophageal duplication and Klippel-Feil syndrome.

Case Presentation Summary

A 2 month old girl infant, was admitted to the PICU with sepsis. She previously had been discharged on day 21 of life for a *Proteus mirabilis* neonatal meningitis. Empiric treatment was started after a sepsis screen and in the culture of her CSF grew *Escherichia coli*. At 4 month of age, one week after discharge, she was readmitted with a bacteriemia due to *Clostridium hathewayi* anda meningitis due to *Staphylococcus epidermidis*. Immunodeficiency workup was negative.

Imaging study revealed vertebral fusion in the context of a Klippel-Feil syndrome; a cystic mass and a fistulous tract through the body of C3 connecting the cyst to a retropharyngeal mass. The UGI study confirmed the presence of a Y shaped esophagus with its left branch reaching the retropharyngeal space.

With the diagnosis of neurenteric cyst, esophageal duplication and Klippel-Feil syndrome, is dismissed with prophylactic treatment until reconstructive neurosurgery was made.

Unfurtonately, she was re-hospitalized, at 7 month, due to *Acinetobacter genospecies* meningitis.

Two weeks later, the esophageal duplication, the retropharyngeal lesion and the intradural cyst were removed and the bone defect was repaired with an excellent recovery.

Learning Points/Discussion

RBM is uncommon in children. The type of bacteria isolated can lead to suspicion of the predisposing condition particularly a neurenteric fistula when GNB are involved, or the possible underlying deficiency. This case is unique because of the anatomical defect and also

because of the etiology due to *Clostridium hathewayi*, in our best knowledge this is the first report of disease caused by this microorganism in children.

ESP16-0422
MEET THE PROFESSOR 8 - PAEDIATRIC INFECTIONS IN A HOT PLACE

SCRUB TYPHUS: A REEMERGING PEDIATRIC INFECTION FROM UNION TERRITORY OF CHANDIGARH, INDIA

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Background

Scrub typhus is a rickettsial infection caused by *Orientia tsutsugamushi.* Serology remains the mainstay of diagnosis. In India, the hilly state of Himachal Pradesh (HP) is endemic for scrub typhus. Recently, Union territory of Chandigarh, adjacent to HP, witnessed a spurt of scrub typhus and is hereby reported.

Methods

We prospectively enrolled all febrile children, 2 months to 14 years, presenting to Pediatric emergency at our hospital from January 2013- December 2014 and suspected to be suffering from scrub typhus based on clinical examination. Children who already had dengue serology and/or malaria positive from outside lab or on outpatient basis were excluded. The diagnosis was confirmed by positive IgM antibody ELISA. Demographic profile and treatment history of all the children who were positive for scrub typhus IgM antibodies was noted.

Results

Of 197 febrile children screened, 44 (22.31%) were positive for scrub typhus IgM antibodies. Median age of study population was 72 months (42,120). There was no sex predilection. Common presenting symptoms were fever (100%), vomiting (52%), rash (27%),abdominal pain (57%), oedema (25%), altered sensorium (40%), seizures (22%),cough (43%), respiratory distress (3%) oliguria (7%), itching (7%). Examination findings included eschar (7%), exanthema (9%), lymphadenopathy (7%), respiratory distress (7%), bleed (48%), hepatosplenomegaly (50%), serositis (25%). Among laboratory findings, thrombocytopenia was most common (59%) followed by anaemia (38.6%), 16% requiring blood transfusion; hyponatremia (24%), azotemia (23%), elevated transaminases (18%), hypokalemia (2%). All children received doxycycline. Nine percent received mechanical ventilation and 11% received ionotrope support. All children were discharged well except one child who succumbed to her illness. Immediate cause of death was pulmonary hemorrhage.

Conclusions

Scrub typhus responds well to doxycycline but disease manifestations are varied and overlap with other acute febrile illnesses.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0659
MEET THE PROFESSOR 8 - PAEDIATRIC INFECTIONS IN A HOT PLACE

CHALLENGING CASE OF PURULENT PERICARDITIS

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Title of Case(s)

CHALLENGING CASE OF PURULENT PERICARDITIS

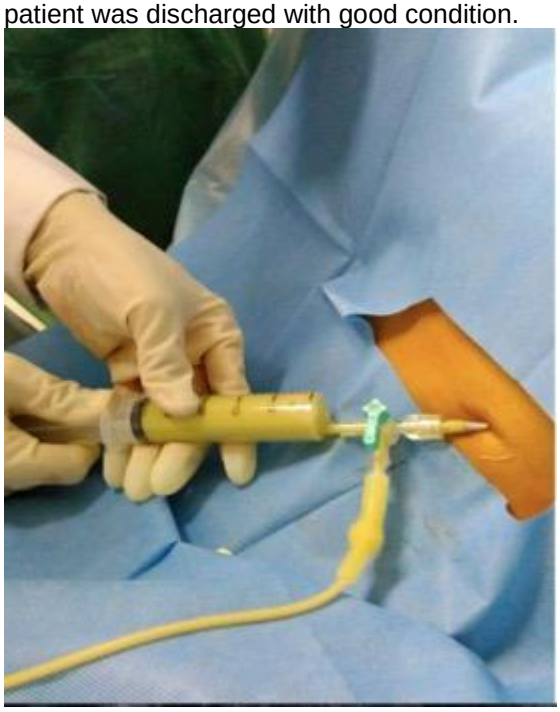
Background

Purulent pericarditis is a rare condition. It is a life-threatening disease, which is commonly produced by the extension from nearby infection or by hematogenous spread. The main etiologic agents are *Staphylococcus aureus* and *Streptococcus pneumonia* followed by fungi and anaerobic sources. Unfortunately, the etiology is not easy to investigate.

Case Presentation Summary

A 10-year-old boy admitted with dyspnea, chest pain and fever. He had a history of trauma to the left hip 2 months before. We found tachycardia, tachypnea, asymmetrical chest expansion with dullness and rales of the right chest, muffled heart sound, and pain of the left hip joint with limited ROM. Investigations revealed pericardial and pleural effusion, also hip joint effusion with soft tissue thickening. A 470 mL of purulent discharge was obtained from pericardial tap. Patient was diagnosed as purulent pericarditis, pleural effusion and tuberculosis coxitis. He was treated with ampicillin-sulbactam, prednisone, and anti-tuberculosis drugs. Tuberculin, ADA, immunology test was normal. Blood culture was sterile. Pericardial fluid analysis showed an exudate. Pleural fluid showed a transudate. Acid-fast bacilli smear, gram staining, M. *tuberculosis* PCR, aerobic, anaerobic and tuberculosis culture of sputum, pleural and synovial fluid were negative, except *Staphylococcus epidermidis* on pericardial fluid. No malignant cell in cytology of pleural nor pericardial fluid. Histopathology revealed active chronic pericarditis and tubercle on synovial tissue. After 36 days of treatment,

patient was discharged with good condition.



Learning Points/Discussion

Classic clinical findings were found in this patient. No direct cause were found but there was site of infection in the hip. Even though, we cannot prove the correlation between etiologic of hip infection and purulent pericarditis, both tuberculosis and *Staphylococcus epidermidis* was still suspected as an etiology.

ESP16-0906
MEET THE PROFESSOR 8 - PAEDIATRIC INFECTIONS IN A HOT PLACE

A CASE SERIES OF PAEDIATRIC EBOLA VIRUS DISEASE: TEENAGERS OFTEN PRESENT WITH MILDER DISEASE THAN YOUNGER CHILDREN

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Title of Case(s)

Paediatric Ebola Virus Disease

Background

Until the recent Ebola virus disease (EVD) outbreak in West Africa, case numbers of children with filovirus disease were low and understanding of paediatric disease poor. The West African outbreak has allowed greater insight into the presentation of EVD in children. A previously poorly known condition now has several thousand new cases for reference, highlighting a range of presentations at different ages with dramatically different outcomes, and mortality rates of almost 90% at under 1 year and approximately 50% at 10-15 years.

Case Presentation Summary

In the summer of 2014 three male teenagers, two aged 12 and one aged 14, were managed at the ELWA treatment centre in Liberia. Two did not present with fever at triage and both had a mild course of disease, all survived. Comparatively in Sierra Leone the disease affected larger numbers of children. We present three children aged under four years, two of whom succumbed to the disease within 48 hours of admission to a treatment facility, and a nine-month-old infant who survived the disease. We describe the differences in presentation and the challenges of managing these different groups of children, as well as the implications for treatment strategies in future epidemics.

Learning Points/Discussion

Older children aged 10-15 years present with the lowest mortality of all age groups from the West African Ebola epidemic, this is in contrast to children under 2 years of age where mortality rates exceeded 80%. Teenagers often presented with milder forms of disease and some did not present with fever at triage, this is important in light of original triage guidelines emphasising fever in the case definition criteria. Younger children may succumb to disease rapidly and require prompt, careful fluid management.

ESP16-0791
MEET THE PROFESSOR 9 - RECOGNITION OF SERIOUSLY ILL CHILDREN

A RARE CASE OF SPONTANEOUS RETZIUS SPACE ABSCESS IN A PREVIOUSLY WELL TEENAGER

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Title of Case(s)

A case of retzius space abscess

Background

Retzius space abscesses are rare and are often complicated by diagnostic delay and significant morbidity.

Case Presentation Summary

A 15yr old Polish girl was admitted by the surgical team with a few days history of fever and abdominal pain. She was diagnosed as probable appendicitis. Bloods showed WCC13.7, N 10.2 and CRP181. Urine analysis was negative. She underwent laparoscopy and her appendix was noted to be normal and therefore not resected. Exploration was negative except for minimal free fluid.

She was commenced on Tazocin and 3 days into her admission she remained pyrexic, with rigors. WCC 13.4 N10.7 and CRP 284. Urine culture was negative.

Care was handed over to the paediatric team on day 4 of admission. Further investigations included Chest X-ray, abdominal USS, inflammatory markers, autoimmune screen and consideration for echocardiogram and abdominal MRI after the weekend.

Her clinical condition remained unchanged with chaotic temperatures and rigors despite addition of gentamicin to her treatment.

Abdominal USS revealed splenomegaly and no other abnormalities with a caveat that bladder was not sufficiently filled and pelvic contents were difficult to visualise.

She had an MRI of the abdomen on Day 6/7. This showed an irregular cystic lesion anterior to the bladder in the midline lower abdomen, with extrinsic pressure on the bladder. This radiological impression was a prevesical (**Retzius space**) abscess. The other possibility was urachal abscess with inferior tracking.

Surgical drainage was performed followed by gradual but complete resolution of abdominal symptoms and defervescence over a 2 day period.

Pus swabs revealed mixed anaerobes.`

Learning Points/Discussion

The space of Retzius, which is extra-peritoneal, is rarely a site of spontaneous infection. Infections are typically occult and insidious, often with diagnostic delay and significant morbidity.

ESP16-0810
MEET THE PROFESSOR 9 - RECOGNITION OF SERIOUSLY ILL CHILDREN

SERIOUS, INVASIVE INFECTIONS DUE TO METHICILLIN-SUSCEPTIBLE PANTON-VALENTINE LEUCOCIDIN POSITIVE S. AUREUS IN PREVIOUSLY HEALTHY CHILDREN

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Title of Case(s)

Serious, invasive infections due to methicillin-susceptible Panton-Valentine Leucocidin positive *S. aureus* in previously healthy children

Background

Panton-Valentine Leucocidin (PVL) producing *Staphylococcus aureus* is well recognized as a cause of severe skin and soft tissue infections, but can also cause invasive infections including necrotising haemorrhagic pneumonia, osteomyelitis, septic arthritis and abscesses. We present the cases of 2 previously healthy children both caused by methicillin-susceptible PVL-positive *S. aureus* (PVL+ MSSA).

Case Presentation Summary

Case 1: A 12 year-old boy presented with fever, general malaise, back pain and neck stiffness. He had a single skin lesion on his left leg during the last week. He was diagnosed with spondylitis of the 8th thoracic vertebra (T8). The patient developed enhanced inflammatory response, with respiratory distress and hepato-splenomegaly. **Case 2:** A 7-year old male presented with fever and impaired motility of the right hip after injury. He was diagnosed with septic right hip arthritis, multifocal femoral osteomyelitis, adjacent pyomyositis and deep femoral vein thrombosis. During hospitalization he developed thrombosis in the lobar branches of the right pulmonary artery and bilateral pneumonia. PVL+ MSSA was detected in both children from cultures of blood as well as hip joint articular fluid (second patient). Both children received cloxacillin intravenously for 2 weeks, followed by oral antibiotic treatment per os for another 4 weeks. The second patient also received anticoagulant therapy and required at least 4 operations of the infected hip and femur-infected area. Full recovery of the first patient was late, whereas the second patient required long orthopedic follow-up with

necrosis of the bone.

Case 1	Day 1	Day 2	Day 13	Case 2	Day 1	Day 14	Day 30
WBC	13600	9200	8300	**WBC**	21100	11200	8100
Neu	88%	86%	62%	**Neu**	78%	68%	52%
CRP	293	146	27	**CRP**	287	202	66
ESR	65		105	**ESR**	94	131	137

Table 01: Laboratory findings of the 2 cases

Learning Points/Discussion

PVL+ *S. aureus* is very pathogenic and can lead to life-threatening invasive disease, even in immunocompetent children and needs high level of suspicion.

ESP16-0224
MEET THE PROFESSOR 9 - RECOGNITION OF SERIOUSLY ILL CHILDREN

FREE LIGHT CHAINS (FLC) INDICES FOR THE EARLY DIAGNOSIS OF VARICELLA ZOOSTER ENCEPHALITIS: A CASE REPORT

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Title of Case(s)

Free Light Chains (FLC) indices for the early diagnosis of Varicella Zooster Encephalitis: a case report

Background

Cerebrospinal Fluid (CSF) Kappa and Lambda Indices were recently proposed as Central Nervous System (CNS) immune activation markers but their use is still limited in the clinical practice.

Case Presentation Summary

A 3 years old boy was admitted to our Emergency Department with hyporeactivity, ataxic gait, drowsiness, slowed speech and severe headache. He had a history of chickenpox 8 days before with rash on head, scalp and trunk and fever for 48 hours. CSF analysis was negative for albumin quotient, quantitative IgG synthesis, isoelectricfocusing (IEF), enteroviruses, HSV, EBV, VZV and CMV PCR. Very high CSF intrathecal IgM fraction (48%) was detected and highly positive CSF VZV specific Antibody Indices IgM (8,74 n.v.<1,5) and IgG (2,41 n.v.<1,5). CSF FLC Kappa and Lambda Indices were highly positive: 34,12 (nv<6,39) and 17,78 (nv<5,51) respectively. The MRI showed pulvinar and lenticular nucleus involvement. The patient was treated with intravenous acyclovir. After an initial progressive decrease of motor control of trunk and cranial nerves, then he showed clinical improvement.

Learning Points/Discussion

This is a case of VZV encephalitis, confirmed only by specific CSF serology and CSF FLC. CSF PCR is usually positive only in first days of VZV encephalitis, later on, specific antibodies are synthesized. IgG IEF is considered the best screening test to detect immune activation CNS; in our case, it was negative since there was mainly an IgM response.
Our case demonstrated that CSF FLC can be used as CNS immune activation screening test, since it is positive also in case of specific or predominantly CNS IgM intrathecal synthesis.

ESP16-1110
MEET THE PROFESSOR 11 - CHALLENGING MENINGITIS CASES

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[1], *Germany*

sgaahysgd fhdh

ESP16-0469
MEET THE PROFESSOR 11 - CHALLENGING MENINGITIS CASES

A CLASSICAL AND A NON CLASSICAL PRESENTATION OF ASEPTIC MENINGITIS DUE TO VARICELLA-ZOSTER VIRUS REACTIVATION IN CHILDREN

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Title of Case(s)

A classical and a non classical presentation of aseptic meningitis due to varicella-zoster virus reactivation in children

Background

Varicella-Zoster virus (VZV) remains latent in the cranial and dorsal root ganglia and there are increased reports of reactivation of VZV as aseptic meningitis in immune-competent individuals, usually with zoster exanthema.

Case Presentation Summary

We report two cases of aseptic meningitis in immune-competent children, one with the classic zoster manifestation and the other without cutaneous lesions. In both cases meningitis was confirmed by detection of VZV-DNA in cerebrospinal fluid using polymerase chain reaction (PCR). Both patients were treated with intravenous acyclovir with complete recovery.

Learning Points/Discussion

Our cases illustrate that VZV should be considered as an agent of aseptic meningitis in children even without classical skin manifestations. Several cases of reactivation of VZV as aseptic meningitis in immune-competent patients without skin manifestations have been reported in the literature.The accessibility of PCR analysis increases the detection rate of VZV as an agent of viral meningitis and it may contribute to the theory that the dorment virus in the spinal ganglia has the ability to travel directly to the central nervous system without producing skin involvement.

ESP16-0542
MEET THE PROFESSOR 11 - CHALLENGING MENINGITIS CASES

HHV 7 MENINGITIS AND ATYPICAL KAWASAKI DISEASE

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Title of Case(s)

HHV 7 meningitis and atypical Kawasaki disease

Background

As below

Case Presentation Summary

A 19 month old boy presented with fever for 3 days, coryza, cough, vomiting and lethargy. He had a nonspecific rash with one petechial spot on the abdomen. He was tachycardic and had a partial septic screen that revealed a raised CRP of 55.3. He was admitted and commenced on Ceftriaxone. The next day he became irritable and more lethargic so underwent a LP that showed 65 WBC with lymphocyte predominance but no organisms. Acyclovir was added.

Over the next two days he deteriorated with a fluctuating and reducing GCS, widespread vasculitic rash, marked oedema, hyponatraemia , hypotension and thrombocytopenia. Fever persisted. He was transferred to HDU, fluid restricted and switched to Meropenem. Clarithromycin was added to the acyclovir to cover meningitis/encephalitis pathogens. CT head was normal. LP and blood cultures showed no bacterial growth and HSV PCR was negative. Differential diagnoses included meningitis complicated with SIADH, encephalitis and vasculitis/Kawasaki's.

Echocardiogram showed mild mitral regurgitation and a small pericardial effusion but normal coronaries. His abdominal ultrasound showed gallbladder hydrops and further viral panels from the initial blood and CSF samples revealed HHV7.

On day 6 he had immunoglobulin and started high dose aspirin and improved clinically. On day 8 his fever returned with bilateral conjunctivitis and peeling of his hands. He was transferred to a tertiary centre for a bone marrow aspirate and MRI/A prior to starting steroids.

He required a second dose of immunoglobulin, 3/7 IV methylprednisolone and aspirin. He made a full recovery and repeat echo was entirely normal.

Learning Points/Discussion

1. Nonspecific onset and rapid clinical deterioration withHHV7 meningitis/encephalitis

2. Diagnostic difficulties as atypical features ofKawasaki with concomitant viral infection

ESP16-1071
MEET THE PROFESSOR 11 - CHALLENGING MENINGITIS CASES

CRYPTOCOCCAL MENINGITIS IN A BOY WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Title of Case(s)

Cryptococcal Meningitis In a Boy With Systemic Lupus Erythematosus

Background

Cryptococcal meningitis (CM) is a rare and potentially fatal infection in immunocompromised patients with systemic lupus erythematosus (SLE). It represents a serious diagnostic challenge for even the most experienced clinicians, due to its non-specific manifestations, frequently misdiagnosed as SLE relapse.

Case Presentation Summary

We report on a 15-year-old boy with diagnosed SLE at age of 12-years, who developed SLE nephritis during the second year of disease. Immediately, an aggressive immunosuppressive treatment, according to Euro-lupus nephritis protocol, has been started. The patient was in the remission of underlining disease when he began complaining of severe headache and double vision. Physical examination was unremarkable. He had no papilloedema nor meningeal irritation. Cerebrospinal fluid (CSF) showed hypoglycorrhachia, mild proteinorachia and pleocytosis. Magnetic resonance demonstrated multiple cortical and subcortical lesions of basal ganglia and corpus callosum with ventriculomegaly. CSF culture yielded Cryptococcus neoformans. The specific antifungal therapy with liposomal amphotericin and voriconazole was started with subsequent oral fluconazole treatment. Unfortunately, the patient had one more episode of CM. The same therapy was repeated after which the oral fluconazole has been continued as prophylaxis. The patient had no more relapses of infection nor SLE during the next two years of follow-up.

Learning Points/Discussion

Normal neurological and even CSF examination do not exclude the possibility of cryptococcal infection in the immunocompromised patient. Timely diagnosis, followed by early and effective antifungal therapy, substantially improves the prognosis of cryptococcal meningitis in SLE patients.

ESP16-0976
MEET THE PROFESSOR 13- REFUGEE MEDICINE

LOUSE-BORNE RELAPSING FEVER - AN (RE) EMERGING INFECTIOUS DISEASE IN BAVARIA, GERMANY

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Title of Case(s)

Louse-borne relapsing fever – an (re)emerging infectious disease in Bavaria, Germany

Background

Relapsing fevers, transmitted by arthropods, are rarely encountered in Germany, thus they are often not considered as differential diagnosis in febrile children and adolescents. Causative agents are spirochetes of the genus *Borrelia*, capable of reaching high densities in patient's blood. Depending on the vector and the region, different species are prevalent worldwide. These spirochetes have been responsible for epidemic outbreaks, in former times also in Europe, especially in times of war, famine and other crises of societies.

Case Presentation Summary

We describe exemplary clinical courses of three Somalian adolescents treated for LBRF. Diagnostic work-up confirming *Borrelia recurrentis* as causative agent included Giemsa stain of blood films, dark field- and fluorescence microscopy from EDTA samples and sequencing of 16S rDNA, glpQ, p41 and uvrA. All individuals developed a Jarisch-Herxheimer reaction upon treatment initiation, one patient required intensive care support. Between July and December 2015, >30 cases of LBRF have been reported among asylum seekers in Bavaria. Some patients had to be admitted to ICU, one patient died despite therapy. Young male refugees originating from the Horn of Africa using the North-African route to Europe seem to be at increased risk for acquiring LBRF. Transmission is also expected to occur in Libya and Italy.

Learning Points/Discussion

Healthcare workers and laboratory personnel should be aware of LBRF as an important differential diagnosis of febrile illness in travelers and asylum seekers and their children First-line antibiotics include tetracycline and penicillin, acquired resistance has not yet been reported. Frequently, patients develop a Jarisch-Herxheimer reaction shortly after initiation of therapy, requiring hospitalization or intensive care treatment. Managing patients in an exclusively outpatient setting, such as GP practices, is not recommended.

ESP16-0990
MEET THE PROFESSOR 14 - DIAGNOSIS OF FUNGAL INFECTIONS IN CHILDREN

INVASIVE GASTROINTESTINAL MUCORMYCOSIS: AN UNRECOGNIZED KILLER IN A CRITICALLY ILL CHILD – A CASE REPORT

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Title of Case(s)

Invasive Gastrointestinal Mucormycosis: an unrecognized killer in a critically ill child – a case report

Background

Invasive gastrointestinal Mucormycosisis a fatal condition in critically ill children. The initial presentation would be nonspecific and is seen even in immunocompetent host.

Case Presentation Summary

A 2-year old boy presented with fever and rash of 7 days and seizures with altered sensorium for one day. He was previously well, developmentally normal and fully immunized. He had respiratory failure, oliguria and hypotensive shock, requiring ventilation, fluids and vasoactive infusion. He had petechial rash and hepatomegaly. Possibility of bacterial sepsis, scrub typhus or primary viral infection was considered. Investigations revealed Hb-7.4gm/dl, TLC-33,500/mm^3 with 75% polymorphs, platelet count-17000/ mm^3, BUN– 42 mg/dl, serum creatinine-0.6 mg/dl, AST-472 IU/L, ALT -146 IU/L, CRP -111mg/L, metabolic acidosis and normoglycemia. Serum IgM ELISA for scrub, widal, blood culture, dengue serology, and malaria smear were negative. Ascitic fluid grew Escherichia coli. He underwent peritoneal dialysis for acute Kidney injury.

During second week, he developed significant ascites and bilious aspirates. With new onset fever, increasing CRP, and worsening thrombocytopenia, possibility of healthcare associated infection was considered. Antimicrobials were changed and amphotericin-B was added. Blood and urine for fungus and serum galactomannan were negative. CT abdomen showed large, left perinephric collection communicating with small bowel (Figure 1). Exploratory laparotomy revealed gross fecal contamination, multiple perforations in small bowel, and a gangrenous descending colon. He succumbed to multi organ dysfunction syndrome. Biopsy report of colon revealed transmural gangrene with multiple aseptate broad fungal hyphae suggestive of invasive Mucormycosis.

Learning Points/Discussion

Invasive gastro-intestinal mucormycosis is indolently progressive and fatal. A high clinical suspicion and prompt surgical intervention are mandatory.Clinical diagnosis of such invasive mucormycoses in children can be a veritable challenge.

ESP16-0982
MEET THE PROFESSOR 16- ADMISSION AND DISCHARGE DECISION MAKING IN ACUTE RESPIRATORY INFECTIONS

MEDICO-ECONOMIC IMPACT OF THE SOFIA® INFLUENZA A+B FIA - RAPID DIAGNOSTIC TEST IN A PEDIATRIC EMERGENCY DEPARTMENT

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Background

The aim of rapid diagnostic tests (RDTs) for influenza is to detect the flu earlier in order to reduce its transmission and avoid some additional examinations and unnecessary hospitalizations. The objective of this study was to evaluate the medico-economic impact of the Sofia® Influenza A+B FIA RDT in a pediatric emergency department (PED).

Methods

We did a retrospective, observational, cross sectional study in the PED of our University hospital during the 2013-2014 and 2014-2015 seasons of influenza epidemics. Patients aged one month to 18 years for whom influenza RDT was performed were included. Clinical data, therapeutical management and related hospitalizations were compared between positive and negative RDT groups. A comparison of the length of stay in PED and of the number of additional tests between the two groups was made. A budgetary evaluation of potentially avoided costs was realized.

Results

238 tests were listed during the two seasons: 119 tests were positive, 110 negative and 9 invalids. The mean length of stay in PED was significantly lower in positive RDT group: 4.0h vs. 7.4h, $p<10^{-6}$. A significant reduction of biological tests (20% vs. 56%, $p<10^{-7}$) and radiographs (23% vs. 52%, $p<10^{-5}$) was highlighted in patients with positive RDT. The number of hospitalizations in short-stay unit was also significantly lower in patients with positive RDT (0.8% vs. 9.1%, p=0.009). No significant difference was shown concerning the number and the duration of hospitalizations in conventional unit. It was estimated that the use of the Sofia® Influenza A+B FIA RDT would have enabled a saving of about 6,190€ overall.

Conclusions

This study showed a significant medical and budgetary impact of the use of Sofia Influenza RDT A+B FIA® in the PED of our University hospital.

Clinical Trial Registration (Please input N/A if not registered)

N/A

Oral Abstracts

ESP16-0967
ORAL PRESENTATION SESSION 1 - DIAGNOSTICS

APPLYING A PCR SCREEN FOR COMMON PATHOGENS IN CHILDREN WITH SUSPECTED SEVERE BACTERIAL INFECTIONS

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Background

Attributing an infectious aetiology to children presenting with severe febrile illness is diagnostically challenging. We examined the range of organisms identified and the diagnostic yield in a cohort where both blood culture and targeted PCR were applied as diagnostic tools.

Methods

Study subjects were recruited by the EUCLIDS consortium between January 2012 and November 2015 following febrile presentation with suspected sepsis or focal infection. EDTA blood samples from 1,036 children across 5 nodes (Austria, Gambia, Netherlands, Spain, UK) were assessed using a standard protocol. Samples were pre-treated with lysozyme/lysostaphin and silica bead disruption before total nucleic acid extraction using an MDx Biorobot (Qiagen). Nested PCR was then applied to detect ten bacterial targets (*Acinetobacter baumanii*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Neisseria meningitidis*, *Streptococcus pneumonia*e, *Haemophilus influenza*e, *Streptococcus pyogenes*, *Streptococcus agalactiae*).

Results

In 1,036 patients whose samples were tested using both techniques, 212 bacterial pathogens were identified by PCR and 238 by blood culture (including 52 identifications of an organism not in the PCR panel). 632 (61%) patients were both blood culture and PCR negative whilst concordance between blood culture and PCR positive results occurred in 31% of cases. *Neisseria meningitidis* and *Haemophilus influenzae* were more commonly identified by PCR whilst *Streptococcus pyogenes* and *Staphylococcus aureus* were more commonly identified by blood culture. Twelve bacterial genera that were not included in the PCR panel were identified in blood cultures.

Conclusions

Applying a standard PCR screen to our patient cohort increased the overall diagnostic yield. However, test sensitivity is still a concern as 61% of patients tested concordantly negative. In this difficult to diagnose group, new testing paradigms appear to be needed to improve rates of diagnosis.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0424
ORAL PRESENTATION SESSION 1 - DIAGNOSTICS

ROTAVIRUS VACCINE FAILURE OR DIAGNOSTIC ERROR?

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Background

Rotavirus vaccine is highly used in many areas of Europe. Rotavirus (RV) diagnosis in stools is mainly done by immunochromatography (ICG), with reported high sensitivity and specificity. Positive predictive value (PPV) is related to prevalence of disease. The objective of the study was to estimate number of false positive RV tests in vaccinated children in Valencia.

Methods

We used the RedMIVA database of the Valencian Region of Spain (contains all microbiology results from all the 24 public hospitals of Valencia). All RV tests 2008-2012 in <37 months of age were analysed. We estimated a sensitivity and specificity of 99% and 96% for ICG. Rotavirus season was defined: December to May. In absence of a PCR as gold standard we used a Bayesian estimation of the parameters of the diagnostic test.

Results

42,839 RV tests were performed. Of those 9430 (22%) in vaccinated children: 3963 (42%) during the rotavirus season and 468 in hospitalized vaccinated children. The percentage of positive was related to the prevalence of the disease, i.e. the vaccination status, hospitalization or not and the rotavirus season, ranging from 2.9 to 60.1%. PPV was low in vaccinated, especially if not hospitalized and out of the rotavirus season (29.7%). In vaccinated children, 49.2% of the positive results (256 out of 520 tests) were considered false positive; in unvaccinated the false positive results were 17% (965 out of 5676).

Conclusions

ICG tests yield a high percentage of false positives in vaccinated children. Misdiagnosis may decrease the confidence in the vaccine and may decrease the estimation of the vaccine effectiveness.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0507
ORAL PRESENTATION SESSION 1 - DIAGNOSTICS

DYNAMICS OF QMPCR IN INVASIVE PNEUMOCOCCAL DISEASE AMONG INDIAN CHILDREN

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Background

In-time diagnosis of *Streptococcus pneumoniae* can play a significant role in decreasing morbidity and mortality of infection. However, establishing *Streptococcus pneumoniae* as an etiology of invasive pneumococcal infection is still challenging due to the limitations of the culture methods. Molecular methods have gained popularity as they offer a rapid and more sensitive strategy with high selectivity compared to the traditional diagnostic tests. This study was designed to evaluate the enrolled cases for the prevalence of pneumococcal infection by quantitative multiplex real time PCR (qmPCR) assay in comparison with culture method

Methods

Fifteen hundred and four (n=1504) children ≤5 years clinically diagnosed with IPD having abnormal Chest-X-ray, raised CBC, positive CRP and PCT test results were included into the study. qmPCR targeting *ply, lytA, psaA* & *spn9802* genes were standardized and validated against 99 culture positive and 50 culture negative samples. Blood culture and corresponding serum qmPCR were performed in all patients

Results

Culture were positive for *S. pneumoniae* in 108 (7.2%) of the 1504 cases. Serum qmPCR identified the pneumococcal infection in 456 (30%) of cases. The mean value of PCT in qmPCR positive and negative samples was 15.5ng/ml and 7.2ng/ml respectively. The sensitivity and specificity of the assay was 100% with lower limit of detection of 4 genome copies/µl.

Conclusions

Infections due to *S. pneumoniae* in IPD are underestimated due to lack of sensitivity of conventional culture methods. Use of qmPCR in serum specimens has emerged as a valuable clinical diagnostic tool. This methodology offers an opportunity to readdress the problem of the diagnosis of *S. pneumoniae* infections. Widespread use of this technique will contribute to the success of treatment and provide true estimate of disease burden

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0614
ORAL PRESENTATION SESSION 1 - DIAGNOSTICS

LIVER STEATOSIS IN CHILDREN WITH CHRONIC HEPATITIS C

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Background

There are only scarce data on liver steatosis in children with chronic hepatitis C (CHC) available. The aim of this study was to evaluate the prevalence, predictors and impact of hepatic steatosis children with CHC.

Methods

Liver biopsy results in 48 patients aged 10.7±3.7 years (86% with genotype 1 HCV) were analyzed. Steatosis was scored on a five-point scale, as follows: absent; minimal (≤ 5% hepatocytes affected); mild (6-33%); moderate (34-66%); and severe (> 66%). Stepwise logistic regression was used to determine the factors associated with steatosis and moderate-to-severe steatosis.

Results

Steatosis was observed in 13/48 (27%) patients, including 5/48 (10%) with moderate-to-severe grade. A trend toward an association between steatosis and BMI *z*-score was observed (p=0.08). Liver steatosis occurred more frequently in patients with HCV genotype 3 compared with other genotypes (p=0.013). In patients with non-3 genotype HCV, steatosis was associated with the duration of infection (OR=0.74, 95%CI: 0.55-0.97) and stage of fibrosis (OR=3.35, 95%CI: 1.01-11.07). Moderate-to-severe steatosis was positively associated with the BMI *z*-score (OR=3.62, 95%CI: 1.22-10.75) and stage of fibrosis (OR=3.89, 95%CI: 1.05-14.47). There was also a trend toward a higher grade of necroinflammatory activity in this group (p=0.06). In patients infected with non-3 genotype HCV, a trend toward higher BMI *z*-score amongst patients with moderate-to-severe steatosis was observed (p=0.06).

Conclusions

Steatosis is a common finding in children with chronic viral hepatitis. It seems to be associated mainly with viral determinants. However, metabolic and viral factors may have a combined effect, leading to more advanced grades of steatosis in children with higher BMI *z*-scores. Moderate-to-severe steatosis is associated with more advanced fibrosis.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1005
ORAL PRESENTATION SESSION 1 - DIAGNOSTICS

DIAGNOSIS OF CHILDHOOD TUBERCULOSIS USING A MINIMAL HOST RNA EXPRESSION SIGNATURE

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Background

Childhood TB remains a major cause of death globally, while traditional diagnostic methods are unreliable in children. HIV co-infection promotes progression to active TB, hinders diagnosis and increases mortality. In this study we sought to identify host transcriptional biomarkers in African children to discriminate TB from other phenotypes using host gene expression profiling.

Methods

Paediatric cohorts were established in Malawi, South Africa and Kenya (177, 157, and 150 individuals respectively). Gene expression arrays were used to examine whole blood RNA from children with culture-confirmed tuberculosis, culture-negative tuberculosis, diseases other than tuberculosis, or latent tuberculosis infection. A novel computational variable selection method was employed to identify the smallest set of "best discriminator" genes in the discovery group, which were then tested in the validation group.

Results

A minimal diagnostic gene signature distinguishing tuberculosis from latent TB infection and from other diseases was identified in the discovery cohort (South Africa and Malawi) and validated in the validation cohort (Kenya). A disease risk score for every patient based on this handful of genes distinguished TB from latent TB (ROC-AUC 91%) and from other diseases (ROC-AUC: 86%) in the validation group. The classification in culture negative TB groups reflected the clinical certainty for diagnosis.

Conclusions

A minimal gene set was able to discriminate between different phenotypes and could be used for diagnosis of paediatric TB, regardless of HIV status and location of the population. The

gene signature holds great potential for development as a diagnostic test exploiting recent significant advances in the field of bio-technology and bio-engineering that allow for the development of point-of-need diagnostics.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0443
ORAL PRESENTATION SESSION 1 - DIAGNOSTICS

DIAGNOSTIC PERFORMANCE OF INFLUENZA VIRUSES AND RSV RAPID ANTIGEN DETECTION TESTS (RADT) IN CHILDREN IN TERTIARY CARE

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Background

Rapid antigen detection tests (RADTs) are increasingly used to detect influenza viruses and respiratory syncytial virus (RSV) in children. However, their sensitivity and specificity are a matter of debate, which challenges their usefulness in clinical settings.
We compared diagnostic performances of BinaxNOW Influenza AB® (BNI) and BinaxNOW RSV® (BNR), to those of real-time reverse transcriptase PCR (RT-PCR), virus isolation and direct immunofluorescence (D-IF) in paediatric patients.

Methods

Between November 2005 and September 2013 521 nasal washings from symptomatic children (age <5 years) attending our tertiary care centre were tested, with a combination of the respective assays using RT-PCR as gold standard.

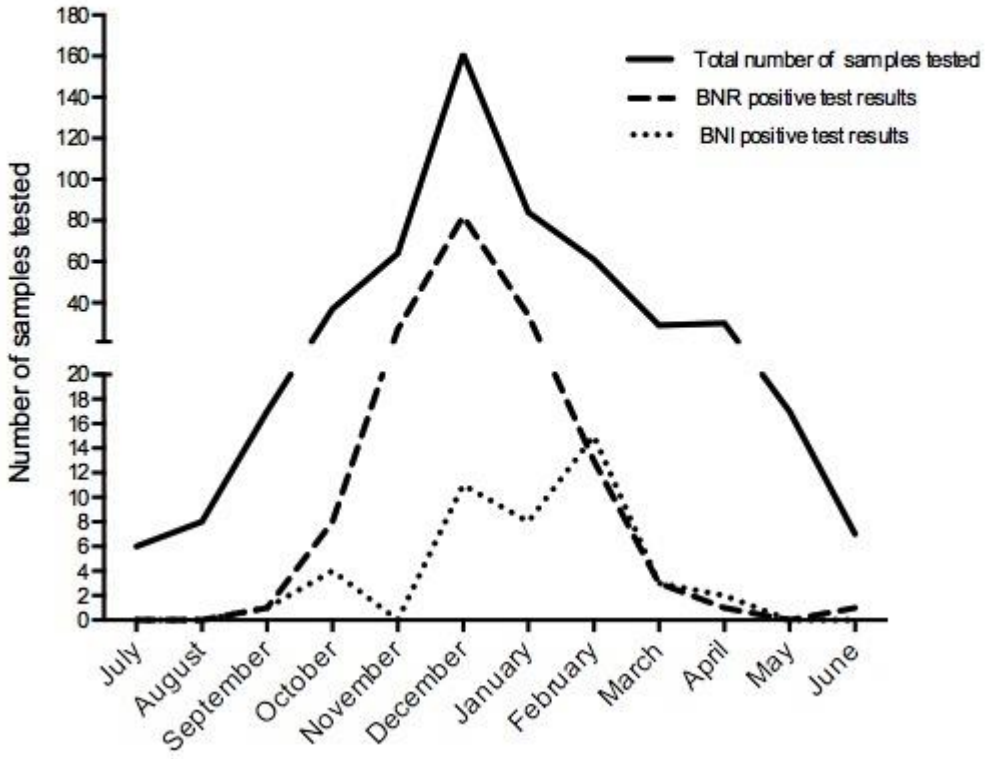
Results

Of 521 samples both influenza RT-PCR and BNI data were available, 514 of these were also tested for RSV (Figure1). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of BNI were 69% (confidence interval [CI] [51-83]), 96% [94-97], 55% [39-70] and 98% [96-99] respectively. Of eleven false-negative samples, RT-PCR Ct-values were higher compared to all RT-PCR positive test results (27 vs 22, p=0.012). Of twenty false-positive samples, none were culture positive and two tested positive in D-IF.

Sensitivity, specificity, PPV and NPV for BNR were 79% [73-85], 98% [96-99], 97% [93-99] and 88% [84-91]. Of the 42 false-negative samples the median Ct-value was higher than that of all RT-PCR positive samples (31 vs 23, p<0.0001). Only five false-positive samples were detected. Three of these tested positive for RSV in virus isolation and D-IF. No differences were found in Ct-values of hospitalized and non-hospitalized patients within the respective

case groups.

Figure 1.
Total number of samples tested with BinaxNOW influenza AB® and BinaxNOW RSV® rapid tests and all positive test results for BNI and BNR in children between 0-5 years at Erasmus MC-Sophia from 2005 – 2013.



Conclusions

RADT have a high specificity with BNR being superior to BNI.However, their relative low sensitivity severely limits their usefulness for clinical decision making in a tertiary care paediatric hospital.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0932
ORAL PRESENTATION SESSION 2 - VACCINE SCIENCE 1

SALIVARY IMMUNE RESPONSE TO ROTAVIRUS: A WHOLE MUCOSAL HOST IMMUNE RESPONSE

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Background

Salivary glands are known immune effector sites and part of the whole mucosal immune system. The aim of the present study is to assesssalivary immune response to rotavirus in infected and vaccinated patients through the analysis of the cytokine immune profile in saliva samples.

Methods

Prospective comparative study of serial saliva samples from a) 27 rotavirus-infected patients (at recruitment during acute phase in the hospital and at convalescence - i.e. at least 3 months after recovery), and b) 36 rotavirus-vaccinated infants (baseline and 40 ± 3 days after 3rd vaccine dose). Concentration of 10 salivary cytokines were determined in a multiplex assay by Luminex (IFN-γ, IFN-α_2, IL-1β, IL-6, IL-8, IL-10, IL-15, IL12p70, TNF-α; Millipore) and ELISA (IFN-λ_1; R&D).

Results

Table.1.

	Baseline	Post-Vaccination	Infected	Post-Infected	*p value* Baseline *vs* Post Vaccine	*p value* Baseline *vs* Infectedf
IFN α_2	216.1±228.1	233.8±135.8	30.09±37.54	76.45±176.1	*0.6848 ns*	*<0.0001 ****
IL-8	74.30±537.5	122.6±545.6	387±820.5	237.4±477.8	*0.1655 ns*	*<0.0001 ****
IL-1β	1.623±3.765	2.000±14.91	3.973±395.7	3.719±6.660	*0.5471 ns*	*<0.0001 ****
IL-15	1.910±2.727	1.527±1.891	2.679±3.033	2.313±6.073	*0.1731 ns*	*0.1943 ns*
IL-10	13.66±9.209	7.932±11.76	4.404±25.28	4.405±15.72	*0.0012 ***	*0.0015 ***
IL12p70	3.910±8.612	2.408±8.847	7.821±11.42	6.671±13.43	*0.7893 ns*	*0.0801 ns*
IL 6	3.779±6.109	1.606±4.935	1.988±50.99	1.419±3.931	*0.0040 ***	*0.1714 ns*
TNF-α	1.008±1.496	0.7140±1.210	2.544±34.07	2.891±7.128	*0.2703 ns*	*0.0080 ***
IFN-γ	4.597±6.026	6.789±5.319	4.432±4.603	4.333±6.169	*0.3100 ns*	*0.5881 ns*
IFN-λ_1	*nd*	*nd*	*nd*	*nd*	---	---

Concentrations of salivary cytokines (pg/ml) and comparisons between baseline/post-vaccine and acute infection/convalescence, are shown in Table 1. In infected patients IFN-α_2, IL-8, IL-1 β, IL-10 and TNF-α levels were significantly different during infection *vs*. convalescence. In vaccinated patients, only IL-10 and IL-6 levels were different before/after vaccination. IFN- λ_1 was not detected in any saliva sample.

Conclusions

Rotavirus induces a host salivary immune response**;** and immune mucosal response to rotavirus infection is not confined to the intestinal mucosa. Rotavirus infection produces a large increase in several innate immune salivary cytokines as IL-8, IL-1β and TNF-α and decreases the salivary production of the anti-viral IFN-α_2 and the immune-regulatory IL-10. Rotavirus vaccination seems to produce a decline in the IL-10 and the IL-6 production by the salivary mucosa.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0412
ORAL PRESENTATION SESSION 2 - VACCINE SCIENCE 1

SEX-DEPENDENT IMMUNE RESPONSES TO INFANT VACCINATION: AN INDIVIDUAL PARTICIPANT DATA META-ANALYSIS OF ANTIBODY AND MEMORY B CELLS

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Background

Biological sex has previously been identified as an important source of variation in infection and immunity. We aimed to investigate sex-dependent differences in immune response to childhood vaccination.

Methods

We undertook an individual participant data meta-analysis of vaccine trials from one centre, in which children under three years of age were randomised and immunological parameters measured. Log-transformed antigen-specific antibody and memory B cell data were combined in a meta-analysis. Differences between girls and boys were reported as geometric mean ratios.

Results

Vaccine immunogenicity data were available from nine trials and 2378 children. Six trials investigated meningococcal vaccines, two studied pneumococcal vaccines, and one studied the effect of different needle sizes. Blood samples were taken at one month post-priming, pre-boost, post-boost and at 24 months of age. Not all time points were available in all studies. Significant differences between girls and boys were observed for anti-diphtheria antibody and capsular group A, W, and Y meningococcal serum bactericidal activity. Serotype-specific anti-pneumococcal antibody concentrations were significantly different for at least one time point in 12 of 13 serotypes. No sex-differences were observed for responses to *Haemophilus influenzae* type b, capsular group C meningococcal or tetanus toxoid vaccines.

Conclusions

In young children, immune responses to vaccines were consistently higher or equivalent in girls compared with boys. In no instance were male responses significantly higher. While these data show some significant differences in immune responses which appear to be determined by biological sex, the clinical significance of such differences remains unclear. Investigation of the biology of these differences may inform improved design of vaccines to direct optimal immune responses and potentially to improve population protection.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESP16-0238
ORAL PRESENTATION SESSION 2 - VACCINE SCIENCE 1

ARM PARALYSIS FOLLOWING VARICELLA AND HEPATITIS A VACCINATIONS DURING A COMMUNITY-WIDE OUTBREAK OF ENTEROVIRUS-D68: A COMPLEX EVALUATION OF A REPORTED ADVERSE EVENT FOLLOWING IMMUNIZATION (AEFI)

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Title of Case(s)

Arm paralysis following varicella and hepatitis A vaccinations during a community-wide outbreak of Enterovirus-D68: A complex evaluation of a reported adverse event following immunization (AEFI)

Background

Flaccid monoplegia in a previously healthy 1-year-old child was initially suspected to have been caused by vaccines received 1 week before onset. Wild-type varicella zoster virus (Wt-VZV) was the only pathogen identified in molecular studies of CSF. The child presented during a community-wide EV-D68 outbreak associated with flaccid paralysis. This case illustrates the complexity of AEFI causality assessments.

Case Presentation Summary

Eight days after receiving hepatitis A and varicella vaccines, a 1-year-old healthy child received an antibiotic for febrile, bilateral otitis media. Two days later, he developed proximal weakness of the left arm, generalized maculopapular rash, vomiting, and diarrhea. He had a decreased left biceps reflex and muscle tone, good movement of the left hand, and a slightly decreased grip. CSF revealed no organisms, RBC 4188 per mm^3, WBC 46 per mm^3, protein 39 mg/dl, and glucose 57 mg/dl. Wt-VZV DNA was identified in the CSF by PCR. Multiplex

respiratory PCR panel and CSF were negative for enteroviruses, though serum was positive for high-titer (IgG) neutralizing antibodies against EV-D68 virus. Diagnostic testing for multiple other pathogens were negative. VZV IgG avidity was consistent with a *primary* VZV antibody response. MRI of the brain and spine with contrast were normal. Serial EMGs were consistent with injury of the motor neurons or ventral roots at C5-7 level. The child remained paralyzed 1.5 years later.

Learning Points/Discussion

Molecular methods aided a complex AEFI causality assessment and excluded vaccination as a cause of paralysis. Wt-VZV, a known neurotropic virus, may have caused or contributed to the child's paralysis.

ESP16-0735
ORAL PRESENTATION SESSION 2 - VACCINE SCIENCE 1

DECREASE OF OTITIS MEDIA EPISODES IN CHILDREN IN GERMANY FOLLOWING INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINES

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Background

The routine immunization with pneumococcal conjugate vaccines (PCVs) of children until the age of 2 years started with PCV7 in 2007. Higher-valent PCVs were introduced in 2009 (PCV10 in April, PCV13 in December). This analysis aimed to evaluate the impact of PCVs on the epidemiology of Otitis Media (OM) in children in Germany, with a focus on the higher-valent PCVs.

Methods

TheIMS Health VIP® panel was used to analyse the data continuously and retrospectively. The alterations of frequencies of ICD 10 (10th revision of International Statistical Classification of Diseases and Related Health Problems) OM diagnosis (H66=suppurative OM/ H65=non-suppurative OM) were primary endpoints. The period before launch of vaccines (2003-2006) was used as baseline and compared with diagnoses collected from 2007 to 2014. According to age cohorts the respective reduction was evaluated. The Poisson model was applied for statistical analysis.

Results

During baseline period, in average 1.403.497/391.828 suppurative/non-suppurative OM-episodes were diagnosed yearly in children between 0-4 years. The diagnosis rates of suppurative/non-suppurative OM decreased over the years significantly ($p<0.0001$), in 2009 by 15.2%/17.5% and in 2013 even by 31.4%/24.4%, respectively compared to baseline. A similar decrease was apparent for children between 5 and 10 years. From 2007 to 2014, cumulated 5,786,206 less children from 0 to 10 years were diagnosed with suppurative or non-suppurative OM. The reduction of antibiotic prescriptions in 2007-2014 due to OM cumulates to a total number of more than 2.563 million in children 0-10 years.

Conclusions

This analysis reveals a significant decrease in OM episodes in children after introduction of PCV7 by more than 5.7 million (2007 – 2014), including a substantial impact by higher-valent PCVs. OM related prescription of antibiotics was reduced in all age groups.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0718
ORAL PRESENTATION SESSION 2 - VACCINE SCIENCE 1

OVERALL EFFECTIVENESS OF HIGHER-VALENCY PNEUMOCOCCAL CONJUGATE VACCINES ON INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN UNDER 5 YEARS (2010-2014): RESULTS OF SPIDNET2 – A EUROPEAN MULTICENTRE STUDY

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Background

SpIDnet2 project aims to enhance surveillance of invasive pneumococcal disease (IPD) in 10 European Union countries. The heptavalent Pneumococcal Conjugate Vaccine (PCV7) was used during 2001-2009 in 12 sites, PCV13 has been used in 6 sites, PCV10/PCV13 in 5 sites since 2010, and PCV10 in 1 site since 2011. We measured the impact of higher-valency PCV (HVPCV) on IPD in children <5 years (2010-2014).

Methods

We compared annual IPD incidence after HVPCV introduction by serotype categories (all types, PCV7, PCV10nonPCV7, PCV13nonPCV10, nonPCV13) to the average incidence of prePCV7 and PCV7 periods. We used random effects meta-analysis to calculate pooled incidence rate ratios (IRR), 95% confidence intervals (CI) and heterogeneity (I^2 test).

Results

After 5 HVPCV years, all type IPD incidence decreased by 63% (IRR=0.37, 95%CI: 0.33-0.40, I^2=0%) versus prePCV7 and 50% (IRR=0.50, 95%CI: 0.43-0.59, I^2=53%) versus PCV7 period. PCV7 serotype IPD incidence decreased by 96% (IRR=0.04, 95%CI: 0.02-0.09, I^2=71%) and by 82% (IRR=0.18, 95%CI: 0.08-0.42, I^2=81%) versus prePCV7 and PCV7 periods, respectively. IPD incidence due to PCV10nonPCV7 serotypes decreased by 80% (IRR 0.20, 95%CI: 0.12-0.32, I^2=0%) versus prePCV7 and 90% (IRR 0.10, 95%CI: 0.05-0.21, I^2=66%), versus PCV7 period. IPD incidence due to PCV13nonPCV10 serotypes decreased by 64% (IRR 0.36, 95%CI: 0.25-0.50, I^2=15%) and 70% (IRR 0.30, 95%CI: 0.18-0.50, I^2=68%) respectively. NonPCV13 IPD incidence increased 2.33 fold (95%CI: 1.47-3.69, I^2=72%) versus prePCV7 and 1.58 fold (95%CI: 1.26-1.99, I^2=48%) versus PCV7 period.

Conclusions

SpIDnet2 results indicate an additional decrease in IPD incidence after introduction of HVPCV, due to decline of serotypes included in these 2 vaccines. NonPCV13 IPD incidence increased as compared to both reference periods. Continuous enhanced surveillance is needed to better explore IPD trends.

Acknowledgements: SpIDnet2 project is co-funded by study sites and ECDC.

ESP16-0082
ORAL PRESENTATION SESSION 2 - VACCINE SCIENCE 1

A PROSPECTIVE COHORT STUDY OF INFLUENZA SURVEILLANCE IN HONG KONG CHILDREN

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Background

Influenza imposes substantial healthcare burden in children, which can be prevented by seasonal influenza vaccination. However, there is limited data on influenza disease spectrum and vaccine effectiveness (VE). This study ascertained spectrum of influenza in Hong Kong preschool and school-age children and investigated VE in preventing childhood influenza.

Methods

This prospective cohort study recruited children aged 2-12 years from 15 kindergartens and primary schools. Parents completed a questionnaire on subjects' health status and history of influenza vaccination. Flocked nasopharyngeal swabs (NPSs) were collected during biweekly school visits during influenza seasons and illness visits for children with influenza-like illness (ILI). Influenza A and B were detected by real-time PCR, and typed and viral load measured according to WHO guidelines. Study outcomes included ILI and laboratory-confirmed influenza between vaccinated and unvaccinated children.

Results

623 children provided a total of 2,633 NPS samples in 2014-2015. Two samples were obtained from 607 (97.4%) of subjects. Thirty-six (11.2%) subjects had influenza A or B in 2014 whereas all 19 (6.3%) subjects had influenza A in 2015. Ninety-nine subjects reported ILI and nine illness visits were arranged. Seasonal influenza vaccination was protective against ILI but not laboratory-confirmed influenza by surveillance. Influenza VE for ILI varied between 42.1% and 51.9% depending on the year of vaccination. Logistic regression confirmed protective effect of influenza vaccination against ILI. There was no reported transmission of influenza within subjects' classes and household.

Conclusions

Mildly symptomatic influenza is common in children during influenza seasons. Influenza vaccine uptake is moderate in Hong Kong children. Seasonal influenza vaccination is effective against ILI but not influenza detected by surveillance. (Grant sponsor: Health and Medical Research Fund [reference no. 13120422] of Hong Kong SAR)

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0230
ORAL PRESENTATION SESSION 3 - VACCINE SCIENCE 2

A SINGLE SUBCUTANEOUS WHOLE-PARASITE IMMUNIZATION INDUCES PROTECTION AGAINST EXPERIMENTAL CEREBRAL MALARIA IN MICE

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Background

Malaria causes approximately 500000 deaths per year, mainly due to the development of cerebral malaria. Despite many years of research, currently available malaria vaccines remain of limited efficacy. The objective of our study was to assess the immunogenicity and protective efficacy of a simple, one-time whole-parasite immunization approach to prevent the onset of cerebral malaria in the rodent model.

Methods

Within the rodent *Plasmodium berghei (Pb)* ANKA-C57BL/6 infection model, we immunized groups of mice by a single intravenous or subcutaneous administration wild-type sporozoites (SPZ) under chloroquine prophylaxis (CQ-CPS) or by intravenous administration of $3*10^4$ irradiated SPZ (RAS;). Six weeks after the immunization process, mice were challenged with SPZ or infected red blood cells (iRBC) iv. We observed the clinical outcome and development of neurologic disease by clinical examination, microscopic evaluation of parasitemia and MRI assessment. Immunological assessment included FACS and CBA analyses.

Results

A single immunization with RAS or CQ-CPS induces complete protection against experimental cerebral malaria. Mice were not only protected after challenge with SPZ, but also following a challenge with iRBC. Immunization resulted in delayed development of parasitemia, and in increasing levels of cd4+ effector memory cells.

Conclusions

It is known that immunization with attenuated SPZ can confer complete, sterile protection against malaria, which is mediated by cytotoxic CD8+t-cells. However, this high degree of protection can only be achieved by multiple intravenous administration of huge amounts of SPZ, thus rendering the approach unfeasible for routine vaccination. Our investigations in the rodent model show that protection against severe malaria can be achieved by a single intravenous or subcutaneous SPZ Administration. This approach might offer a novel, simple and feasible way to protect children in malaria endemic countries against severe, life-threatening malaria.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0490
ORAL PRESENTATION SESSION 3 - VACCINE SCIENCE 2

PERTUSSIS VACCINATION DURING PREGNANCY IN BELGIUM: FOLLOW-UP OF INFANTS UNTIL 1 MONTH AFTER THE FOURTH INFANT PERTUSSIS VACCINATION

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Background

We present the final results of a clinical study on pertussis vaccination during pregnancy. The overall aim is to measure the influence of maternal pertussis vaccination on antibody titers in infants before and after a primary series of 4 pertussis containing vaccines.

Methods

Women were either vaccinated with an acellular pertussis vaccine (Boostrix®) during pregnancy (vaccine group) or received no vaccine (control group).

All infants were vaccinated with Infanrix Hexa® according to the standard Belgian vaccination schedule (8/12/16 weeks, 15 months). We report results from blood samples collected before and 1 month after the fourth vaccine dose.

Immunoglobulin G (IgG) antibodies against Pertussis Toxin (PT), Filamentous Haemagglutinin (FHA), Pertactin (Prn), Tetanus Toxoid (TT) and Diphtheria Toxoid (DT) are measured using commercially available ELISA.

Results

Demographic characteristics are similar in the vaccine and control group. Before the fourth vaccine dose, significantly lower antibody titers are found in the vaccine group compared to the control group for anti-Prn IgG ($p=0.003$) and anti-DT IgG ($p=0.023$). One month after the fourth dose, antibody titers are only significantly lower in the vaccine group for anti-PT IgG ($p=0.006$). For all antigens, there is a rise in antibody titer after the fourth dose.

GMC (95% CI)	Before fourth vaccine dose		1 month after fourth vaccine dose	
	Vaccine	Control	Vaccine	Control
N	46	24	45	23 (22 for FHA and Prn)
Tetanus toxoid (IU/ml)	0.25 (0.21-0.30)	0.15 (0.11-0.21)	3.83 (3.39-4.32)	3.40 (2.67-4.33)
p-value	0.007		0.394	
Diphtheria toxoid (IU/ml)	0.45 (0.35-0.58)	0.73 (0.56-0.94)	3.32 (2.94-3.74)	3.85 (3.44-4.31)
p-value	0.023		0.221	
Pertussis toxin (IU/ml)	5.44 (4.49-6.58)	7.27 (5.80-9.12)	36.29 (30.93-42.57)	56.60 (42.36-75.65)
p-value	0.071		0.006	
Filamentous Haemagglutinin (IU/ml)	14.83 (12.37-17.77)	15.98 (12.43-20.56)	100.86 (84.93-119.77)	139.42 (112.68-172.51)
p-value	0.636		0.651	
Pertactin (IU/ml)	4.44 (3.66-5.39)	7.62 (5.67-10.25)	92.73 (67.04-128.25)	81.20 (58.40-112.90)
p-value	0.003		0.272	

Table 1: Geometric Mean Concentrations (GMC) with 95% confidence interval (CI) in International Units per Milliliter (IU/mL) for IgG against tetanus toxoid, diphtheria toxoid, pertussis toxin, filamentous haemagglutinin and pertactin in both groups of infants.

Conclusions

Blunting of the infant immune response after 3 doses of a pertussis-containing vaccine, administered at 8, 12 and 16 weeks of age, has been communicated, when infant vaccination is performed in the presence of high titers of maternal antibodies. The present results indicate still a minor blunting effect 1 month after a fourth vaccine dose at 15 months of age for anti-PT antibodies. However, a good humoral immune response on all measured antigens is found in both groups of children.

Clinical Trial Registration (Please input N/A if not registered)

Clinical trials.gov number: NCT01698346

ESP16-0869
ORAL PRESENTATION SESSION 3 - VACCINE SCIENCE 2

A WHOLE CELL PERTUSSIS VACCINE WITH LOW LEVELS OF ENDOTOXIN (PLOW) PROTECTS MICE AGAINST BORDETELLA PARAPERTUSSIS CHALLENGE

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Background

Whopping caught (or pertussis) is caused by the gram-negative bacteria *Bordetella pertussis* and *Bordetella parapertussis*. An increased prevalence of *B. parapertussis* has being observed as an epidemiological consequence of global immunization with pertussis. The Instituto Butantan is developing a less reactogenic whole cell pertussis vaccine (Plow), with low-endotoxin content. Aims:This work evaluated the impact of the vaccination with Plow in the infection of the upper respiratory tract of mice with *B. parapertussis.*

Methods

Balb/c female mice were subcutaneously immunized with Plow (1/5 of a human whole cell pertussis vaccine dose) in two doses, within 15 days interval. The animals were intranasally challenged 105 days after the immunization, with virulent *B. pertussis* or *B. parapertussis* (10^7 CFU/20µl in PBS). Total IgG anti-Plow and anti- *B. parapertussis* was measured by ELISA 105 days after immunization and 20 days after challenge. The number of CFU in the mice nasotracheal washes was measured 5 or 20 days after challenge.

Results

Plow induced very high antibodies titers against pertussis and parapertussis, with a reduction of 95.8% in the colonization of the upper respiratory tract of the mice with *B. pertussis*, 5 days after challenge and 100% after 20 days, as compared to the residual number of colonies in the saline control group. The animals immunized with Plow and challenged with *B. parapertussis,* showed 52.5% of reduction in the colonization 5 days after challenge, and 100% after 20 days.

Conclusions

Our data demonstrate that Plow was able to induce an effective humoral immune response and protection against pertussis and parapertussis, with recruitment of memory immune response more than three months after immunization.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0926
ORAL PRESENTATION SESSION 3 - VACCINE SCIENCE 2

USAGE OF PROPHYLACTIC INTRAVENOUS IMMUNOGLOBULIN FOLLOWING EXPOSURE TO MEASLES IN INFANTS YOUNGER THAN 6 MONTHS WHOSE MOTHERS WERE NOT IMMUNIZED

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Background

When the measles vaccine is contraindicated, intramuscular and intravenous immunoglobulin (IG) administration is recommended within the first 6 days for healthy children below the age of 12 months, pregnant women and immunodeficient patients. We aimed to perform a retrospective assessment of IVIG for post-exposure prophylaxis after exposures among infants younger than 6 months of age whose mothers were not immunized against measles.

Methods

The Istanbul Public Health Directorate (IHM) identified 105 confirmed measles cases in Istanbul between August 24, 2012 and June 16, 2013. Additionally, 187 infants younger than 6 months with measles IgG- negative mothers and who had been in close contact with these cases were identified. Under the supervision of the IHM, IVIG (0.4 g/kg) was administered to these infants within the first 6-10 days following exposure. The sex, age, exposure type, time after exposure at which IVIG was administered and measles development status were recorded for each subject retrospectively.

Results

Only 2 of the 187 infants developed measles after IVIG prophylaxis. No significant difference in measles frequency was observed between infants who received IVIG within the first 6 days after exposure and those who received IVIG within 7-10 days. The risk of developing measles was greater for infants who experienced contact at home compared to other types of close contact (p=0.003).

Conclusions

Measles did not develop after exposure to measles following prophylactic IVIG administration in 99% of infants younger than 6 months of age whose mothers were seronegative for measles antibodies. Measles frequency was similar in the within 6 days post-exposure IVIG group and the 7-10 day post-exposure IVIG group. Contact with a confirmed case at home, in particular, causes a higher risk of measles.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0709
ORAL PRESENTATION SESSION 3 - VACCINE SCIENCE 2

THE TRANSMISSION POTENTIAL OF MEASLES AFTER THE IMPLEMENTATION OF SUPPLEMENTARY IMMUNIZATION ACTIVITIES IN CHINA

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Background

Measles is a contagious disease to humans and the primary group of infection is children. In order to eliminate measles from China, officials implemented the supplementary immunization activities (SIA) in addition to the routine measles-mumps-rubella vaccines since 2009. Although the measles incidence was reduced by years, the impact of SIA on the transmissibility of the diseases has not yet been investigated to date. Based on the serologic survey, the study aims to evaluate the potential for sustained measles transmissions.

Methods

Two population-based cross-sectional serological surveys of measles antibodies were conducted in Hubei province of China in mid-2010 and mid-2011 after the implementation of SIA in 2009. Immunoglobulin G (IgG) antibodies against measles were measured by enzyme-linked immunosorbent assay (ELISA). Based on the estimated age-specific susceptibility levels, the effective reproduction number (*R*), a key indicator of disease transmissibility was determine by the next generation matrix in transmission model.

Results

In total, 855 and 1723 samples were collected in 2010 and 2011. The overall IgG sero-prevalence were 88.0% (95%CI: 85.6% to 90.4%) and 89.6% (95%CI: 88.0% to 91.2%) respectively in 2 different periods. Comparatively lower sero-prevalence rates were obtained for the children aged less than 24 months and those who attending high school in 2011. The *R*s were 0.76 and 1.53 for the two study periods.

Conclusions

Even though the susceptibility levels were low after the implementation of SIA, the reproduction number in 2011 was greater than unity which indicates a high risk for sustaining measles transmission. The findings suggest that SIA should also focus on the group of high school students as they showed a high transmissibility to other groups, probably due to waning immunity.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0715
ORAL PRESENTATION SESSION 3 - VACCINE SCIENCE 2

INFLUENCE OF MATERNAL IMMUNIZATION DURING PREGNANCY ON THE QUALITY (AVIDITY) OF INFANT ANTIBODY RESPONSES TO PAEDIATRIC VACCINES

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Background

Maternal antibodies induced by vaccination during pregnancy cross the placental barrier and can close the susceptibility gap to infectious diseases in young infants up to the start of primary immunization. However, not only the quantity but also the quality of circulating antibodies is important for the efficacy of prevention against infection. The aim of this study was to assess the effect of maternal immunization on quality (avidity) of infant vaccine-induced IgG antibodies to tetanus toxin (TT), diphtheria toxin (DT), pertussis toxin (PT), filamentous haemagglutinin (FHA) and pertactin (Prn).

Methods

Infants were born from mothers who received a dTap (Boostrix™) vaccine during pregnancy or from control mothers who did not receive any booster vaccine. All infants were immunized with a hexavalent (Infanrix Hexa®) vaccine at 8, 12 and 16 weeks followed by a fourth dose at 15 months of age. The relative avidity index (RAI) was determined using ammonium thiocyanate 1.5M as a dissociating agent. RAI <40% was considered as low, RAI between 40 and 60% as moderate and RAI>60% as high avidity.

Results

Before the fourth dose, infant IgG antibodies were of moderate avidity for TT, PT, FHA and Prn and of low avidity for DT and similar in both study groups.

One month after the fourth vaccine, high avidity was found for TT and PT, but avidity remained moderate for FHA and Prn and low for DT. Avidity was significantly lower for PT

(p=0.003) in the offspring of the vaccine group compared to the control group.

GM of RAI (95% CI)	Before fourth vaccine dose		1 month after fourth vaccine dose	
	Vaccine	Control	Vaccine	Control
N	46	24	45	23 (22 for FHA and Prn)
TT	46.19 (40.75-52.24)	45.12 (37.09-54.88)	74.68 (71.14-78.39)	73.46 (66.76-80.83)
p-value	0.880		0.880	
DT	27.97 (24.54-31.86)	25.76 (22.30-29.75)	28.59 (24.54-33.30)	31.82 (25.44-39.80)
p-value	0.301		0.426	
PT	55.40 (51.14-60.01)	59.64 (53.48-66.52)	68.06 (63.98-72.41)	78.65 (76.04-81.36)
p-value	0.201		0.003	
FHA	47.82 (43.04-53.13)	50.13 (46.05-54.57)	50.51 (44.32-57.57)	58.94 (50.06-69.39)
p-value	0.761		0.092	
Prn	44.13 (39.94-48.76)	46.89 (42.68-51.52)	59.05 (52.56-66.34)	64.82 (57.18-73.49)
p-value	0.582		0.347	

Conclusions

High maternal antibodies after vaccination during pregnancy may have a negative impact on antibody quality of vaccine-induced infant immune responses to PT.

Clinical Trial Registration (Please input N/A if not registered)

Clinical trials.gov number NTC01698346

ESP16-0621
ORAL PRESENTATION SESSION 4 - IMMUNOPATHOGENESIS 1

COMPLEMENT FACTOR H SERUM LEVELS DETERMINE RESISTANCE TO PNEUMOCOCCAL INVASIVE DISEASE

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Background

Streptococcus pneumoniae is an important cause cause of invasive infections in children. Complement activation plays a vital role in opsonophagocytic killing of *Streptococcus pneumoniae* in blood. Initial complement activation via the classical and lectin pathways is amplified through the alternative pathway amplification loop. Alternative pathway activity is tightly regulated. Complement factor H (FH) is a negative regulator of alternative pathway activity. We tested whether the inter individual variability in human serum FH levels have a functional impact on host defence against pnuemococci.

Methods

Streptococcus pneumoniae strain TIGR4 was used in all experiments. Two in vivo mouse sepsis models were applied to study the consequences of different FH levels on penumococcal sepsis. 1) Factor H +/+, +/- and -/- C57BL/6 mice were studied. 2) C57BL/6 mice +/+ mice treated with human FH at the time of inoculation were studied. bacterila load serum cytokines and disease severity were determined. In vitro assays include dpneumococcal C3 opsonization assay and in vitro whole blood pneumococcal killing assay. In some experiments FH depleted serum reconstituted with different concentrations human FH was aplied.

Results

Clearance of *S. pneumoniae* from plasma is enhanced in heterozygous factor H deficient mice. Administration of human factor H to wild-type mice impaired plasma clearance of *S. pneumoniae.*Pneumococcal C3 opsonization is enhanced in heterozygous factor H deficient mice. Human factor H levels influence the degree of pneumococcal C3 opsonization and killing in human blood.

Conclusions

In summary, we found that FH levels determine a delicate balance of AP activity, thus affecting the resistance to invasive pneumococcal disease. Our results suggest that variation

in FH expression levels, naturally occurring in the human population, determine resistance to invasive pneumococcal disease.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0965
ORAL PRESENTATION SESSION 4 - IMMUNOPATHOGENESIS 1

AGE-SPECIFIC CD4+ T-CELL RESPONSES FROM HUMAN NEONATES AND INFANTS AGAINST ANTIGENS OF STAPHYLOCOCCUS AUREUS AND BIFIDOBACTERIUM LONGUM SSP. INFANTIS

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Background

T cells in human neonates, infants, and adults differ dramatically in the initiation, strength, and stability of their responses. In this study, we investigate cellular mechanisms of $CD4^+$ T cells from neonates, infants and adults to show the antigen specific response to *Staphylococcus aureus* and *Bifidobacterium longum ssp. infantis*.

Methods

$CD14^+$ monocytes from surgically excised adenoids of infants in different ages, cord blood and peripheral blood from healthy donors were incubated with extracts of *Staphylococcus aureus* and *Bifidobacterium longum ssp. infantis* to stimulate enriched T cells. T cells were characterized by flow cytometry and functional assays.

Results

$CD4^+$ $CD45RA^+$ and $CD4^+$ $CD45R0^+$ T cells proliferate and up regulate the activation-associated molecule CD25 in response to antigens of *Staphylococcus aureus* whereas stimulation with *Bifidobacterium longum ssp. infantis*-antigenhad almost no effect. Interestingly, an inverse correlation between the percentages of *Staphylococcus aureus*-antigen induced proliferating T cells and age of infants is observed. In all groups, the stimulation with *Staphylococcus aureus*-antigen induces the production of cytokines like IL-2, IL-4, IFNγ, and TNFα in T cells whereas the treatment with *Bifidobacterium longum ssp. infantis*-antigendid not. High numbers of IL-4 receptor alpha expressing T cells are identified in adenoids of infants after incubation with *Staphylococcus aureus*-antigencompared withantigens of *Bifidobacterium longum ssp. infantis.* Multi-functional analysis of $CD4^+$ T cells producing a range of cytokines in response to *Staphylococcus aureus*-antigenare identified in cord blood, adenoids of infants, and adults with age-dependent characteristics.

Conclusions

This work highlights the gap between specific T cell responses of neonates, infants, and adults in terms of quality and quantity. Our findings will help to understand the relationship between pathogens and T cells and to optimize future strategies for therapeutic interventions.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0383
ORAL PRESENTATION SESSION 4 - IMMUNOPATHOGENESIS 1

FEASIBILITY OF DUAL RNA-SEQUENCING TO REVEAL HOST-PATHOGEN INTERACTIONS IN SEVERE MALARIA

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Background

The pathogenesis of severe malaria (SM) is incompletely understood, but both host and pathogen factors have been implicated. Global analysis of simultaneous, paired, human and parasite gene expression has the potential to reveal the biological processes underlying severe malaria.

Methods

Whole blood (average 3mL) from 46 Gambian children with malaria (25 SM, 21 uncomplicated (UM)) was collected into PAXgene™ tubes. After extraction of RNA, we performed Illumina Hi-Seq 100bp paired-end RNA-sequencing on ribosomal and globin RNA-depleted libraries. We used transcriptional profiles of pure leukocyte populations and *in vitro* synchronized parasites to perform deconvolution of leukocyte mixtures and parasite stage, and adjust for these in differential expression analyses.

Results

We obtained per sample medians of 36 million reads, 91% uniquely mapped, 21 million human and 9 million of parasite origin, giving sufficient depth for robust simultaneous host and parasite global gene expression analysis. Estimates derived from multi-gene signatures of major leukocyte populations and parasite developmental stages showed strong correlations with measured cell counts and accurately discriminated proportions in synthetic datasets, allowing correction for inter-subject variation in leukocyte differential, and parasite stage and synchronicity. Preliminary analyses reveal differential expression of hundreds of both host and parasite genes between SM and UM.

Conclusions

It is feasible to perform simultaneous global gene expression analysis of both host and pathogen on whole blood “straight out of the arm” of children with malaria. Despite complex changes in the mixture of cell types and parasite stages in blood during infection, bioinformatic approaches can eliminate these confounding effects on differential gene expression. Dual RNA-sequencing offers an unprecedented opportunity for detailed assessment of host-pathogen interactions causing severe disease in humans.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0405
ORAL PRESENTATION SESSION 4 - IMMUNOPATHOGENESIS 1

A NOVEL MACROPHAGE SUBSET INSTRUCTS IMMUNITY IN STAPHYLOCOCCAL SKIN INFECTION

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Background

Dermal macrophages constitute the major resident immune cell type in the resting dermis. Dermal macrophages are critical for both initiation and contraction of immunity in staphylococcal skin infection. In mice, prenatally seeded dermal macrophages are replaced by monocyte-derived macrophages in the neonatal period. The impact of this development on the immunity against S. aureus is unknown.

Methods

We employed an intradermal S. aureus infection model in various fate-mapping and reporter mice to study dermal macrophage immunology at the beginning of life.

Results

We identified a relatively small and phenotypically discrete dermal macrophage subset, which establishes and persists independently of bone marrow-derived cells. This subset is essential for the timely expansion and contraction of the inflammatory response in staphylococcal skin infection. Analysis of neonatal mice, pulse labeling and fate-mapping suggest that thismacrophage subset originates from the yolk sac and retains the ability to expand in situ. Functionally, the subset exhibits an exceptionally high phagocytic and inflammatory activity in response to staphylococci.

Conclusions

We conclude that a distinct, quantitatively minor dermal macrophage population drives skin immunity against staphylococci.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0814
ORAL PRESENTATION SESSION 4 - IMMUNOPATHOGENESIS 1

HUMAN NEWBORNS MOUNT AN IGM-BASED INNATE HUMORAL RESPONSE TO RESPIRATORY SYNCYTIAL VIRUS

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Background

B cells play an important role in the immune response during viral respiratory tract infections but their function is distinct at birth. Although IgG production is generally impaired in newborns, comparable IgM production has been observed. This raises the question whether early B-cell activation and IgM production are impaired in human newborns during viral infections, in particular RSV infections.

Methods

Age-dependent RSV-induced B cell responses in newborn and adult B cells *in vitro* were determined. Mononuclear cells from newborns and adults or isolated B cells were stimulated with RSV or type I IFNs. CD69 as activation marker was used to determine B cell activation. Blocking anti-IFNAR antibodies were used for functional assays. RSV-IgM-secreting cells and plasma levels of RSV-IgM in newborns and adults were measured by ELISpot and ELISA, respectively. IgM was purified from newborn plasma with anti-human IgM-agarose. The neutralizing capacity of newborn IgM on RSV infection of epithelial cells was determined.

Results

RSV infection activated newborn and adult B cells and enhanced the percentage of IgM- and RSV-IgM-secreting cells. Newborns demonstrated reduced IgM-secreting cells compared to adults, but comparable RSV-IgM-secreting cells. RSV and IFN-β induced similar IFNAR-mediated activation of newborn and adult B cells. Newborn plasma contained RSV-IgM and newborn IgM reduced RSV infection of epithelial cells.

Conclusions

Newborns mount robust RSV- and IFN-ß-induced B cell responsiveness and IgM production comparable to adults correlating with endogenous RSV-IgM-secreting cells and neutralizing plasma levels of RSV-IgM at birth. The observed B cell activation, the presence of RSV-IgM and the neutralizing capacity of newborn IgM suggest that pathways we have described may be relevant in vivo and may be clinically relevant as a first line of defense during RSV infections in early life.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0947
ORAL PRESENTATION SESSION 4 - IMMUNOPATHOGENESIS 1

HOST IMMUNITY TO MYCOBACTERIUM TUBERCULOSIS AND THE RISK OF TUBERCULOSIS: A LONGITUDINAL STUDY AMONG GREENLANDERS

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Background

Humanimmune responses to latent*Mycobacterium tuberculosis (Mtb)* infection (LTBI) may have preventive potential and enable some individuals to successfully control their *Mtb* infection and halt progression to tuberculosis disease (TB), a hypothesis also applied in novel TB vaccines. This study aimed to evaluate whether immune responses to LTBI antigens was associated with prevention of TB in an Arctic setting virtually free of cross-reacting non-tuberculous mycobacteria.

Methods

A population-based cohort study comprising Greenlanders aged 5-31 years from 2012-2014. Participants were invited using a personal identification number, which allowed follow-up through national registers including the TB notification system. *Mtb* infection was defined by either Quantiferon-TB Gold testing (ongoing infection) or prior notified TB (prior infection). Immune responses to LTBI antigens (Rv1284, Rv2659, Rv2660) were assessed by whole blood antigen stimulation and subsequent interferon gamma measurements.

Results

978 participants were included; 67 had prior notified TB. Both *Mtb* infected and non-infected participants had immune responses to LTBI antigens; range 6-50% and 2-40%, respectively. *Mtb*-infected, both ongoing and prior, had 2-3 fold increased odds of having an immune response to LTBI antigens. Among 911 participants without prior notified TB, 31 were notified with TB during follow-up. An immune response to LTBI antigens was not associated with prevention of subsequent TB; Rv1284 HR 0.92 (95%CI 0.28-3.04), Rv2659 HR 1.05 (95%CI 0.51-2.13) Rv2660 HR 3.06 (95%CI 0.70-13.37).

Conclusions

Host immunity to *Mtb* infection, evaluated by cross-sectional measurements of immune responses to LTBI antigens, was similar among individuals with ongoing and prior *Mtb* infection. Furthermore, immune responses to LTBI antigens did not reduce the risk of subsequent TB. A high proportion of participants who were categorised as non-infected were shown to have immune responses to LTBI antigens.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0228
ORAL PRESENTATION SESSION 5 - USE OF VACCINES

A POST-MARKETING OBSERVATIONAL EVALUATION OF THE SAFETY OF LIVE ATTENUATED INFLUENZA VACCINE IN CHILDREN AND ADOLESCENTS WITH HIGH-RISK CONDITIONS

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Background

More than 90 million doses of live attenuated influenza vaccine (LAIV) have been distributed since it was first authorised in the US in 2003. However, information concerning the safety of LAIV among children with high-risk medical conditions is relatively limited. In the European Union, LAIV is approved for children with high-risk medical conditions, excluding severe asthma.

This study assessed the safety of LAIV among children and adolescents aged 2–17 years with high-risk medical conditions in the UK.

Methods

This was a post-marketing, observational, prospective cohort study. LAIV recipients in influenza season 2013–14 were identified from the Clinical Practice Research Datalink (CPRD), a large computerised database of anonymised longitudinal medical records from primary care in the UK. High-risk conditions were defined according to UK policy.

The incidence rate of all-cause hospitalisations was monitored through 42 days and 6 months following LAIV administration and compared with rates among inactivated influenza vaccine (IIV) recipients and unvaccinated controls, matched by type of high-risk condition, age, healthcare utilisation and region. Incidence rates of hospitalisation for lower respiratory events (LRE) were also analysed.

Results

A total of 4613 eligible LAIV recipients were retained for analysis; most of them (n=3391; 74%) had a diagnosis of asthma or a chronic respiratory disease.

Incidence rate and relative risk of events of interest

	Period at risk	Incidence rate (per 1000 person-years) [95% CI]			Relative risk [95% CI]	
		LAIV recipients n=4613	IIV recipients n=4612[a]	Unvaccinated controls n=13,769[a]	LAIV versus IIV recipients	LAIV recipients versus unvaccinated controls
Any hospitalisation	42 days	234 [193; 276]	433 [376; 489]	236 [210; 261]	0.52 [0.41; 0.65]	0.96 [0.77; 1.18]
Hospitalisation for LRE[b]	42 days	95 [69; 122]	165 [130; 200]	94 [77; 110]	0.58 [0.40; 0.81]	0.97 [0.69; 1.34]
Any hospitalisation	6 months	186 [166; 206]	257 [234; 280]	170 [158; 183]	0.68 [0.58; 0.79]	1.05 [0.91; 1.20]
Hospitalisation for LRE[b]	6 months	73 [61; 85]	107 [92; 122]	73 [65; 82]	0.67 [0.53; 0.84]	1.01 [0.82; 1.24]

[a]LAIV recipients were matched 1:1 with IIV recipients and 1:3 with unvaccinated controls.

[b]LREs are those associated with ICD 10 diagnosis codes of whooping cough, acute obstructive laryngitis (croup), asthma/status asthmaticus, acute respiratory failure, influenza and pneumonia, and other acute lower respiratory infections.

Risk of hospitalisation after LAIV administration did not vary significantly versus matched unvaccinated controls and was consistently lower than after IIV administration, within 42 days or 6 months post vaccination, for all hospitalisations and LRE hospitalisations (Table).

Conclusions

This study did not identify any increased risk of hospitalisation after administration of LAIV in UK children and adolescents aged 2–17 years with high-risk medical conditions.

This study was sponsored by MedImmune, the biological division of AstraZeneca.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0414
ORAL PRESENTATION SESSION 5 - USE OF VACCINES

A SAFETY STUDY OF A LIVE-ATTENUATED JAPANESE ENCEPHALITIS VACCINE (JE-CV) IN 10,000 THAI CHILDREN

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Background

JE-CV, a live-attenuated Japanese encephalitis vaccine, has been licensed in more than 10 Asian countries. We conducted a prospective Phase IV open-label study in 10 academic hospitals in Thailand to further characterize the safety profile of the vaccine and detect rare AEs. With 10,000 subjects aged between 9 months and <5 years, the probability of observing any AE with a true frequency of 1/3,333 was 95%.

Methods

The primary objective was to collect SAEs up to 60 days after 1 dose of JE-CV given as primary vaccination (Group 1: 70% of subjects) or as booster for subjects primed with an inactivated JE vaccine 1 year before (Group 2: 30 % of subjects). The secondary objective was to describe grade 3 systemic AEs within 30 minutes after vaccination.

Results

The study was conducted from November 2013 to April 2015. Mean age at enrolment was 1.2 years in Group 1 and 3.6 years in Group 2. Each group included more male than female

subjects. Among the 6,851 subjects included in Group 1, 204 (3.0%) reported 231 SAEs; 59 subjects (1.9%) out of 3,149 included in Group 2 reported 63 SAEs. The most frequent SAEs, occurring at a frequency of <0.4% in each group, were all considered unrelated to vaccination and included gastroenteritis, pneumonia, febrile convulsions, bronchitis, and influenza. Three cases of urticaria, assessed as moderate hypersensitivity, in 2 subjects in Group 1 were considered to be related SAEs by the Investigator. No grade 3 immediate systemic AEs were reported.

Conclusions

Increasing the size of the overall safety database to >15,000 subjects vaccinated in clinical trials, our study confirms the satisfactory safety profile of JE-CV, making this vaccine a good candidate for EPI vaccination.

Clinical Trial Registration (Please input N/A if not registered)

NCT01981967

ESP16-0564
ORAL PRESENTATION SESSION 5 - USE OF VACCINES

PNEUMOCOCCAL VACCINATION ASSOCIATED WITH FEWER ANTIBIOTIC PRESCRIPTIONS IN DUTCH INFANTS

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Background

Previous research has shown reductions in antibiotic prescribing after introduction of pneumococcal vaccines in infancy. We assessed the impact of 10-valent pneumococcal conjugate vaccination (PCV10) subsequent to PCV7 on antibiotic prescribing in the Netherlands.

Methods

We included infants who were insured by Achmea Health at birth and collected all-cause antibiotic prescription claims data up to the age of 2 over the years 2006-2013. We used negative binomial regression analyses accounting for seasonal variation and calculated incidence rate ratios (IRR) by comparing the crude antibiotic prescription rate in the PCV10 period (March 2011 to December 2013) to that in reference period (January 2006 to February 2011). The IRR was then calculated for municipalities with low (≤79.9%), moderate (80%-95%) and high (≥95%) PCV immunisation coverage.

Results

Over the years 2006-2013, 255,154 infants were included in our analysis. During a total follow-up of 461,352 child-years, 275,337 antibiotic prescriptions were purchased. PCV10 was associated with a significant change in antibiotic prescriptions; crude prescription rates decreased from 601 (95% CI: 598 to 604) in the reference period to 591 (95% CI: 588 to 595) per 1,000 child-years in PCV10 years (IRR: 0.98 [95% CI: 0.98 to 0.99]). In municipalities with high immunisation coverage, antibiotic prescription rates decreased by 4% (IRR 0.96, 95% CI: 0.95 to 0.97), in those with moderate immunisation coverage prescription rates remained stable (IRR 1.01, 95% CI: 1.00 to 1.02) and in municipalities with low immunisation coverage they increased by 6% (IRR: 1.06, 95% CI: 1.00 to 1.13).

Conclusions

Introduction of PCV10 in the Netherlands has led to fewer antibiotic prescriptions issued to infants.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0737
ORAL PRESENTATION SESSION 5 - USE OF VACCINES

EPIDEMIOLOGY OF HERPES ZOSTER AMONG CHILDREN IN GERMANY FOLLOWING INTRODUCTION OF VARICELLA VACCINATION IN 2004

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Background

Pre-vaccine data on herpes zoster (HZ)-associated hospitalization showed increasing incidences for persons aged >10 years in Germany. Following introduction of varicella vaccination in Germany (2004), increasing vaccination coverage (VC) and decreasing varicella incidences were observed. Previous US-studies found a greater risk of developing HZ for unvaccinated compared to vaccinated children. We analyzed available data to determine the effects of varicella vaccination on HZ in 0-14-year-old children in Germany.

Methods

A countrywide sentinel of about 500 primary care pediatricians transmitted case based reports on HZ from April 2005 to December 2014. Yearly HZ practice indices (PI) were computed as cases/100 pediatricians for age groups 0-4, 5-9 and 10-14 years. Based on data on HZ-associated hospitalization from 2005 to 2014 annual age-group-specific hospitalization incidences (HI) of HZ (cases/100.000 inhabitants aged 0-4, 5-9 and 10-14 years) were calculated. Incidence rate ratios (IRR) were calculated using Negative Binomial Regression to detect trends.

Results

Sentinel pediatricians reported a total of 3,158 HZ-cases among 0-14-year-olds from April 2005 to December 2014. PI significantly increased for 10-14-years-olds (IRR=1.14; $p<0.001$), no significant time trends were observed for the younger age groups. Overall 3,616 HZ-cases aged 0-14 years were hospitalized from 2005-2014. HZ-HI significantly declined for age group 0-4 (IRR=0.91; $p<0.001$) and significantly increased for 10-14-year-olds (IRR=1.05; $p<0.001$); no time trend was found for 5-9-year-olds (IRR=0.98; $p=0.22$).

Conclusions

Our data are inconclusive to suggest an impact of increasing varicella VC on pediatric HZ epidemiology. The incidence increase in children >10 years has continued. Declining HZ incidence in cohorts dedicated for vaccination was only shown partly and by one data source. Ongoing monitoring and analysis are needed to detect and comprehend changes in HZ epidemiology in the post-vaccine era.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0860
ORAL PRESENTATION SESSION 5 - USE OF VACCINES

PNEUMOCOCCAL CARRIAGE IN HOUSEHOLDS IN KARONGA DISTRICT MALAWI, BEFORE AND AFTER INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINATION

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Background

Thirteen-valent pneumococcal conjugate vaccine (PCV-13) was introduced in Malawi in November 2011 and is given as part of the EPI schedule at 6, 10, 14 weeks of age. The vaccine is expected to reduce vaccine type (VT) nasopharyngeal carriage, leading to reduced transmission and herd protection.

Methods

This household surveillance survey compared pneumococcal carriage in rural Karonga District, Malawi in 2009-2011 (n=783 persons) and 2014 (n=483 persons), before and after vaccine introduction. Nasopharyngeal swabs were collected monthly or biweekly from a cohort of infants, mothers and household members <15 years. Serotyping was performed using latex agglutination. Carriage prevalence ratios before and after vaccine introduction were calculated using log-binomial regression, adjusted for age, seasonality and household composition.

Results

VT carriage prior to PCV-13 introduction was 11.4%, 45.1%, 28.2%, 21.2% and 6.6% for 6-week old infants, 18-week old infants, children 1-4 years, children 5-15 years and mothers, respectively. After vaccine introduction, VT carriage decreased amongst 18-week old infants (adjusted prevalence ratio (APR) 0.14 (95% CI 0.05-0.41) and vaccinated children 1-4 years (0.42, 0.24-0.75). VT carriage also decreased in unvaccinated children 1-4 years, children 5-15 years and mothers: APR 0.56 (0.34-0.94), 0.40 (0.18-0.90) and 0.40 (0.17-0.95) respectively. No decrease in VT carriage was observed for 6-week old infants (APR 1.31 (0.44-3.88). Non-VT carriage increased only amongst vaccinated children 1-4 years (APR 1.41 (1.00-1.97). Vaccine coverage with 3 doses PCV-13 at 1 year of age was 89.4% in 2014.

Conclusions

There is evidence of reduced carriage of VT pneumococcus three years after vaccine rollout in this rural Malawian population with good vaccine coverage using a 3+0 schedule. Six-week old infants continued to carry at a high rate; reasons for this need further investigation.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0872
ORAL PRESENTATION SESSION 5 - USE OF VACCINES

IMPACT OF ROTAVIRUS VACCINATION IN BELGIUM 8 YEARS POST-VACCINATION

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Background

Rotavirus vaccination has been recommended in Belgium for all infants starting at 8 weeks of age since October 2006 and been partially reimbursed since November 2006. Shortly after, vaccine uptake reached a high level (81-85% in 2007, 86-89% in 2012).
This study analyses the impact of rotavirus vaccination in children 0-2 years up to eight years after its introduction.

Methods

We assessed trends in rotavirus activity using data from a representative sentinel laboratory-network over the period 1999-2015 (with interruption in 2002-2004, and preliminary results for 2015). Additionally we analysed national hospitalisation discharge data for rotavirus gastro-enteritis for 1999-2012 (ICD9 code 008.61). Data from the pre-vaccination years (average of 1999-2001 and 2005-2006 for confirmed cases and average of 2000-2006 for hospitalisations) were compared to the most recent year post-vaccination (2014-15 for confirmed rotavirus cases and 2011-2012 for hospitalisation discharge data) and presented as a percentage reduction.

Results

In children 0-2 years, the number of laboratory-confirmed rotavirus cases dropped from 6887 on average during the pre-vaccination period to 2221 during the 8th year post-vaccination, i.e. a 68% reduction (95%CI 67-69%). A pattern of biennial increases in rotavirus activity was observed in the most recent post-vaccination years, with relative increases occurring during 2012-2013 and 2014-2015, but these remained well below pre-vaccination levels.
In children 0-2 years the number of hospitalisations for rotavirus gastroenteritis decreased from an average of 3916 pre-vaccination to 785 post-vaccination, i.e. a decrease by 80% (95% CI 78-81%).

Conclusions

A substantial and sustained decline in rotavirus activity and rotavirus related hospitalisations was observed up to eight years post-vaccination, affirming continued high effectiveness in

preventing rotavirus gastroenteritis in young children. Biennial fluctuations in rotavirus activity seem to emerge in the four most recent years.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0981
ORAL PRESENTATION SESSION 5 - USE OF VACCINES

EARLY HERD EFFECT IN DAY CARE CENTRES AFTER THE INITIATION OF THE PCV-10 VACCINATION IN ICELAND

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Background

Pneumococcal conjugate vaccination (PCV-10) was initiated in 2011 in Iceland for all children born in 2011 and later with vaccinations at 3, 5 and 12 months of age, without catch-up schedule.

Aim: To determine the impact of pneumococcal conjugate vaccine on nasopharyngeal carriage of pneumococci in unvaccinated children attending Day Care Centres (DCC).

Methods

The study is an ongoing, repeated cross-sectional study conducted in Iceland where nasopharyngeal swabs have been collected annually in March from 2009 from healthy children attending 15 DCCs. The swabs were selectively cultured for pneumococci and the pneumococci serotyped. Only children born before 2011 were included. Children sampled in the year 2011 and earlier (PreVac) were compared to children sampled in 2013 and later (PostVac). Children sampled in 2012 were excluded as a transition year. To attain compatible age distribution only children ≥3 year of age were included.

Results

In the PreVac and PostVac groups 1020 and 1072 children were sampled respectively. The total pneumococcal carriage rate was similar (63.8% vs 64.6%), dual carriage was 5.1% and 6.0%, a total of 710 and 748 pneumococcal isolates respectively. The PreVac were younger than PostVac (4.67 vs 4.81, $p<0.05$). No gender difference was found. Vaccine types were 40.0% and 19.8% of pneumococcal isolates for the PreVac and PostVac groups respectively. Pooled vaccine efficacy for acquisition of pneumococci for the PostVac compared to the PreVac was 58% (47-66%). For vaccine-associated serotypes, a 41% (11-60%) reduction was found for 6A and a non-significant reduction for 19A.

Conclusions

A significant reduction in vaccine-serotypes was found in unvaccinated healthy children attending DCCs. We conclude that PCV-10 causes early herd effect in older, unvaccinated children in DCCs, possibly also including serotype 6A.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0083
ORAL PRESENTATION SESSION 5 - USE OF VACCINES

IS HAEMAGGLUTINATION INHIBITION A USEFUL METHOD FOR ASSESSING INFLUENZA IMMUNITY IN CHILDREN?

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Background

Haemagglutination inhibition (HAI) assay is a standard method for assessing influenza immunity in adults, but there is limited data on its usefulness in young children. This prospective cohort study investigated the relationship between HAI results, history of influenza vaccination and occurrence of influenza infection in Hong Kong children.

Methods

Children aged 2-12 years from 10 kindergartens and five primary schools were recruited. Parents provided information on subjects' influenza vaccination. Flocked nasopharyngeal swabs were collected during biweekly school visits during influenza seasons in 2014. Influenza was detected and typed by molecular assays. Subjects' sera were tested in parallel by HAI against the five circulating strains. HAI titre ≥1:40 was used as threshold that indicated ≥50% protection against infection in adults.

Results

189 children consented for blood testing, and HAI was successfully done on 181 samples. After excluding HAI data due to earlier influenza detected by our surveillance, results for three influenza A (n=177) and two influenza B (n=158) were analysed. Seropositivity rates for A/H1N1 pdm, A/H3N2, A/H3N2_Switzerland, B/Victoria and B/Yamagata were 92%, 91%, 68%, 49% and 85%, respectively. Sixty-seven subjects received influenza vaccine within one year. The mean reciprocal HAI titres for A/H1N1 pdm was higher in children who were vaccinated within one year (192 versus 112; *P*=0.032). Neither HAI titres nor seropositivity rates differed between subjects with and without influenza-like illness or laboratory-confirmed influenza detected by surveillance.

Conclusions

HAI titres and seropositivity at ≥1:40 are not useful surrogates for influenza immunity in children. Our results show weak cross immunogenicity between A/H1N1 pdm and A/H3N2 contained in seasonal vaccine of 2014/15 and the emerging A/H3N2_Switzerland strain.
(Grant sponsor: Health and Medical Research Fund [reference no. 13120422], Hong Kong SAR)

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0632
ORAL PRESENTATION SESSION 5 - USE OF VACCINES

IMMUNE RESPONSES TO CIRCULATING INFLUENZA AND VACCINE VIRAL STRAINS IN HIV-INFECTED AND UNINFECTED CHILDREN WHO RECEIVED THE 2013/2014 QUADRIVALENT LIVE ATTENUATED INFLUENZA VACCINE (LAIV4)

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Background

LAIV is generally more efficacious than inactivated influenza vaccines in children. LAIV is not recommended for HIV-infected children because of insufficient data. We compared cellular and antibody responses in HIV-infected and uninfected recipients of LAIV4 2013-2014. We tested responses against H1N1-09 and B Yamagata (BY) vaccine strains, which had low and high effectiveness, respectively, and against the circulating H1N1-14 strain, which had significant mutations compared to H1N1-09.

Methods

46 HIV-infected and 56 uninfected participants with prior influenza immunization had the following measurements before and after LAIV4: IFNg T- and IgG/IgA memory B-cell ELISPOT; hemagglutination inhibition (HAI), microneutralization (MN) and nasal IgA antibodies.

Results

The HIV-infected participants had median CD4+ T cells=645 cells/µL and plasma HIV RNA=20 copies/mL; and 84% were on cART. Regardless of HIV status, significant increases in T cell responses were observed against BY, but not against H1N1-09. Furthermore, H1N1-09 T cell immunity was higher than H1N1-14 before and after vaccination. LAIV4 significantly increased memory IgG B cells against H1N1-14 and BY in uninfected, but not in HIV-infected participants. Regardless of HIV status, memory IgG B cells to H1N1-09 were higher than H1N1-14 and lower than BY. There were significant HAI titer increases after vaccination in all groups and against all viruses. H1N1-14 MN titers were significantly lower than H1N1-09 before and after vaccination. Regardless of HIV status, LAIV4 increased nasal IgA concentrations against all viruses; the fold-increase in H1N1-09 IgA was lower than BY.

Conclusions

In conclusion, HIV-infected and uninfected children had comparable responses to LAIV4. H1N1-09 immune responses were lower than BY and higher than H1N1-14, suggesting that both low immunogenicity of H1N1-09 and mutations in H1N1-14 may have contributed to the decreased H1N1 effectiveness of 2013-2014 LAIV4.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0839
ORAL PRESENTATION SESSION 6 - EPIDEMIOLOGY

PAN INDIA DISTRIBUTION OF PNEUMOCOCCAL SEROTYPE (PIDOPS) STUDY: A MULTICENTER LABORATORY-BASED, 2-YEAR SURVEILLANCE OF INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN (<5 YEARS) IN INDIA

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Background

Diseases caused by *S.pneumoniae* are a major public health problem in India. Reports of high prevalence of Invasive pneumococcal disease and excessive infection burden are not supported by laboratory data. There is lack of current reliable base line data as regards to the burden, serotype prevalence, antibiotic resistance and vaccine coverage. In the back drop of scarcity of data, a multisite surveillance study engaging 7 institutional & 51 sentinel sites across the countrywas conducted with conventional and molecular methods.

Methods

1504 children aged 6 months-5years clinically suspected of IPD or Pneumonia with abnormal radiological findings, raised CBC, CRP and Procalcitonin were enrolled. Blood and serum samples were processed by culture and qmPCR for *S.pneumoniae* detection and isolation. Identification and Antibiogram was performed using WalkAway 40 system. Isolates were serotyped by Quellung reaction and PCRseqTyping was made use of for culture negative, qmPCR positive serum samples.

Results

Of the 1504 blood cultures 108(7%) specimens yielded growth of *S. pneumoniae.* 456(30%) of 1504 serum samples were positive for *S.pneumoniae* by qmPCR assay. Penicillin, cefotaxime and Levofloxacin showed 11%, 7% and 7% respectively. High resistance of 48%, 45% and 32% was observed with Co-Trimoxazole, Tetracycline and Erythromycin correspondingly.32 of 108(32.4%) revealed Multi drug resistance. 1, 6B and 14 were the most frequent serotypes with quellung and qmPCR. 78% of the serotypes were covered by PCV 13.

Conclusions

The strength of the study is that it provides baseline information on the epidemiology of IPD at national level, facilitating assessment of drug resistance, appraisal of prevalent serotypes and true burden of the disease. This Pan India surveillance study for *S.pneumoniae* supports large scale introduction of Pneumococcal vaccines and prioritization of policy.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0945
ORAL PRESENTATION SESSION 6 - EPIDEMIOLOGY

GROUP B STREPTOCOCCAL (GBS) DISEASE IN UK AND IRISH INFANTS YOUNGER THAN 90 DAYS OF AGE IN 2014-15

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Background

GBS is the leading cause of neonatal sepsis and meningitis in many countries. Since the last national surveillance in 2000-1 a risk-based intrapartum antibiotic prophylaxis (IAP) strategy has been introduced in the UK and Ireland. We therefore aimed to define the current burden of GBS disease in infants < 90 days and their clinical presentation, risk factors, mortality and the serotypes (ST) responsible for invasive disease.

Methods

Prospective, enhanced, active surveillance was undertaken through the British Paediatric Surveillance Unit, microbiology reference laboratories and national public health agencies. Cases were identified by paediatricians and microbiologists. Paediatricians were asked to complete a questionnaire. Microbiologists were encouraged to submit isolates to the relevant reference laboratories. Isolates were characterised by serotyping and antimicrobial susceptibility testing.

Results

In the 13 months from April 2014 817 cases were identified (149 meningitis): incidence 0.89/1000 live births (95% CI; 0.87-0.91); 0.54/1000 (0.51-0.57) for early-onset (EO) disease,

0.36/1000 (0.33-0.39) for late-onset (LO) disease. 38 infants died (5.8%; 16 EO and 22 LO). Where full clinical information was available (80%), 21% of EO cases and 39% of LO cases were in premature infants and 44% of EO cases had ≥ 1 risk factors. ST were characterised in 50% of the cases; STs III (n=228) and Ia (n=63) were most prevalent. 17% of isolates were clindamycin resistant.

Conclusions

Since the national surveillance of 2000- 2001 there has been a significant increase in the overall incidence of invasive GBS disease in the UK and Ireland, proportionately greater for LO disease, but also evident for EO disease despite the presence of national IAP guidelines. New strategies for prevention of GBS in this age group are urgently required.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0946
ORAL PRESENTATION SESSION 6 - EPIDEMIOLOGY

EPIDEMIOLOGICAL SITUATION OF DENGUE IN BRAZIL IN THE YEARS 2014 AND 2015: A COMPARISON

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Background

Dengue is one of the major health system problems in Brazil, whose spread has increased in the last 30 years with various outbreaks. This study presents the epidemiological situation in the last 2 years of the disease front of all efforts and public health measures adopted by the government in recent years.

Methods

It was used as database the last epidemiological surveillance bulletin released by Brazil's health ministry with the number of recorded cases of Dengue in 2014 and in the period of 04/01/15 to 02/01/16. Data was analyzed in absolute terms, in incidence rate and monthly distribution. Reported cases were divided by gravity, period and region.

Results

In 2014 there were 589.107 reported cases of dengue in Brazil. In 2015, it were recorded 1.649.008 cases, an increase of about 2.8 times. Last year the recorded incidence was 813.1 cases /100,000 inhabitants, while in 2014 the incidence was 289.4/100,000 inhabitants. They were recorded 8.436 cases of Dengue with alarm signals in 2014 and a significant increase to 20.329 in 2015. The number of confirmed deaths in 2014 was 473, and in 2015 were recorded 863 deaths.

Conclusions

Dengue has increased considerably its impact last year, setting as a persistent public health problem in Brazil. The absence of vaccine and chemoprophylaxis hamper disease control. The development of a vaccine and the adoption of more effective measures to control the disease main vector are priorities for the next future, in view of parallel growth of Chikungunya fever cases and Zika virus infections.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1007
ORAL PRESENTATION SESSION 6 - EPIDEMIOLOGY

CHILDHOOD DEATHS ATTRIBUTABLE TO INVASIVE PNEUMOCOCCAL DISEASE IN ENGLAND AND WALES 2004-2014

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Background

The pneumococcal conjugate vaccine (PCV) was introduced into the United Kingdom childhood immunisation programme in 2006 and has been shown to be highly effective in preventing invasive pneumococcal disease (IPD) across all age groups through direct and indirect (herd) protection. However, deaths attributable to pneumococcal infection do still occur. This study aimed to described the children who died of IPD since P30CV introduction in England and Wales

Methods

Public Health England conducts enhanced IPD surveillance in England and Wales. All PCV-eligible children with IPD were actively followed-up by postal questionnaires and, for fatal cases, detailed information was requested from general practitioners, paediatricians, histopathologists and coroners.

Results

During September 2006 to August 2014 (8 years), there were 3,146 IPD cases in <5 year-old children, 210 of whom died. After follow-up, 59 cases were excluded; 49 deaths were sudden unexpected deaths in infancy (SUDI) or Unascertained, 7 had survived IPD and died later of underlying co-morbidities, and 3 were not UK residents. Of the 151 IPD-associated deaths (case fatality rate, 5%), 133 isolates were serotyped and 83 (63%) were not vaccine-preventable (64 non-PCV13 serotypes, 19 additional PCV13 serotyped prior to PCV13 introduction in 2010). The vast majority of deaths occurred in infants (<1 year-olds, 88/151 cases, 58%) and one year-olds (36/151 cases, 24%). One-third (35%; n=53) had a known risk factor for IPD. Meningitis was the most common clinical presentation among the fatal cases (48%; n=73). Clinical presentation varied by age-group (Figure 1).

Conclusions

The majority of fatal cases of IPD are currently not vaccine preventable. Additional strategies will be required for reducing the burden of childhood pneumococcal deaths in countries with established pneumococcal vaccination programmes

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1012
ORAL PRESENTATION SESSION 6 - EPIDEMIOLOGY

COMPARISON OF CAPSULAR AND PILUS TYPING OF INVASIVE STREPTOCOCCUS AGALACTIAE ISOLATES FROM INFANTS AND ADULTS: RESULTS FROM A NATIONWIDE SURVEILLANCE STUDY IN GERMANY

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Background

Invasive group B streptococcal (GBS) infections are a major cause of morbidity and mortality in infants. They are also emergent pathogens in elderly adults. GBS vaccines based on capsule and pilus antigens are under development. Our study compared capsular and pilus typing of invasive GBS strains from infants and adults in Germany.

Methods

Invasive GBS strains from infants and adults in Germany were collected through a prospective nationwide surveillance study over a two-year period (2009-2010). Capsular type (serotyping and PCR genotyping) and pilus type (PCR genotyping) were determined according to standard methods. For discrepant strains, assignment of capsule type was done according to genotype.

Results

In total, 173 infant, two pediatric and 803 adult invasive GBS isolates were collected. Capsular serotyping was performed on 977 and capsular genotyping on 281 isolates. Agreement between both methods was 100% for type Ia, III, V, and VI. Discrepancies primarily were seen for type IX strains. The five most common capsular types were type III (31.5%), V (25.1%), Ia (21.5%), Ib (10.5%) and II (7.3%). Type Ib, II, and V were overrepresented among adult strains, while type III was underrepresented. Pilus typing was performed on 173 GBS isolates. In 89.6% of isolates, a pilus type was able to be assigned, most often PI1+2a (37.6%), PI1+2b (24.9%), PI2a (20.2%) and PI1a (6.4%). Infant strains more frequently carried PI1+2b, whereas adult strains more commonly carried PI1+2a.

Conclusions

A vaccine consisting of capsular types Ia, III and V would cover 91% of all invasive infant and 75% of all invasive adult GBS strains in Germany. The three most common pilus types (PI1+2a, PI1+2b and PI2a) represent 83% of all invasive GBS strains in Germany.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0859
ORAL PRESENTATION SESSION 6 - EPIDEMIOLOGY

DAYCARE AND CHRONOLOGICAL BURDEN OF RESPIRATORY TRACT INFECTIONS

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Background

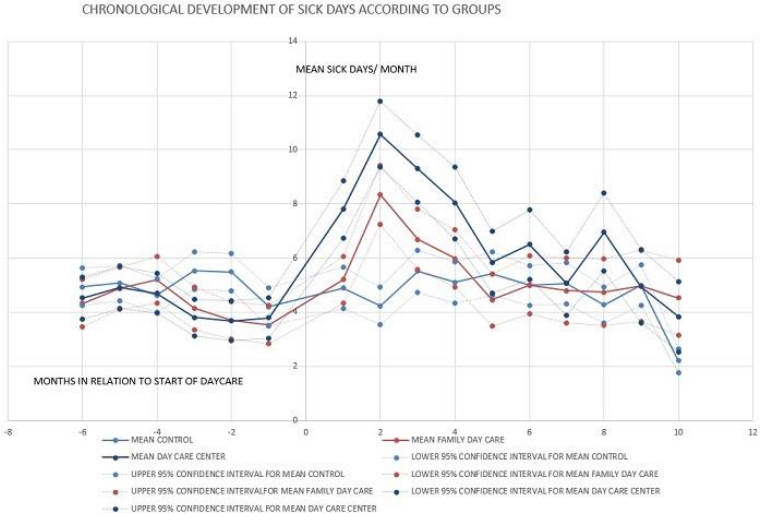
Daycare is a known mediator of infection in children under 2 years of age. Since the majority of children in modern society commence daycare in this age range it constitutes an important public health factor. We explored the chronology of the respiratory infectious disease burden with regard to daycare.

Methods

We followed up a birth cohort of 1827 children until the age of 24 months collecting diary-based data on respiratory tract infections and daycare. Using repeated measures analyses of variance for unbalanced data we analysed sick days, days with antibiotic treatment and parental absence from work for each month 6 months prior to and 10 months after the start of day care, which was further stratified into groups of family day care (n =252) and center-based day care (n =317) . Children of same age in home care (n =369) served as a control group.

Results

We documented a significant effect of time (p<0.0001) and mode of daycare (p<0.0001 sick days; p<0.001 antibiotic treatments; p=0.017 parental absence from work) as well as a significant interaction between them (p<0,0001 sick days and antibiotics; p=0,003 parental absence) for all outcome measures. There was a relative rise of measures after the start of daycare with a subsequent decrease within the following 10 months. Confounding factors (sex, older siblings, maternal education, furry pets, parental asthma, parental smoking, time of year during the start of daycare) were evenly distributed throughout the different groups.



Conclusions

Our study shows the rapid increase in respiratory infections with regard to starting daycare, and a relatively fast decrease in infections in the course of time with continued daycare. This finding highlights the importance of support to families around the start of daycare.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0661
ORAL PRESENTATION SESSION 6 - EPIDEMIOLOGY

ACUTE RESPIRATORY ILLNESS AND RESPIRATORY VIRUS DETECTIONS IN A COMMUNITY COHORT OF INFANTS IN THE FIRST 2-YEARS OF LIFE

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Background: Community-based, longitudinal studies on the incidence and aetiology of acute respiratory illness (ARI) in unselected infants using sensitive molecular-based techniques for detecting respiratory viruses are generally limited, with sampling confined to symptomatic episodes, few control specimens collected and a narrow spectrum of viruses tested. We describe the incidence, epidemiology, and relative pathogenicity of respiratory viruses associated with ARI in a birth cohort of infants.

Methods: An observational, longitudinal, community-based birth cohort study was conducted in Brisbane, Australia from 2010 to 2014. Parents were approached antenatally for their newborn infants to be recruited progressively into the study. A daily tick-box diary captured pre-defined respiratory symptoms from birth until their second birthday. Weekly parent-collected nasal swabs were mailed in and tested for 17 respiratory viruses.

Results: Parents of 154 infants recorded 88,032 child-days of observation (78.2% of maximum expected) during 1,651 ARI episodes (1,370 URTI; 281 LRTI; 0.56 ARIs per child-month (95% CI: 0.54, 0.59)). Of the 11,192 (68.0% of maximum expected) weekly nasal swabs submitted, 3,012 (26.9%) were virus-positive (286 co-detections, 9.5%), of which 1,921 (63.8%) were associated with symptoms. Overall, viruses were detected in 1,200/1,651 (72.7%) ARI episodes. Rhinoviruses predominated, accounting for 2,337 (77.6%) positive swabs. There was moderate evidence for causal attribution for most viruses (attributable fraction (AF) 45-65) in infants with ARI, with weaker evidence for polyomaviruses and bocavirus (AF 18-37).

Conclusions and relevance: ARIs are common in the first 2-years of life, with an average of 13 episodes and almost 5-months of respiratory symptoms. Virus detection in infants aged < 2-years is frequent and often asymptomatic. Given the frequency of asymptomatic viral detection, attributing ARIs to specific viruses in community settings should be done with caution.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0403
ORAL PRESENTATION SESSION 6 - EPIDEMIOLOGY

DYNAMICS OF ANTIBIOTIC-RESISTANCE AMONG NASOPHARYNGEAL NON-VACCINE SEROTYPE PNEUMOCOCCI IN YOUNG CHILDREN FOLLOWING PCV7/PCV13 INTRODUCTION

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Background

Widespread PCV7/PCV13 use reduces PCV13 serotype (VT13) pneumococcal carriage, with a near complete replacement by non-VT13 pneumococci. Most antibiotic-nonsusceptible and multi-resistant pneumococci (NSSP, MDRSP) were VT13 in the pre-PCV period. However, NSSP was already somewhat prevalent in non-VT13 before PCV introduction and was predicted to increase post PCV as result of replacement and continuous antibiotic pressure. Thus, it is important to document post-PCV NSSP colonization in children. Our objective was to evaluate the NSSP colonization dynamics in children <5 years visiting the Pediatric Emergency Room (PER) before and after PCV introduction.

Methods

An ongoing, prospective, population-based, active surveillance, Nov-2009 through Jun-2015. The first 8 children presenting to the PER of the only hospital serving the entire southern Israel population were enrolled daily. PCV7/PCV13 were introduced in Jul-2009/Nov-2010, and coverage (≥2 doses) reached ≥90% within 2 years. Methodology of nasopharyngeal cultures, microbiology, serotyping and susceptibility testing were previously described (Dagan, JID, 211:1144, 2015).

Results

Of 8,446 nasopharyngeal swabs, 4,166 (49%) were positive. Of all isolates, proportions of VT13 pneumococci declined by 67%, and those of non-VT13 pneumococci increased by 189%. A significant increase in prevalence of non-VT13 strains nonsusceptible to penicillin, macrolides, clindamycin and MDR was observed with a 15% reduction in fully susceptible isolates (**Table 1**). Six non-VT13 (15A, 15B/C, 16F, 23B, 23A, 11A) + non-typeable pneumococci constituted 53% of all isolates in 2014-2015. Increases in NSSP within these common non-VT13 serotypes was observed: macrolide resistance (15A, 15B/C, 11A), penicillin (11A, 15B/C, 16F, non-typeable pneumococci), MDR (15A; 15B/C) (**Table 2**).

Table 1. Antibiotic Nonsusceptibility Proportions Among Pneumococcal Non-VT13 isolates in Children <5 Years Attending Pediatric Emergency Room, Southern Israel

	Years						Ratio of proportions, 2014-15 *vs.* 2009-10	P value
	2009-10	2010-11	2011-12	2012-13	2013-14	2014-15		
No. of pneumococcal isolates	579	898	652	696	656	685		
No. (%) of non-PCV13 pneumococcal serotypes of all isolates	261 (45)	526 (58)	474 (73)	559 (80)	558 (85)	584 (85)	1.89	<0.001
Yearly proportions (%) of each susceptibility pattern among all non-PCV13 Isolates								
Susceptible (S) to all*	44	38	32	38	34	38	0.85	0.068
Penicillin MIC ≥0.1 µg/ml	40	43	47	44	52	47	1.20	0.007
Penicillin MIC ≥1.0 µg/ml	9	7	9	11	18	15	1.67	0.023
Erythromycin non S	6	6	9	9	14	15	2.58	<0.001
Clindamycin non S	4	6	9	8	9	10	2.66	0.002
Non S to ≥2 drug classes	19	23	32	25	33	35	1.89	<0.001
Non S to ≥3 drug classes (MDR)	6	7	10	9	16	17	1.60	<0.001

*Antibiotics tested: Penicillin, Resprim, Chloramphenicol, Tetracyclin, Erythromycin, Clindamycin

Table 2. Dynamics of Nonsusceptibility Prevalence Within Selected Pneumococcal non-VT13 Isolates in Children <5 Years, Attending Pediatric Emergency Room, Southern Israel: 2014-15 *vs.* 2009-10

	Serotype													
Proportions (%) of yearly susceptibility patterns, among selected non-VT13 isolates	15A n=178		15B/C n=367		11A n=160		16F n=220		23B n=202		23A n=141		Untypable n=174	
	2009-10	2014-15	2009-10	2014-15	2009-10	2014-15	2009-10	2014-15	2009-10	2014-15	2009-10	2014-15	2009-10	2014-15
Susceptible to all*	63	41	**30**	**9**	50	45	50	19	54	49	100	87	0	13
Penicillin MIC ≥0.1 µg/ml	37	55	47	59	**0**	**23**	39	54	36	47	0	3	100	80
Penicillin MIC ≥1.0 µg/ml	5	0	**0**	**13**	0	3	**15**	**35**	0	0	0	0	**22**	**35**
Erythromycin non S	16	41	**5**	**43**	0	10	0	0	0	0	0	3	78	56
Clindamycin non S	16	38	**8**	**41**	0	6	0	2	0	0	0	0	11	22
Non S to ≥2 drug classes	26	48	**40**	**58**	**0**	**29**	**21**	**48**	36	47	0	3	90	80
Non S to ≥3 drug classes (MDR)	16	41	**8**	**42**	0	10	0	0	0	0	0	3	67	61

BOLD=P value <0.05 ; linear trend in proportions for all years 2009-10 to 2014-15
*Antibiotics tested: Penicillin, Resprim, Chloramphenicol, Tetracyclin, Erythromycin, Clindamycin

Conclusions

Carriage of non-PCV13 NSSP and MDRSP increased in a pattern that strongly suggests a dual effect: vaccine-induced serotype replacement on one hand, and continuous antibiotic pressure on the other hand.

ESP16-0924
ORAL PRESENTATION SESSION 6 - EPIDEMIOLOGY

THE ECOLOGICAL EFFECTS OF SHORT-COURSE INTRAVENOUS ANTIBIOTICS IN CHILDREN: PILOT CHANGES IN THE GUT MICROBIOME

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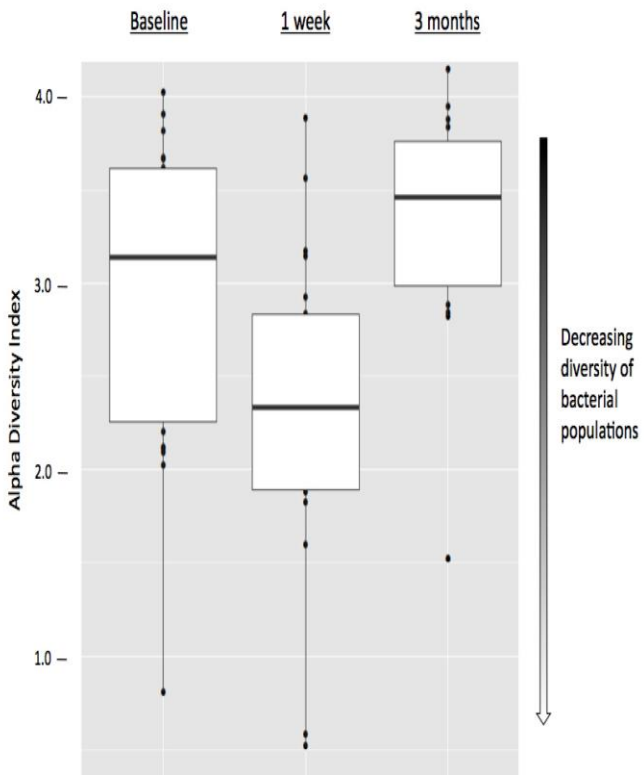
Background and Aims: Antibiotic use is associated with selection of resistant bacteria and in adults disrupts the gastrointestinal microbiota for years. The effects of antibiotics on the gut microbiome in children remain largely unknown and the few published studies have focused largely on neonates. We aimed to assess longitudinally the effects of intravenous antibiotics on the diversity of the gut microbiome.

Methods: Children aged 6 months-18 years presenting to Emergency with moderate/severe cellulitis treated with short-course intravenous followed by oral antibiotics were included. Stool samples were collected at 3 time points: baseline, 1 week (maximal antibiotic pressure) and 3 months (post antibiotic washout) after the first dose of intravenous antibiotics. After DNA extraction, microbiome diversity was assessed by amplicon sequencing analysis of the 16S rRNA V3-V4 region.

Results: Stool samples were collected from 45 children. Stool samples were collected from 45 children. There was a significant difference in bacterial population diversity between baseline and 1 week (median diversity index 3.2 versus 2.3, $p=0.01$), but there was no difference by 90 days (3.2 versus 3.5, $p=0.29$) (figure). Phylogenetic analysis showed specific Firmicutes and Bacteroidetes were reduced at 1 week ($p<0.001$) but the majority recovered by 90 days ($p>0.05$). Two *Bacteroides* species were persistently low at 90 days ($p<0.001$) and uniquely *Coprococcus* had increased ($p<0.001$).

Conclusions: This is the first time that it has been shown that even short-course intravenous antibiotics can reduce bacterial diversity in the gut, but overall changes do not persist. How different antibiotics affect the microbiome and the implications on short-term selection of resistance will be part of a larger study. However, these pilot data reassure about short course antibiotic use in healthy children.

Figure attached



ESP16-0115
ORAL PRESENTATION SESSION 7 - RESPIRATORY TRACT INFECTIONS

HUMAN BOCAVIRUS IN HOSPITALIZED CHILDREN AND COMPARISON WITH OTHER RESPIRATORY VIRUSES.

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Background

The clinical characteristics of human bocavirus(hBoV) infections and its role are not yet well established. Our aim was describing and comparing hBoV infections in hospitalized children with respiratory syncytial virus(RSV), rhinovirus(RV), and human metapneumovirus(hMPV) single infections in the same population.

Methods

From September 2005 to August 2014 a prospective study was conducted on children under 14, admitted with respiratory infection to the Severo Ochoa Hospital(Spain). Specimens of nasopharyngeal aspirate were taken for virological study by using polymerase chain reaction, and clinical data were recorded.

Results

3275 episodes of respiratory infections were analyzed. At least one virus was detected in 76.5%(2504). A total of 320 episodes were associated to hBoV(9.8%), 80 single infections, and 240 coinfections. Single hBoV infections were mainly in November and December(50%), in children of 24.7+24 months of age. 69% had fever, 52% hypoxia and 47% infiltrate in X-ray. Recurrent wheezing(60%) and pneumonia(22%) were the most common diagnoses.

Single infections (665 RSV, 555 RV and 108 hMPV) were compared with single hBoV infections(80). RSV single infections affected younger children (9 vs 24 months,p<0,001), had more frequently hypoxia, (71% vs 52%,p<0.001), and the most frequent diagnosis was bronchiolitis (63%, vs 17%,p<0.001). Days of admission (p=0.002) at hospital and duration of hypoxia (p=0.04) was longer in RSV group. hBoV patients had more frequent pneumonia, higher C-reactive protein (p<0.001) and antibiotic treatment (41% vs 17%,p<0.001).

RV children had less frequently fever (69% vs 41%,p<0.001), and pneumonia (11% vs 23%,p<0.001). hMPV children had less proportion of pneumonia (8.4% vs 23%,p=0.14) and CRP (35+41 vs 67+79,p=0.004) and leukocytosis(p=0.019).

Conclusions

HBoV infections are frequent in hospitalized children and associate to fever, pneumonia, increased CRP and antibiotic treatment. There are significantly differences with other respiratory virus infections.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0127
ORAL PRESENTATION SESSION 7 - RESPIRATORY TRACT INFECTIONS

THYMIC STROMAL LYMPHOPOIETIN AND PERIOSTIN IN HOSPITALIZED INFANTS WITH VIRAL BRONCHIOLITIS

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Background

Much attention has recently been focused on thymic stromal lymphopoietin (TSLP) and periostin in allergic disease, but less is known about their role in viral bronchiolitis. Objective: to evaluate the immune response in the airway of infants hospitalized due to bronchiolitis and determine whether immune response is related to disease severity or viral etiology.

Methods

One hundred thirty-seven infants under 2 years of age who were hospitalized with bronchiolitis from October 2013 to January 2015 were enrolled alongside 23 healthy infants. Nasopharyngeal aspirates(NPA) were screened for respiratory viruses by polymerase chain reaction. TSLP, periostin, IL-10, and IFN- γ were measured in NPAs. Clinical data were recorded.

Results

At least one virus was detected in 123(89.7%) hospitalized infants: respiratory syncytial virus(RSV), 93(68%); rhinovirus, 32(23%); parainfluenza virus, 9(6.6%); adenovirus, 6(4.3%); human bocavirus, 4(3%); and human metapneumovirus, 3(2%). Infants with bronchiolitis had higher levels of cytokines than healthy controls (TSLP $p<0.001$, periostin $p<0.05$, IL-10 $p<0.001$, IFN-γ $p=0.003$). Detectable levels of TSLP and periostin were more frequent in virus-positive than in virus-negative patients ($p<0.005$). TSLP was also more common in coinfections (RSV+rhinovirus) than in single infections ($p<0.005$). All viruses elicited Th1 and Th2 responses, but there was a predominance of Th2 cytokine in the rhinovirus group as evidenced by higher TSLP/IFN ratio in rhinovirus infections (dual $p<0.05$ or single infections $p=0.06$). Higher TSLP/IFN ratio was associated with oxygen saturation ≤ 89%($p=0.07$) and with admission ≥5 days ($p=0.08$), suggesting a more severe clinical course in those infants with predominant Th2 response.

Conclusions

Severe bronchiolitis caused by the most common respiratory viruses is associated with elevated nasal TSLP, periostin, IL-10, and IFN- γ. Our findings suggest that rhinovirus, RSV, and hMPV bronchiolitis may shift immune response towards Th2.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0434
ORAL PRESENTATION SESSION 7 - RESPIRATORY TRACT INFECTIONS

INFLUENZA B VIRUS, IRON DEFICIENCY ANAEMIA AND FOOD ALLERGY ARE PREDICTORS OF SEVERE INFLUENZA IN HOSPITALISED YOUNG CHILDREN

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Background

Influenza infection can result in severe disease with debilitating complications. Young children have the highest rate of influenza hospitalisations with various factors influencing susceptibility to and severity of, infection. This study aimed to determine the disease burden and assess risk factors for severe influenza in hospitalised children under 5 years of age by completing a detailed clinical audit of all children admitted to the tertiary paediatric hospital in South Australia from 2008-2012.

Methods

Data on laboratory-confirmed influenza cases were collected, including infecting influenza strain, co-infections, prematurity, pre-existing co-morbidities and other potential risk factors. A standardised data collection tool was used and 10% of data audited to ensure accuracy. Predictors of high level care were assessed using univariate and multivariable logistic regression.

Results

A total of 267 children with laboratory-confirmed influenza were hospitalised. Of these, 147 hospitalisations (53%) occurred in children without underlying medical risk factors. Eighteen children (7%) required high level care, of which 11 (61%) had no underlying medical conditions. The majority of children were unimmunised against influenza, with only four having documented evidence of influenza vaccination. Co-infections were identified in 40% of children (n=107). Influenza B virus was associated with requirement for higher care (OR 3.7, CI 1.3-10.9, p=0.0.02) as was a history of food allergies (OR 9.7, CI 1.5-61.4, p=0.0.02) and iron deficiency anaemia (OR 4.8, CI 1.4-16.1, p=0.01).

Conclusions

Influenza can be a severe illness, even in healthy children without underlying medical conditions. The identification of influenza B virus, history of food allergies and iron deficiency anaemia as predictors of severe disease in hospitalised cases warrants further investigation and has important implications for preventative strategies to reduce the burden of childhood influenza, including improved coverage against influenza B viruses.

ESP16-0187
ORAL PRESENTATION SESSION 7 - RESPIRATORY TRACT INFECTIONS

NO EFFECT OF ORAL ZINC ON PLASMA CYTOKINE CONCENTRATION IN CHILDREN WITH SEVERE OR NON-SEVERE PNEUMONIA: A RANDOMIZED PLACEBO CONTROLLED TRIAL

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Background

Children in low-and middle-income countries have a high burden of respiratory tract infections and zinc deficiency is common. An appropriate balance between pro-and anti-inflammatory cytokines is required for effective immune responses against pathogens, and normal zinc homeostasis is identified as an important component in regulation of the immune response. The objective of this study was to measure the effect of oral zinc on plasma cytokine concentrations in children with community acquired pneumonia (CAP).

Methods

Children aged 2 – 35 months with severe (n=43) and non-severe (n=387) CAP was included and randomized to receive oral zinc (10 mg to infants and 20 mg to older children) or placebo for 14 days in addition to standard antibiotic treatment. The plasma concentrations of 27 cytokines were measured at baseline and 14, 45 and 90 days after enrolment.

Results

There were no differences in the cytokine concentration between the zinc and placebo groups, except for the concentration of platelet derived growth factor- subunit B after 14 days.

Conclusions

In conclusion, oral zinc treatment in children with CAP did not affect the cytokine concentrations.

Clinical Trial Registration (Please input N/A if not registered)

clinicaltrials.gov NCT0014733

ESP16-0840
ORAL PRESENTATION SESSION 7 - RESPIRATORY TRACT INFECTIONS

GENE POLYMORPHISMS OF MANNOSE-BINDING LECTIN AND TOLL-LIKE RECEPTORS 2, 3, 4, 7 AND 8 AND RISK OF RESPIRATORY INFECTIONS AND ACUTE OTITIS MEDIA

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Background

Genetic variations may predispose to infections, but genetic susceptibility to rhinovirus infections and acute otitis media is not well known.

Methods

In a prospective cohort setting, blood samples from 410 Finnish children were analyzed by pyrosequencing for polymorphisms in mannose-binding lectin (MBL) structural gene at codons 52, 54, and 57, TLR2 Arg753Gln, TLR3 Leu412Phe, TLR4 Asp299Gly, TLR7 Gln11Leu, and TLR8 Leu651Leu. Children were followed for respiratory infections until 24 months of age with daily symptom diaries. Nasal swabs were taken at the onset of respiratory symptoms and PCR and antigen tests were used for detection of respiratory viruses.

Results

Of the study children, 33% had variant types in MBL, 5% in TLR2, 53% in TLR3, 17% in TLR4, 40% in TLR7, and 58% in TLR8. Rates of respiratory illness days per year correlated with MBL variant genotype (variant type vs. wild-type, median 53 vs. 45 days per year, p=0.048) and TLR4 variant genotype (median 53 vs. 44 days per year, p=0.045). Rates of acute otitis media were significantly higher in children with TLR2 variant type (median 1.5 vs. 0.5 per year, p=0.008). TLR7 variant genotype was associated with lower rate of rhinovirus infections (p=0.025). TLR3 and TLR8 polymorphisms were not associated with the rates of respiratory infections, acute otitis media, or rhinovirus infections.

Conclusions

Genetic polymorphisms of MBL and TLR4 are associated with respiratory infections, and variants of TLR2 with acute otitis media.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0173
ORAL PRESENTATION SESSION 7 - RESPIRATORY TRACT INFECTIONS

CLINICAL AND LABORATORY CHARACTERISTICS OF RADIOGRAPHICALLY-DIAGNOSED ALVEOLAR COMMUNITY-ACQUIRED PNEUMONIA (RD-A-CAP) IN THE PCV13 ERA

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Background

Radiographic diagnosis is widely practiced to determine alveolar pneumonia as an outcome measuring efficacy and impact of PCVs. The aim of the present study was to compare selected clinical and laboratory characteristics of RD-A-CAP cases in children <5yrs during the PCV13 era to those occurring before PCV introduction.

Methods

A prospective population-based study, conducted between 2004 and 2015, in southern Israel. All hospital visits of children <5yrs old with RD-A-CAP to the only hospital in the region were included. PCV7 was introduced in the National Immunization Plan in Jul-2009 and was replaced by PCV13 in Nov-2010. Clinical and laboratory data were compared in 2 distinct periods: Pre-PCV (Jul-04 to Jun-08) and PCV13 (Jul13-Jun15). RD-A-CAP was prospectively diagnosed as per the WHO protocol (Greenberg et al, Vaccine 33:4623-9, 2015).

Results

3871 and 1074 episodes were studied in the pre-PCV and PCV13 periods, respectively. Compared with the pre-PCV period, during the PCV13 era children were younger; higher proportion was hospitalized, but for shorter duration; higher proportion had desaturation, cough and runny nose; lower proportion had high temperature, vomiting, presence of pleural fluid, anemia, high blood leukocytes counts and higher CRP concentrations. Detection of

respiratory viruses, mainly RSV, was more common during PCV13 period (**Table**).

Table: Comparison of clinical and laboratory characteristics: Pre-PCV *vs.* PCV13 periods in children <5 years old with RD-A-CAP

	Pre-PCV n=3781*	PCV13 n= 1074*	OR**/r†	95% CI
Mean age, months ± SD (median)	21.0±15.7 (17.3)	18.9±15.5 (14.2)	-	-
Hospitalized n, (%)	2319 (59.9)	793 (73.8)	1.822	1.557-2.133
Duration of hospitalization, days + SD (median)	3.9+7.2 (2.0)	2.9+5.2 (1.0)	-0.072	-0.580 to -1.658
Temperature >38.5^{0}C, n (%)	2667 (70.1)	675 (65.9)	0.854	0.736-0.991
Oxygen saturation <92%, n (%)	979 (25.9)	340 (33.3)	1.355	1.162-1.581
Runny nose, n (%)	2214 (70.7)	710 (80.1)	1.666	1.384-2.006
Cough n (%)	3175 (88.2)	910 (91.5)	1.380	1.077-1.768
Vomiting, n (%)	1184 (38.4)	288 (31.7)	0.767	0.654-0.899
Presence of pleural fluid n (%)	76 (2.0)	6 (0.6)	0.304	0.132-0.701
Blood WBC> 20,000 cell/µL, n (%)	1226 (34.0)	308 (31.3)	0.939	0.803-1.096
Mean maximal ANC cell/µL recorded ±SD (median)	12.2±7.9 (10.4)	10.4±6.7 (9.2)	-0.069	-0.779 to -1.813
Hb <10 g/dL, n (%)	846 (23.4)	143 (14.5)	0.532	0.430-0.636
CRP >70 mg/L, n (%)	212 (56.2)	81 (44.0)	0.693	0.478-1.004
Detection of any respiratory virus, n (%)	509 (44.7)	282 (60.8)	2.000	1.566-2.555
RSV, n (%)	390 (34.2)	194 (42.2)	1.375	1.071-1.765
Influenza, n (%)	33 (2.9)	18 (4.4)	1.522	0.854-2.741

* Not all data were available for all patients

** OR, Odds ratio adjusted for age, ethnicity and season

† Pearson coefficient correlation r in linear regression, adjusted for age, ethnicity and season

CI, confidence interval; ANC, absolute neutrophil count

Conclusions

Compared with the pre-PCV period, the clinical and laboratory findings of children <5 years with RD-A-CAP in the PCV13 era fitted less the characteristic description of what is considered "classical" bacterial alveolar pneumonia; they resembled more the “classical” description of pure viral respiratory disease. It is plausible that some disease interpreted radiographically as alveolar pneumonia, may not be in fact a bacterial disease, and this fraction constitutes a higher proportion after PCV13 introduction compared to the pre-PCV era.

ESP16-0607
ORAL PRESENTATION SESSION 7 - RESPIRATORY TRACT INFECTIONS

THE FREQUENCY OF RESPIRATORY VIRUSES AMONG CHILDREN WITH NON-SEVERE COMMUNITY-ACQUIRED PNEUMONIA

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Background

Community-acquired pneumonia(CAP) is a leading cause of death and hospitalization in children worldwide. The role of respiratory viruses in this condition remains unclear. We estimated the frequency of respiratory viruses detected in children with CAP.

Methods

This study was conducted at one centre in Brazil where children aged 2-59 months with non-severe CAP were diagnosed by paediatricians based on respiratory complaints and radiographic pulmonary infiltrate/consolidation. Out of 820 children recruited in a clinical trial, 774(94.4%) had nasopharyngeal aspirate collected and tested for 16 viruses by PCR. For those with human bocavirus detected, specific IgM and IgG were quantified in 161 paired serum samples.

Results

Viruses were detected in 708(91.5%) of the cases, out of which 491(69.4%) had multiple viruses detected. Rhinovirus (n=357;46.1%), adenovirus (n=297;38.4%), enterovirus (n=205;26.5%), respiratory syncytial virus(RSV) (n=193;24.9%), bocavirus (n=174;22.5%), parainfluenza virus(Paraflu) (n=159;20.5%), metapneumovirus (n=100;12.9%), influenza virus(Flu) (n=66;8.5%) and coronavirus (n=64;8.3%) were identified. In regard to subgroups of the aforementioned viruses, RSVA(14.2%), RSVB(10.5%), Paraflu1(4.0%), Paraflu2(3.6%), Paraflu3(8.8%), Paraflu4(6.1%), FluA(5.4%), FluB(3.4%), coronavirus-Oc43(5.6%), coronavirus-nl63(2.1%), and coronavirus-229e(1.7%) were found. Thirty-nine(5.1%) children had bocavirus infection diagnosed by serology. Except RSV and Flu, all viruses were more frequently found in cases with co-detection.

Conclusions

Respiratory viruses were detected in over 90% of the cases, out of which approximately 70% had multiple viruses. RSV and Flu were similarly found among cases with multiple or sole detection.

ESP16-0158
ORAL PRESENTATION SESSION 7 - RESPIRATORY TRACT INFECTIONS

IMPACT OF PCV13 ON COMMUNITY ACQUIRED PNEUMONIA ACCORDING TO THE C-REACTIVE PROTEIN AND PROCALCITONIN THRESHOLDS IN CHILDREN

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Background

An early and strong impact of PCV13 on community acquired pneumonia (CAP) had been already demonstrated in many countries. As C-reactive protein (CRP) levels and Procalcitonin (PCT) are considered as markers of pneumococcal infection, PCV13 should not change the trend of CAP with low CRP and PCT levels. To demonstrate this assumption we analyzed the evolution of the number of CAP according to the CRP and PCT thresholds, 5 years after PCV13 implementation (june 2010).

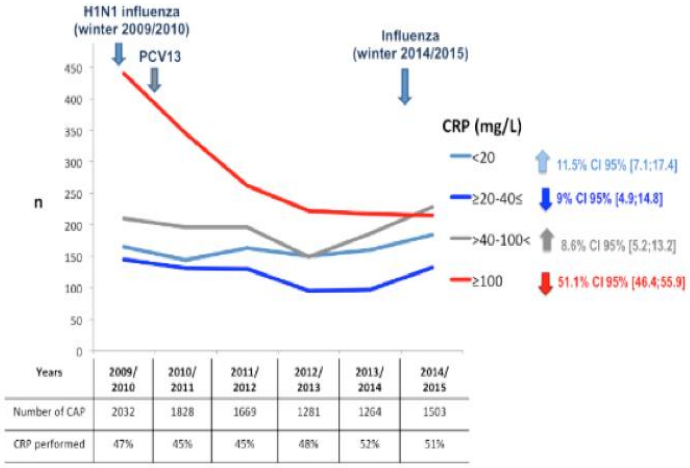
Methods

8 emergency units enrolled prospectively all children (1 month to 15 years) with CAP or empyema (EP) from June 2009 to May 2015.

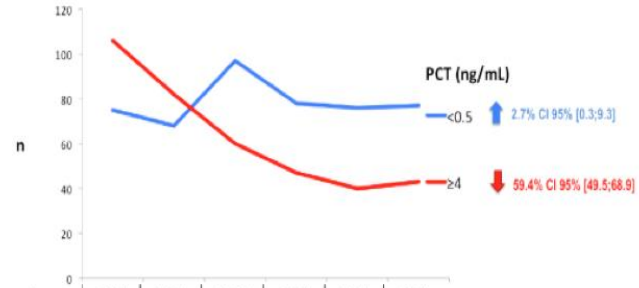
Results

9577 patients were enrolled (median age 3 years), EP and pneumococcal pneumonia accounted for 5.7% and 2% of cases, respectively. From 2009 to 2015, CAP decreased by 26%, hospitalized CAP by 31%, EP by 52% and PP by 86%. The decrease of CAP cases started from a level of CRP at 100 mg/L. In 2014/2015, CAP with CRP ≤20 mg/L slightly

increased.



Years	2009/2010	2010/2011	2011/2012	2012/2013	2013/2014	2014/2015
Number of CAP	2032	1828	1669	1281	1264	1503
CRP performed	47%	45%	45%	48%	52%	51%



Years	2009/2010	2010/2011	2011/2012	2012/2013	2013/2014	2014/2015
PCT performed	13%	13%	13%	14%	13%	12%

Conclusions

As expected, PCV13 has no impact on CAP with low levels of CRP or PCT. 5 years after PCV13 implementation, sustained reduction of CAP is observed and the slight increase in 2014/2015 is probably due to the intensity of influenza winter season.

Acknowledgment: study funded by an unrestricted grant from Pfizer.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0376
ORAL PRESENTATION SESSION 7 - RESPIRATORY TRACT INFECTIONS

TUBERCULOSIS IN HIV-INFECTED CHILDREN IN EASTERN EUROPE

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Background

There is a high burden of tuberculosis (TB) in people living with HIV in Eastern Europe (EE), but few data are available on HIV-infected children in the region.

Methods

We described incidence, presentation, management and outcomes of TB in HIV-infected children aged <16 years, diagnosed with TB in 2011-2013, in EE clinical sites in the Paediatric European Network for Treatment of AIDS, within the Paediatric TB:HIV EuroCoord Study.

Results

Of 2727 HIV-infected children followed-up, 80 (3%) were diagnosed with TB in 11 EE sites (3 Russia, 7 Ukraine, 1 Latvia); estimated TB incidence was 982/100,000 person-years. Median age at TB diagnosis was 5.3 (IQR 3.0, 9.4) years. Most (85%) were diagnosed with TB after HIV at median time 35.2 (IQR 11.1, 68.7) months; of these 21(31%) had anti-TB prophylaxis. Overall, half were on antiretroviral therapy (ART) and 57% (44/77) had no/mild WHO stage immunodeficiency at TB diagnosis. Of those not on ART, 93% (37/40) started at median 1.5 (IQR 0.8, 3.2) months after TB diagnosis. Of TB clinical forms, 38(48%) had pulmonary only, 22(28%) extrapulmonary and 20(25%) pulmonary and extrapulmonary TB. One-third (n=28) had confirmed TB and 8 had multidrug-resistance. Streptomycin was used in 24 (30%) children; of these only 3 had recurrent TB. Second-line drugs with no confirmed/suspected resistance were used in a third of cases (n=24). Six (8%) discontinued any anti-TB drugs for toxicity. Five children had unfavourable TB outcomes: 3 died (one, non-TB related cause), 2

did not complete treatment. Not being virologically supressed on ART at TB diagnosis was univariably associated with unfavourable outcome.

Conclusions

Early ART may reduce TB in this population. Sub-optimal practices (streptomycin use and inappropriate use of second-line drugs) should be addressed through training.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1004
ORAL PRESENTATION SESSION 8 - SEVERE INFECTIONS

CONGENITAL TUBERCULOSIS: A EUROPEAN CASE SERIES - ON BEHALF OF THE PAEDIATRIC TUBERCULOSIS NETWORK EUROPEAN TRIALS GROUP

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Title of Case(s)

CONGENITAL TUBERCULOSIS: A EUROPEAN CASE SERIES on behalf of the Paediatric Tuberculosis Network European Trials group (ptbnet)

Background

Congenital tuberculosis (cTB) is a rare infection of unknown incidence, difficult diagnosis with controversial diagnostic criteria and poor prognosis. No case series have been published in the European setting. Current diagnostic criteria do not include novel diagnostic methods.

Case Presentation Summary

We present a case series of eleven cTB cases from 1995 to 2015 from nine European ptbnet centers. Cantwell's criteria were used for diagnosis of cTB. Three patients were Black African, three White, two Moroccan, two Pakistani and one Chinese White. Six infants were premature and presented earlier than term infants. Time to diagnosis was on average 2.5 weeks. All infants had pulmonary TB of which seven had miliary hepatic infiltrates. Ten infants had microbiological confirmation with culture and/or PCR. Interferon gamma release assays (IGRA) were positive in four out of five infants tested; TST was positive in three out of six tested. Infant mortality was 10%.

Three mothers were known to be symptomatic during pregnancy and/or have known household TB contact. All mothers had antenatal or postnatal symptoms suggestive of TB, on

average for 7.5 weeks before diagnosis of cTB; only one mother was diagnosed before delivery.

Learning Points/Discussion

Maternal TB screening and treatment during pregnancy is imperative to prevent transmission. Comprehensive TB guidelines are needed. cTB should be suspected in any symptomatic baby born to high-risk mothers (HIV positive, living in high TB incidence areas, symptomatic). IGRA test was positive in 4 of 5 cases tested and microbiology was positive in ninety percent.

Current congenital TB diagnostic criteria were not met by 50% of the infants and should be revised to include IGRA and PCR tests.

ESP16-1078
ORAL PRESENTATION SESSION 8 - SEVERE INFECTIONS

EPIDEMIOLOGY OF NEONATAL INFECTIONS IN THE UK FROM THE NEONIN (HTTPS://WWW.NEONIN.ORG.UK). INFECTION SURVEILLANCE NETWORK

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Background

Neonatal infection is a significant cause of morbidity and mortality. It is vital to monitor the epidemiology of neonatal infection and assess associated risk factors in order to inform clinical practice and policy. This study aimed to describe the epidemiology of neonatal infection among a surveillance network of UK neonatal units (NNUs).

Methods

neonIN is an international web-based infection surveillance database of culture proven neonatal infections. Cases from UK-NNUs between January 2004 and December 2014 were extracted. Early-onset sepsis (EOS) was defined as occurring within 48 hrs from birth. Repeated growth of the same organism within 7 days was considered the same episode (or 10 days for Coagulase-negative Staphylococci and fungi).

Results

4,630 episodes were recorded, involving 3,819 infants (56% male), from 30 NNUs. The overall incidence was 6.1/1000 live-births and 49.2/1000 NNUs admissions. A decreasing trend

(p<0.001) was observed in both the overall and LOS rates over the 10-year study period. Further results are shown in Table-1.

	Early Onset Sepsis (n=698)			*Late Onset Sepsis (n=3,932)*				
	GP (n=564)	GN (n=129)	p (GN EOS v GP EOS)	GP (n=3,011)	GN (n=757)	Fungi (n=164)	p (Fungal LOS v GN LOS)	p (GN EOS v GN LOS)
Most common pathogen (n (%))	Group B Streptococcus (225, (39.9))	*E. coli* (95, (73.6))	--	CoNS (2,320, (77.0)) or *S. aureus* (221, (7.3)) (if CoNS excluded)	*E. coli* (240, (31.7))	*C. albicans* (106, (64.6%))	--	--
Gestational age (weeks)	37 (31-40)	29 (25-34)	<0.0001	26 (25-29)	26 (24-29)	25 (24-27)	0.0001	<0.0001
Birth weight (g)	2750 (1500-3500)	1,215 (860-2,020)	<0.0001	850 (680-1233)	830 (658-1200)	760 (655-920)	0.0018	<0.0001
Postnatal age (PNA) (days)	0 (0-1)	0 (0-0)	--	16 (8-35)	22 (10-45)	14 (9-22)	<0.0001	--
Isolated from blood (n (%))	545 (98.4)	125 (97.7)	0.58	2,874 (96.9)	668 (89.7)	112 (68.3)	<0.0001	0.0038
Treated for meningitis (n (%))	59 (11.0)	20 (15.9)	0.12	132 (4.5)	82 (11.1)	16 (10.2)	0.69	0.14
Central line *in-situ* (n (%))	81 (14.5)	38 (29.5)	0.0003	1,686 (56.5)	397 (53.2)	117 (73.1)	<0.0001	<0.0001
Line removed due to infection (n (%))	10 (3.9)	2 (2.8)	0.33	704 (31.2)	148 (27.3)	52 (38.5)	0.0026	<0.0001
CRP (mg/dL)	21 (1-56)	35 (3-76)	0.36	22 (4-68)	73 (13-147)	44 (9-85)	0.0028	<0.0001

Table 1: Median (IQR). EOS: early onset sepsis. LOS: late onset sepsis. GP: Gram positive. GN: Gram negative. CoNS: Coagulase negative staphylococci. CRP(mg/dL): max CRP within 48 hours of culture taken, PNA: postnatal-age. EOS fungal infections are not displayed due to their low number (n=4).

Neonates with Gram-positive (GP) EOS had higher birth-weight and gestational-age than those with Gram-negative (GN) EOS (p<0.001 for both). GN-LOS was associated with a greater postnatal-age and CRP compared to fungal cases (p<0.001 and p<0.002). Infants with GN-LOS had lower birth-weight and gestational-age and higher CRP compared to those with GN-EOS (p<0.001 for all).

Conclusions

The neonIN database provides comprehensive longitudinal data on neonatal infections from a large, well-defined geographic population. This represents a unique opportunity for describing and understanding disease burden, defining empiric antibiotic policies and identifying research priorities.

On behalf of the Neonatal Infection Surveillance Network (neonIN)

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0249
ORAL PRESENTATION SESSION 8 - SEVERE INFECTIONS

CLINICAL FEATURES AND FACTORS ASSOCIATED WITH DEATH IN EBOLA VIRUS DISEASE AMONG CHILDREN AGED ≤5 YEARS: A RETROSPECTIVE COHORT STUDY

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Background

The case fatality in the 2013-16 West African Ebola virus disease epidemic has been highest in young children. Clinical features in children and their relationship to outcome has been neglected and published clinical data in this epidemic have largely been limited to symptoms reported on arrival at treatment facilities, rather than observed during admission.

Methods

In a retrospective cohort study we included all children aged ≤5 years admitted, with laboratory confirmed Ebola virus disease, to the Médecins Sans Frontières (MSF) Ebola Management Centres in Bo and Kailahun, Sierra Leone from June-December 2014.

We describe demographic and clinical characteristics and Ebola virus cycle thresholds, and assess their association with death using Cox regression modelling.

Results

Of the 91 children included, 52 died (57.1%). Case fatality was higher in children <2 years (76.5% [26/34]) than those aged 2-5 years (45.6% [26/57]; adjusted hazard ratio 3.5 [95% CI 1.5-8.5]) and in those with high vs low viral load (81.8% [18/22] vs 45.9% [28/61], respectively; adjusted hazard ratio 9.2 [95% CI 3.8-22.5]).

Symptoms observed during admission included: weakness 74.7% (68); fever 70.8% (63/89); pain 63.7% (58); anorexia 60.4% (55); diarrhoea 59.3% (54); and cough 52.7% (48). At admission, 25% (19/76) were afebrile. Signs significantly associated with death were fever, vomiting, and diarrhoea. Hiccups, bleeding, and confusion were observed only in children who died.

Conclusions

This study confirms the vulnerability of younger children to succumb to Ebola virus disease, especially those with a high viral load at presentation. It illustrates the symptom profile and encourages the broader recognition of pain, with implications for training and care. Collection and analysis of age-specific data on Ebola is critical to ensure that the specific vulnerabilities of children are not over-looked.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1079
ORAL PRESENTATION SESSION 8 - SEVERE INFECTIONS

PRESENTATION, MANAGEMENT AND OUTCOME OF BACTERIAL MENINGITIS IN YOUNG INFANTS IN THE UNITED KINGDOM AND IRELAND

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Background

The incidence of acute bacterial meningitis is highest in young infants and has remained unchanged in the United Kingdom (UK) and Ireland for the last three decades. Understanding the clinical characteristics and management of cases is important in trying to improve outcomes.

Methods

Prospective, enhanced, population-based active surveillance was undertaken to determine the presentation, management, and short-term outcome of bacterial meningitis in infants aged <90 days in the UK and Ireland from July 2010 to July 2011.

Results

A total of 364 cases were identified. Most infants had non-specific features; the “classic” features of meningitis: seizures, bulging fontanelle, coma and neck stiffness were reported in 79 (24%), 64 (19%), 16 (5%) and 9 (3%) cases, respectively, whilst fever was reported in 176 (53%). A bacterium was identified in 298 (82%) cases and varied by age at presentation, route of admission and gestation at birth. For cases where the antimicrobial susceptibility of the pathogen was reported, 240/242 (99%) would have been covered by a combination of cefotaxime plus amoxicillin/ampicillin, while cefotaxime alone would have provided coverage for all cases >30 days. Of the 26% of cases (86/329; 95% CI: 22-31) who either died (n=25) or had a serious neurological complication (n=61), coma, seizures and temperature instability upon admission, high CSF protein and infection with *Streptococcus pneumoniae*, were all independent risk factors.

Conclusions

The presentation of bacterial meningitis in young infants is often non-specific and only half of cases present with fever. Poor outcome in this age group remain unacceptably high.

ESP16-0837
ORAL PRESENTATION SESSION 8 - SEVERE INFECTIONS

NEOMERO-2: A EUROPEAN MULTICENTRE PHASE I-II CLINICAL TRIAL OF MEROPENEM IN INFANTS <3 MONTHS WITH BACTERIAL MENINGITIS (BM)

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Background

Neonatal BM is a serious disease with death in 10-30% and long-term disabilities in 20- 50%. Development of antibiotic resistance among pathogens is of major concern. Meropenem is an attractive candidate for empiric therapy but is unlicensed in this population. NeoMero2 aimed to evaluate the safety and outcomes in infants with BM treated with meropenem.

Methods

Inclusion: Infants <90 days with clinical signs of BM and/or CSF pleocytosis and/or +ve CSF Gram stain. Doses: 40 mg/kg 8 hourly (<32 weeks GA and <2 weeks post-natal age (PNA): 40 mg/kg 12 hourly). Duration: 21±7 days. Favourable outcome was defined at Test of Cure visit, 2 days after end of allocated treatment: alive with clinical / bacteriological resolution, no occurrence of new clinical or laboratory abnormalities requiring a new course of antibiotics, no modification of meropenem therapy for >24 hours. Clinical and biological adverse events (AEs) were recorded until the 45-day follow-up (FU) visit.

Results

Fifty-one infants [median (IQR) PNA 11d (4-22), birth weight 2.9 kg (1.45-3.54)] were enrolled in 21 sites across 6 countries. BM was culture-confirmed in 28 (55%, 50% Gram-negative bacteria) and probable (clinical signs AND pleocytosis ≥ 100 cells/mm^3) in 5 (10%). Twenty infants (61%) had a favorable outcome, 1 (3%) microbiological failure and 12 (39%) did not complete therapy as per protocol. 100% survival was observed to FU with no clinical relapses or new infections. AEs were common, 17 were serious (13 infants), but none reported to have a causal relationship with meropenem.

Conclusions

Meropenem appears to be suitable for the treatment of neonatal BM with a very low rate of microbiological failure, a high rate of survival and a satisfactory safety profile.

Clinical Trial Registration (Please input N/A if not registered)

EudraCT : 2011-001521-25

ESP16-0199
ORAL PRESENTATION SESSION 8 - SEVERE INFECTIONS

IMPACT OF PCV7/PCV13 INTRODUCTION ON INVASIVE PNEUMOCOCCAL DISEASE (IPD) IN YOUNG CHILDREN: COMPARISON BETWEEN MENINGITIS AND NON-MENINGITIS IPD

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[3]HaEmek Medical Center, Pediatric Infectious Disease Unit, Afula, Israel
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Background

The worldwide introduction of PCVs to National Immunization Programs (NIPs) resulted in a rapid and substantial reduction of IPD rates in children. However, the reduction of meningitis *vs*. non-meningitis IPD (nm-IPD) is not yet fully elucidated, and several studies reported less impressive reduction of meningitis *vs*. nm-IPD. Our aim was to compare PCV7/PCV13 impact on pneumococcal-meningitis *vs*. nm-IPD in Israeli children <5yrs.

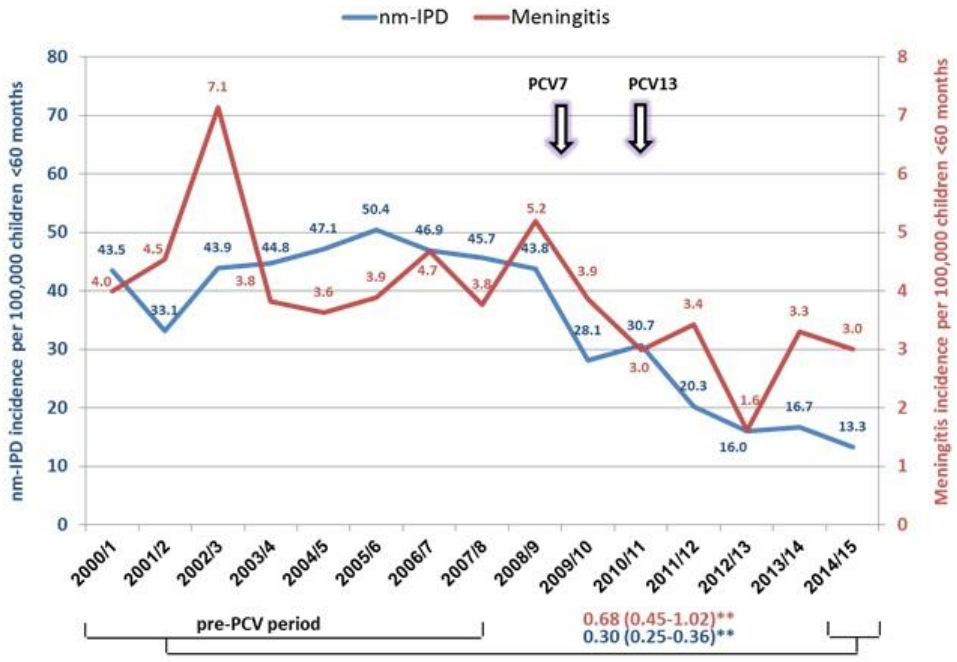
Methods

An ongoing nationwide, prospective, population-based, active surveillance. PCV7 and PCV13 were introduced into the Israeli NIP in Jul-2009 and Nov-2010, respectively. Pneumococcal isolates (blood and/or CSF) from IPD episodes in children <5yrs from Jul-2000 through Jun-2015 were included. Extrapolation methods for missing serotypes (34.7% of all-isolates) were detailed previously (Ben-Shimol et-al. Vaccine 2014).

Results

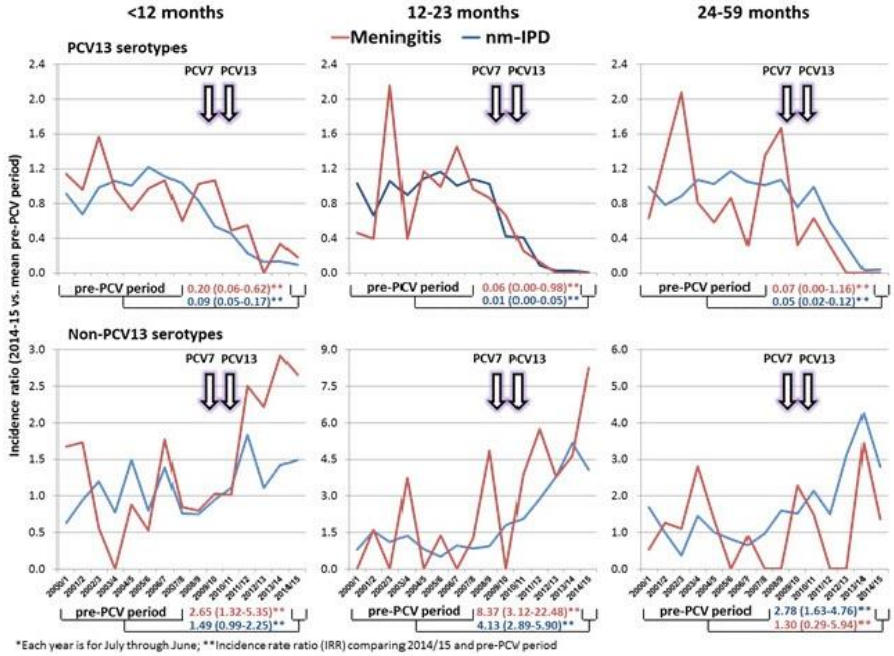
Overall, 4,163 meningitis and nm-IPD cases in children <5yrs were reported; 424 (10.2%) were meningitis. In the pre-PCV period (2000-2008), children <12m constituted 52.1% of meningitis episodes *vs*. 33.7% of nm-IPD (p<0.001). The proportion of non-PCV13 serotypes (non-VT) were 18.2% *vs*. 10.1%, respectively (p<0.001). Comparing rates of the last study year (2014-2015) to the mean rates of the pre-PCV period, meningitis incidence in children <5yrs decreased non-significantly by 32%, while nm-IPD decreased significantly by 70% (**Figure 1**). However, rates dynamics of meningitis and nm-IPD caused by PCV13 serotypes were similar. In contrast, non-VT increased in meningitis relatively to nm-IPD, mainly in children <24m, including an outbreak of serotype 12F between Jul-2010 and Jun-2015 (28.6% and 26.6% of all non-VT meningitis in children <24m and<60m, respectively) (**Figure 2**).

Figure 1: Pneumococcal meningitis and non-meningitis IPD incidence rates (per 100,000 population) in children <60 months old in Israel, July 2000 – June 2015



*Each year is for July through June; **Incidence rate ratio (IRR) comparing 2014/15 and pre-PCV period

Figure 2: Pneumococcal meningitis and non-meningitis IPD incidence rate ratios in children <60 months old in Israel, July 2000 – June 2015



*Each year is for July through June; **Incidence rate ratio (IRR) comparing 2014/15 and pre-PCV period

Conclusions

PCV7/PCV13 impact on meningitis and nm-IPD caused by vaccine-serotypes is similar. The apparent differences in vaccine impact derive from the different age and serotype distribution between the two entities, found both in pre- and post-PCV introduction.

ESP16-0419
ORAL PRESENTATION SESSION 8 - SEVERE INFECTIONS

PREVALENCE, SIX-MONTH PERSISTENCE AND INCIDENCE OF ORAL HUMAN PAPILLOMAVIRUS INFECTION AMONG UNIVERSITY STUDENTS IN VALENCIA, SPAIN

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Background

HPV infections have been recently identified as risk factors in oral and oropharyngeal cancer. Our aim was to estimate the prevalence, six-month persistence and incidence of new infections among university students.

Methods

Cross-sectional study performed in a convenience sample of university students aged 18-25 years living in the Valencia Region, Spain, during November 2012. Participants provided an oral rinse sample. Six months later, a second sample was obtained from HPV-positive subjects to determine the persistence of infection and presence of infections by new genotypes. HPV detection and typing were based on PCR.

Results

The final study sample included 543 participants, 70 (12.9%) of whom had received HPV vaccination, all vaccinees were women. Prevalent oral HPV infections were identified among 7/70 (10%; 95%CI:4.1%-19.5%) vaccinated participants, all of which had non-identifiable genotypes. Among 473 non-vaccinated participants, 32 (6.8%, 95%CI:4.8%-9.4%) had prevalent oral HPV infections, of which 19 (59.4%) had high-risk genotypes. A second sample was obtained six months later from positive subjects, including 29 unvaccinated and 7 vaccinated subjects, to identify persistence of infection and reinfections; 7 and 1 of them, respectively, were found positive. The specimen from the vaccinated student showed untypable genotypes in both isolations. Among the unvaccinated, six-months persistence of the same genotype was 10.3% (95%CI:2.2%-27.4%) and six-month incidence of infection with a new genotype was 17.2% (95% CI:5.8%-35.8%) . High-risk genotypes were identified in all persistent infections and in 3/5 new HPV infections.

Conclusions

Our study provides a first picture of oral HPV infection and its persistence among university students in our region, which may support implementation and monitoring of new public health measures addressed to reduce the burden of the infection.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0504
ORAL PRESENTATION SESSION 8 - SEVERE INFECTIONS

PREDICTORS OF BACTERIAL SEPSIS IN CHILDREN PRESENTING WITH SEVERE LIFE THREATENING INFECTIONS IN AN URBAN GAMBIA SETTING - THE EUCLIDS STUDY IN WEST AFRICA

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Background

Bacterial infections are a major cause of morbidity and mortality in African children. However, predictors of bacteraemia in children presenting with signs of severe sepsis in West Africa are limited**.**

Methods

Patients aged 1 month to 18 years presenting with sepsis or suspected sepsis to two urban hospitals in the Gambia were recruited. Demographic data, clinical features, outcome and bacterial pathogen isolated from sterile sites using standard bacterial culture were documented and the presence of antibiotic was screened for in urine on admission.

Results

A total of 349 children were recruited over a 2-year period; 206 (59.0%) were male, 22(6.3%) had a previous history of severe infection and 65.3% had evidence of pre-hospital antibiotic use on urine antibiogram testing. A pathogen was identified in 26% of cases of which *S. aureus* was the most common (33%). Overall mortality was 12.0% with death occurring within <7 days of admission in 80%. Surprisingly, neither tachypnoea, tachycardia, fever nor hypothermia were predictors of bacteraemia. However, severe anaemia (Hb <8g/dl) and musculoskeletal infection were significantly associated with bacteraemia (p=0.038 and 0.007 respectively).

Conclusions

In an urban Gambian setting, only anaemia and features of musculoskeletal infection were associated with bacteraemia. High rates of pre-hospital antibiotic use have a significant impact on standard microbiological culture and may confound the predictors of bacteraemia.

Clinical Trial Registration (Please input N/A if not registered)

1FP7, GA#279185, http://www.euclids-project.eu ---- submitted on behalf of EUCLIDS cionsortium

ESP16-0287
ORAL PRESENTATION SESSION 8 - SEVERE INFECTIONS

CAUSES OF MENINGITIS IN THE UK IN THE CONJUGATE VACCINE ERA - FINDINGS FROM THE UK CHILDHOOD MENINGITIS AND ENCEPHALITIS PROSPECTIVE COHORT STUDY (UK-CHIMES)

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Background

Introduction into the UK infant immunisation schedule of highly effective bacterial conjugate vaccines has dramatically changed the epidemiology of childhood meningitis such that viral causes are increasingly predominant. Recent studies have suggested that over 80-90% of children with meningitis in the highly immunised populations of developed countries have non-bacterial meningitis, but current UK epidemiology is unknown.

Methods

Data were collected from an ongoing prospective cohort study in 30 UK hospitals from December 2012. Inclusion criteria: child aged <16 years and hospitalisation with suspected meningitis or encephalitis and/or having a lumbar puncture (LP) as part of an evaluation for infection. Data were collected from hospital records. Meningitis was defined as isolation of a pathogen from CSF and/or a CSF WBC >4/μL.

Results

Of the initial 2,251 children recruited into the study, 592 (26%) had meningitis. In children <3 months, 353/1234 (29%) had meningitis, compared with 135/588 (23%) children aged 3-23 months and 97/399 (24%) children aged 2-15 years. Overall 128/592 (22%) children had bacterial meningitis – the commonest pathogens were Group B Streptococcus in infants <3 months old (40% of cases), and *Neisseria meningitidis* in children ≥3 months (55% of cases). Overall 259/592 (44%) cases had a confirmed viral aetiology – enterovirus was the commonest viral cause at all ages (84% of cases). 201/592 (34%) children had no pathogen identified.

Conclusions

In the UK, where bacterial conjugate vaccines are routinely used, 78% of children with meningitis in this study to date have non-bacterial meningitis, and a pathogen was not identified in 43% of these cases. The precise epidemiology of childhood meningitis is currently poorly defined, and better diagnostic methods are urgently required to prioritise prevention and management strategies.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0563
ORAL PRESENTATION SESSION 9 - USE OF ANTIMICROBIALS

DIHYDROARTEMISININ-PIPERAQUINE IS AN EFFICIENT ALTERNATIVE TO ARTEMETHER-LUMEFANTRINE FOR THE TREATMENT OF UNCOMPLICATED MALARIA IN CHILDREN IN GUINEA-BISSAU.

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Background

Since 2008 artemether-lumefantrine (AL) has been the 1st line anti-malarial drug in Guinea-Bissau. However, resistance/tolerance to lumefantrine exists. Consequently, there is a need for another treatment option. To examine whether dihydroartemisinin-piperaquine (DP) is tolerated and as efficacious as AL we performed an RCT at the Bandim Health Centre, Guinea-Bissau.

Methods

Children aged 6 months to 15 years with uncomplicated malaria were randomised to supervised treatment with either AL or DP, and monitored for 42 days. PCR analyses were used to distinguish between true recrudescence and re-infections. In the intention-to-treat analysis (ITT) all early treatment failures (ETF), late treatment failures (LTF), and re-infections were counted as treatment failures. In the per-protocol analysis (PP) ETF on day 0 was considered violation of inclusion-criteria and re-infections were censored on the day of re-infection.

Results

In the DP and the AL-group 157 and 155 children were included, respectively. In the ITT 2 and 6 children, respectively, had ETF (of these 2 in each group on day 0); 0 and 3 had LTF; 2 and 0 had re-infection; 17 and 18 were lost-to-follow up/withdrew consent.
The table shows the treatment-outcome. No side-effects were recorded.

Conclusions

In Guinea-Bissau both AL and DP have high efficacy, however in the PP-analysis DP is slightly better than AL. DP would be a good alternative to AL.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov Identifier:: NCT01704508

ESP16-0774
ORAL PRESENTATION SESSION 9 - USE OF ANTIMICROBIALS

THE IMPACT OF GESTATIONAL AGE AND GEOGRAPHICAL REGION ON ANTI-INFECTIVES' USE IN EUROPEAN NEONATAL INTENSIVE CARE UNITS (NICU)

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Background

Anti-infectives are the most commonly used medicines in NICUs. We aimed to describe variations related to geographical region (GR) and gestational age (GA) in the use of anti-infectives in Europe.

Methods

We performed a Point Prevalence Survey in 2012 including 89 NICUs from 21 European countries. During one day all neonatal prescriptions and demographic data were registered in a web-based database. Medicines were classified based on WHO Anatomical Therapeutic Chemical (ATC) classification system according to the 1st, 3rd and 5th level. Prescription rates (number of prescriptions/100 neonates) were calculated. Neonates were grouped based on gestational age (22-27 weeks, extremely preterm; 28-31 weeks, very preterm; 32-36 weeks, late preterm; ≥37 weeks, term). Participating countries were classified into GR (according to the United Nations Statistics department instructions). The impact of GA and GR on anti-infectives' use were analysed using uni- and multivariate logistic regression analysis; East region and extremely premature neonates were used as reference group.

Results

In total, 572 prescriptions of anti-infectives to 315 (43% of 726) neonates were recorded. The prescription rate was highest for penicillins (28/100), aminoglycosides (23/100), other beta-lactams (12/100) and other antibacterials (9/100). In univariate analysis GA or GR significantly affected the use of anti-infectives except penicillins. In multivariate analysis compared to reference group the use of anti-infectives in general was higher in South and lower in very- and late preterms. The use of aminoglycosides was significantly higher in South and North, penicillins in North, other antibacterials use was higher in South and lower in late preterm and term neonates (Table).

Table.
Geographical region and gestational age-based differences in multivariate logistic regression model (reference groups East and Extremely preterm neonates); * Significant odds ratios (OR) at α = 0.05

	Geographical region			Gestational age group		
ATC group (ATC code) Frequently used active ingredients	**North OR (95% CI)**	**South OR (95% CI)**	**West OR (95% CI)**	**Very preterm OR (95% CI)**	**Late preterm OR (95% CI)**	**Term OR (95% CI)**
Anti-infectives (total) Gentamicin, Ampicillin, Benzylpenicillin	1.03 (0.7-1.52)	**1.65 (1.06-2.58)***	0.66 (0.4-1.09)	**0.55 (0.32-0.95)***	**0.48 (0.29-0.81)***	0.74 (0.44-1.25)
Penicillins (J01C) Ampicillin, Benzylpenicillin, Amoxicillin	**1.68 (1.09-2.6)***	1.35 (0.82-2.23)	0.99 (0.56-1.74)	1.18 (0.62-2.23)	1.47 (0.8-2.68)	1.75 (0.95-3.2)
Aminoglycosides (J01G) Gentamicin, Amikacin	**2.17 (1.35-3.5)***	**2.4 (1.42-4.07)***	0.67 (0.33-1.36)	0.86 (0.44-1.7)	1.02 (0.54-1.93)	1.58 (0.85-2.96)
Other antibacterials (J01X) Vancomycin, Teicoplanin, Metronidazole	0.66 (0.3-1.47)	**2.47 (1.16-5.26)***	0.82 (0.33-2.05)	0.63 (0.29-1.34)	**0.21 (0.09-0.5)***	**0.23 (0.1-0.54)***

Conclusions

While GA-dependent differences in anti-infectives consumption are well understood, regional variations are more difficult to explain suggesting a lack of uniformity in use of anti-infectives in Europe.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1002
ORAL PRESENTATION SESSION 9 - USE OF ANTIMICROBIALS

EXTENDED-SPECTRUM-β-LACTAMASE (ESBL) PRODUCING ENTEROBACTERIACEAE IN NEONATES AND ASSOCIATION WITH MATERNAL URINE CULTURES

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Background

Enterobacteriaceae has become a major cause of neonatal sepsis over the past decades. Pregnant women are potential carriers of extended-spectrum-β-lactamase producing Enterobacteriaceae (ESBL-PE). Neonates can acquire ESBL-PE during passage through the birth canal. There is a need to measure the influence of ESBL-PE prevalence in neonates on morbidity and mortality, and to analyze vertical transmission of these resistant bacteria. The study was aimed to analyze the correlation between the presence of ESBL-PE in pregnant women's urine cultures and the finding of ESBL-PE in related neonates' cultures and to examine the impact of ESBL-PE on neonatal morbidity and mortality.

Methods

A retrospective cohort study was conducted with data obtained from the centralized Clalit Health Services (CHS) database. The study population included neonates born in one of seven CHS hospitals between 2009-2013.

Results

The study population included 137,580 neonates. Of the 31,921 (23.2%) neonate cultures taken, 2,647(8.3%) were positive. The odds ratio (OR) of ESBL-PE in urine cultures of mothers of neonates with positive ESBL-PE cultures was 2.69 fold (95%CI: 1.06-6.80) greater than in women with negative cultures. Hospital stay in 3 months after birth was 38.8 days (median) vs. 16.5 days in neonates with and without ESBL-PE. The finding of ESBL-PE in neonatal cultures is associated with increased neonatal mortality (OR=2.11, 95%CI: 1.17-3.82).

Conclusions

Our study demonstrates that maternal carriage of ESBL-PE is an important risk factor in passing it on to their neonate. ESBL-PE is associated with increased morbidity and mortality in neonates. The policy to prevent ESBL-PE outbreaks in neonatal units should include maternal and neonatal screening and cohorting, and active notification of medical staff when ESBL-PE positive women and their neonates are admitted.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1093
ORAL PRESENTATION SESSION 9 - USE OF ANTIMICROBIALS

ANTIMICROBIAL RESISTANCE (AMR) IN NEONATAL UNITS (NNUS) PARTICIPATING IN THE UK NEONATAL SURVEILLANCE NETWORK, NEONIN (WWW.NEONIN.ORG.UK)

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Background

AMR has been shown to lead to increased duration and cost of treatment as well as worse patient outcomes. Surveillance of AMR is essential in order to develop appropriate strategies to address changing AMR patterns. This study describes the AMR rates among pathogens causing neonatal infections in UK NNUs participating in a neonatal infection network with a focus on Gram-negative isolates (GNI).

Methods

neonIN (www.neonin.org.uk) is an international surveillance database for culture proven neonatal infections. Antimicrobial susceptibility data on UK bloodstream isolates identified between January 2004 and December 2014 were extracted. Early-onset sepsis (EOS) was defined as occurring within 48 hours of birth.

Results

1568 episodes (excluding *Coagulase-negative Staphylococci*) from 30 NNUs (involving 1236 neonates) were reported. Of those 1105 (46%) were due to GNI. In EOS most common pathogen was GBS 158/328 (48.2%) followed by *E. coli* 65/328 (19.8%) and *Enterococcus* spp 15 (4.6%). *E.coli* 193/1240 (15.6%) was the most frequent isolate in LOS followed by *Enterococcus* spp 183/1240 (14.7%), *S. aureus* 181/1240 (14.6%) and *Klebsiella* spp 145/1240 (11.7%). Overall susceptibility to common antibiotic combinations and antimicrobial susceptibility for GNI specifically, is detailed in the table.

	Antibiotic combinations		Overall antimicrobial susceptibility to common empiric antibiotic combinations			Antimicrobial susceptibility in GNI		
			N Tested	N Susceptible	% Susceptible	N Tested	N Susceptible	% Susceptible
EOS	Benzylpenicillin	Gentamicin	238	222	93%	81	74	91%
	Amoxicillin	Cefotaxime	228	216	95%	78	69	88%
	Amoxicillin	Gentamicin	238	229	96%	81	76	94%
LOS	Flucloxacillin	Gentamicin	833	742	89%	564	489	87%
	Amoxicillin	Cefotaxime	783	665	84%	523	420	80%
	Amoxicillin	Gentamicin	876	770	88%	605	515	85%
	Piperacillin/Tazobactam	Gentamicin	317	279	88%	233	199	85%
	Vancomycin	Cefotaxime	763	700	91%	457	401	88%
	Cefotaxime		538	475	88%	457	401	88%
	Amoxicillin & Clavulanic acid		657	526	80%	405	281	69%

Table: Antimicrobial susceptibility to common empiric antibiotic combinations in EOS and LOS and for GNI

Conclusions

Susceptibility to commonly used empiric antibiotic combinations, including those of narrow spectrum, remains high for EOS. LOS pathogens demonstrate higher levels of antimicrobial resistance yet there is no clear evidence that broader spectrum combinations provide better coverage. More work is required to identify better ways of targeting appropriate empiric antibiotics.

On behalf of the Neonatal Infection Surveillance Network (neonIN)

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1037
ORAL PRESENTATION SESSION 9 - USE OF ANTIMICROBIALS

AN EVALUATION OF THE EFFICACY OF CONTINUOUS INFUSION VANCOMYCIN IN A NEONATAL POPULATION

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Background

Whilst continuous infusion vancomycin is widely used in the neonatal population, pharmacokinetic data is limited and there is little consensus on an optimal dosing regimen. At Evelina London Children's Hospital (ELCH) it has been noted that babies receiving continuous infusion vancomycin have been failing to achieve therapeutic vancomycin levels.

Objectives

To determine whether the current dosing regimen for continuous infusion vancomycin at ELCH is consistently achieving and maintaining therapeutic vancomycin levels in a neonatal population.

Methods

Data collection was retrospective. Patients were identified using the JAC pharmacy system of patients who had been supplied vancomycin via the Centralised Intravenous Additive Service (CIVAS) from July 2014 to July 2015. Medical notes for the patients were requested from Medical Records in order to review the dosing of vancomycin. Biochemical results, such as vancomycin and creatinine levels, were obtained from the Electronic Patient Records.

Results

A total of 17neonates were included in the study, resulting in 28 courses of continuous infusion vancomycin being analysed. Of the 28 courses, only 18 (67.9%) achieved a therapeutic vancomycin level at some stage within the course and only 2 (11.1%) achieved this within 24 hours after completion of load. From the 18 courses, just 8 maintained a vancomycin level within a target range of 15mg/L to 25mg/L 48 hours following initial achievement. 33.2% of the therapeutically beneficial courses required 2 or more loading doses and 66.7% required 1 or more daily dosage increase to achieve a therapeutic vancomycin level.

Conclusions

The current dosing regimen in place for neonates at ELCH is failing to achieve and maintain therapeutic vancomycin levels consistently. Further pharmacokinetic/pharmacodynamics studies are required to ensure adequate dosing regimens.

ESP16-0395
ORAL PRESENTATION SESSION 9 - USE OF ANTIMICROBIALS

POPULATION PHARMACOKINETICS OF MEDI8897, AN EXTENDED HALF-LIFE ANTI-RSV MONOCLONAL ANTIBODY (MAb), IN HEALTHY ADULT VOLUNTEERS AND INFANTS AND SUBSEQUENT DOSE SIMULATIONS IN INFANTS

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Background

MEDI8897 is an RSV monoclonal antibody with an extended half-life intended to protect all infants through an entire RSV transmission season with a single, fixed intramuscular (IM) dose. A modeling and simulation analysis was conducted using adult and interim infant pharmacokinetics (PK) data to simulate infant PK profiles.

Methods

MEDI8897 PK data from 102 healthy adults in a phase 1 (single, fixed-doses of 300, 1000, or 3000 mg intravenously or 100 or 300 mg IM) and interim data from 63 infants in a Phase 1b/2a (single 10, 25 or 50 mg IM dose) studies, were used for the model development. Body weight was used as a covariate on clearance and volume. Gender or the presence of anti-drug antibodies had no effect on PK and were not included. PK profiles were simulated in 1000 infants after allometrically scaling parameters whilst accounting for age-based maturation in clearance.

Results

The adult and infant PK was well described by a 2-compartment model with linear PK. Observed infant PK was consistent with prior predictions. Simulations in infants across different age groups up to 8 months of age, predict median half-life to range from 83-94 days after a single 50 mg IM dose in infants with normal clearance. The maximum concentration and time to peak ranged from 54-200 µg/mL and 4-5 days, respectively.

Conclusions

A population PK model for MEDI8897 was developed in healthy adults and infants. Subsequent simulations in infants support single dose of MEDI8897 to provide protection for the duration of the RSV season.

This study was sponsored by MedImmune.

Clinical Trial Registration (Please input N/A if not registered)

NCT02114268 NCT02290340

ESP16-0843
ORAL PRESENTATION SESSION 10 - VACCINE IMMUNOGENICITY

A LONG-TERM EFFECTIVENESS, IMMUNOGENICITY, AND SAFETY STUDY OF GARDASIL™ (HUMAN PAPILLOMAVIRUS [TYPES 6,11,16,18] RECOMBINANT VACCINE) IN YOUNG MEN (V501-020)

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Background

Human papilloma virus (HPV) infection in men causes anogenital warts, anal cancer, and a proportion of penile cancers. Men are the main source of HPV infection in women. The V501-20 base study demonstrated the efficacy, immunogenicity, and safety of GARDASIL™ in young men.

Methods

The extension of V501-020 evaluates the immunogenicity, safety and effectiveness of GARDASIL™ in preventing vaccine-type genital warts, external genital lesions (EGL), and anal intraepithelial neoplasia (AIN)/cancer in 16 to 26 year old men for 10 years after vaccination. The V501-020 base study was a double-blind, placebo-controlled, multicenter, international study, in which young men were randomized 1:1 to receive GARDASIL™ or placebo. Subjects in the placebo group were offered catch-up vaccination. All subjects who received at least one dose of GARDASIL™ in the base study (early vaccination group, EVG) or thereafter (catch-up vaccination group, CVG) were followed annually in this extension. This interim analysis was performed 8 years post-vaccination.

Results

936 subjects in the EVG were followed for a median duration of 8.9 years after receipt of the first vaccine dose; 867 CVG subjects were followed for 4.2 years. No cases of HPV 6/11 genital warts or HPV 6/11/16/18 EGL were observed in the EVG per-protocol population during the extension. In a subpopulation evaluated for AIN, no high-grade disease and a single case of AIN1 was observed (0.3/100 person-years-at-risk, compared to 5.8 per 100 person-years-at- risk in the base study). Seropositivity rates for HPV 6/11/16/18 remained high and no vaccine-related serious adverse experiences were reported.

Conclusions

Vaccination with GARDASIL™ is immunogenic, well-tolerated, and provides durable protection from vaccine-type genital warts, EGLs, and AIN up t ~9 years following administration in 16 to 26 year-old men.

Clinical Trial Registration (Please input N/A if not registered)

Clinical Trial Registration: EudraCT-2004-002945-10, CT-Gov-NCT00090285

ESP16-0464
ORAL PRESENTATION SESSION 10 - VACCINE IMMUNOGENICITY

IMMUNOGENICITY AND SAFETY OF A 2 OR 3 DOSE PRIMARY SERIES OF MENINGOCOCCAL SEROGROUP B VACCINE IN INFANTS, AND A 2-DOSE CATCH-UP SERIES IN CHILDREN

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Background

Young children have the highest rates of invasive meningococcal disease. This phase 3b study investigated the immunogenicity and safety of two regimens of rMenB+OMV NZ meningococcal B vaccine in infants 2½ to12 months (Groups I–III), and a 2-dose series in children aged 2 to 10 years (Group IV).

Methods

Group I received 3 doses of rMenB+OMV NZ at 2½,3½ & 5 months of age. Groups II and III received 2 doses at 3½ & 5, and 6 & 8 months of age, respectively, and Group IV (children) received 2 doses two months apart. All infants received a booster dose at 11 months of age. Antibody response was measured by hSBA against fHbp, NadA, PorA and NHBA test strains. Safety was assessed by solicited reactions, adverse events (AEs) and serious AEs (SAEs).

Results

253, 250, 251 infants, and 404 children were enrolled into Groups I, II, III, and IV, respectively. One month after the 2-dose primary series, all infants had hSBA ≥1:4 against fHbp and NadA, 98–99% against PorA, and 44–73% of infants had hSBA ≥1:5 against NHBA. Percentages were similar for children: 99% against fHbp, NadA and PorA; 94% against NHBA (hSBA ≥1:5). Solicited adverse reactions were reported by 97%–100% infants and children, most of which resolved by Day 7. Fever was reported by 75–80% of infants and 14–20% of children. Three infant SAEs were considered possibly related to the study vaccine: pyrexia (2 cases) and juvenile idiopathic arthritis.

Conclusions

Most infants and children achieved seroprotective antibody titres regardless of vaccine schedule. Similar safety profiles were seen across groups. Rates of fever were higher in infants.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov NCT01339923

ESP16-1044
ORAL PRESENTATION SESSION 10 - VACCINE IMMUNOGENICITY

PHASE 3 TRIAL OF IMMUNOGENICITY OF BIVALENT rLP2086, A MENINGOCOCCAL SEROGROUP B VACCINE, IN ADOLESCENTS: BACTERICIDAL ACTIVITY AGAINST A PANEL OF ANTIGENICALLY DIVERSE STRAINS

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Background

Bivalent rLP2086, which targets factor H binding proteins (fHBP), is approved in the US to prevent meningococcal serogroup B (MnB) disease in 10-25-year-olds. Broad protection with bivalent rLP2086 was initially demonstrated in hSBAs with 4 diverse invasive MnB strains expressing fHBPs with sequences different from vaccine antigens. In this pivotal phase 3 trial, broad coverage against MnB disease is further supported by hSBA data with 10 additional MnB test strains representing the diversity of circulating invasive MnB strains.

Methods

Healthy subjects aged 10-<19 years were randomized to receive bivalent rLP2086 at 0, 2, and 6 months, or hepatitis A virus vaccine at 0 and 6 months and saline at 2 months. Immune responses were assessed in hSBAs with 4 primary MnB test strains (primary endpoint; N=1210-1266) and in a population subset using 10 secondary MnB test strains (secondary endpoint; N=266-281). All strains expressed vaccine-heterologous fHBP.

Results

hSBA responses 1 month after doses 2 and 3 among bivalent rLP2086 recipients against 4 primary MnB test strains measured by hSBA titers ≥LLOQ were 64.0%-99.1% and 87.1%-99.5%, respectively (Table). hSBA responses to 10 secondary MnB test strains were 61.1%-100.0% and 75.1%-98.6% 1 month after dose 2 and 3, respectively. hSBA GMTs for each

secondary test strain increased from 4.5-11.4 at baseline to 22.1-93.5 after dose 3.

Table. hSBA activity elicited by bivalent rLP2086 against a panel of invasive, antigenically diverse meningococcal serogroup B strains

Strain (fHBP Variant)	N	% with hSBA titers ≥LLOQ (1:8 or 1:16)			hSBA GMTs	
		Baseline	After dose 2 *	After dose 3	Baseline	After dose 3
Primary strains						
PMB80 (A22)	1266	33.2	94.3	97.8	12.6	86.8
PMB2001 (A56)	1229	27.5	99.1	99.5	8.4	222.5
PMB2948 (B24)	1250	6.4	66.4	87.1	4.5	24.1
PMB2707 (B44)	1210	3.6	64.0	89.3	4.3	50.9
Secondary strains						
PMB3175 (A29)	278	17.5	100.0	98.6	5.7	93.5
PMB3010 (A06)	280	9.4	84.0	95.7	9.3	78.6
PMB3040 (A07)	280	43.1	93.8	96.4	11.4	63.5
PMB824 (A12)	277	3.9	67.4	75.1	8.4	22.3
PMB1672 (A15)	266	20.7	65.6	87.2	5.9	31.0
PMB1989 (A19)	275	11.3	84.5	92.7	9.1	57.6
PMB1256 (B03)	279	4.3	61.1	92.5	4.5	51.7
PMB866 (B09)	276	15.2	76.3	86.2	5.2	22.9
PMB431 (B15)	281	28.7	96.8	98.2	7.3	47.7
PMB648 (B16)	278	7.6	61.6	81.7	4.7	22.1

*For the secondary strains, subset of subjects; n=86–97.
LLOQ = 1:16 for A06, A12, A19, and A22; 1:8 for A07, A15, A29, A56, B03, B09, B15, B16, B24, and B44.

Conclusions

Bivalent rLP2086 vaccination resulted in robust immune responses against diverse MnB strains heterologous to vaccine antigens after 2 and 3 doses. A high proportion of individuals developed protective hSBA titres greater than the correlate of protection (hSBA titre ≥1:4) to 10 additional MnB test strains. Collectively, these phase 3 immunogenicity data support the broad protection afforded by bivalent rLP2086 against MnB disease in adolescents. Funded by Pfizer.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov: NCT01830855

ESP16-0451
ORAL PRESENTATION SESSION 10 - VACCINE IMMUNOGENICITY

IMMUNOGENICITY AND SAFETY OF CONCOMITANT ADMINISTRATION OF MENINGOCOCCAL SEROGROUP B (RMENB+OMV NZ) AND C (MENC-CRM) VACCINES IN INFANTS IN BRAZIL: A PHASE 3B TRIAL

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Background

The predominant disease-causing meningococcal serogroups in Brazil are MenC and MenB. A 3-dose regimen of MenC vaccine (MenC-CRM) was added to the infant immunisation schedule in 2010. We investigated the immunogenicity and safety of concomitant administration of MenC-CRM with MenB vaccine (rMenB+OMV NZ) in infants in Brazil

Methods

Healthy infants were randomised 1:1 to receive 2 primary and 1 booster dose of rMenB+OMV NZ and MenC-CRM (Group A), or MenC-CRM alone (Group B) at 3, 5 and 12 months of age. Antibody responses against four MenB test strains (fHbp, NadA, PorA, and NHBA), and MenC were measured by hSBA at baseline, and at 6, 12 and 13 months of age. Non-inferiority of co-administered MenC-CRM vs MenC-CRM alone was established if the lower limit of 95% confidence interval [LL95%CI] of the difference in percentage of subjects with hSBA ≥1:8 was >-10% one month after the second/booster doses. Solicited reactions, adverse events (AEs) and serious AEs (SAEs) were monitored to assess safety and tolerability

Results

In total, 117/126 (Group A) and 111/125 (Group B) infants completed the study. Non-inferiority was demonstrated for co-administered MenC-CRM (LL95%CI: 2nd dose: -6.4%; booster: -5.2%). One month after the second vaccination, 97%, 96% and 93% of infants in Group A had hSBA ≥1:4 against fHbp, NadA and PorA, respectively, and 68% had hSBA ≥1:5 against NHBA. Most subjects reported solicited reactions (95–100% for any injection), which mostly resolved within 2 days. Rates of AEs and SAEs were similar across groups

Conclusions

Concomitant administration of MenC-CRM with rMenB+OMV NZ was non-inferior to MenC-CRM alone, with similar safety profiles. Nearly all infants administered rMenB+OMV NZ achieved seroprotective titres against MenB test strains

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov NCT01339923

ESP16-0517
ORAL PRESENTATION SESSION 10 - VACCINE IMMUNOGENICITY

SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF PENTAVALENT ROTAVIRUS VACCINE MANUFACTURED BY A MODIFIED PROCESS

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Background

Rotavirus is the leading cause of severe diarrhea in infants and young children. The current formulation of pentavalent rotavirus vaccine (RV5) must be stored refrigerated at 2 to 8°C. A modified formulation of RV5 ($RV5_{mp}$) has been developed with stability at 37°C for 7 days and an expiry extended to 36 months when stored at 2 to 8°C.

Methods

This study evaluated the safety, tolerability and immunogenicity of $RV5_{mp}$ versus the currently marketed RV5 in infants. Immunogenicity endpoints were: (1) serum neutralizing antibody (SNA) titers to human rotavirus serotype G1, G2, G3, G4, and P1A[8]; and (2) proportion of subjects with a ≥3-fold rise from baseline for SNA to human rotavirus serotypes G1, G2, G3, G4, P1A[8], and serum anti-rotavirus IgA.

Results

The $RV5_{mp}$ group (n=505) and RV5 group (n=509) had comparable safety profiles. There were no deaths and no vaccine-related SAEs in this study. The geometric mean titers (GMTs) of vaccine-induced SNA to human rotavirus serotypes G1, G2, G3, G4, and P1A[8] were noninferior in $RV5_{mp}$ recipients compared to RV5 (all $p<0.001$). SNA responses by country and breast feeding status were generally consistent with the overall results.

	$RV5_{mp}$ (N=495)	**$RV5_{mp}$ (N=488)**		
Antigen	**Estimated GMT**	**Estimated GMT**	**GMT Ratio**	**95% CI**
Serotype G1	99.5	107.6	0.92	(0.79,1.07)
Serotype G2	30.7	26.7	1.15	(0.99,1.33)
Serotype G3	82.6	25.8	3.20	(2.75,3.74)
Serotype G4	77.3	72.8	1.06	(0.94,1.20)
Serotype P1A	107.2	92.5	1.16	(1.00,1.35)

Conclusions

$RV5_{mp}$ enhances storage requirements while maintaining the immunogenicity and safety profile of the currently licensed RV5. A vaccine that is stable at room temperatures may be more convenient for vaccinators, particularly in places where the cold chain is unreliable, and ultimately will permit more widespread use.

Clinical Trial Registration (Please input N/A if not registered)

NCT01600092; EudraCT:2012-001611-23

ESP16-0720
ORAL PRESENTATION SESSION 10 - VACCINE IMMUNOGENICITY

KINETICS OF MATERNALLY-DERIVED SEROGROUP A, C, Y AND W-SPECIFIC MENINGOCOCCAL IMMUNOGLOBULIN G MEASURED BY ENZYME LINKED IMMUNOSORBENT ASSAY IN MALIAN WOMEN AND INFANTS

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Background

In 2010, MenAfriVac®, serogroup A meningococcal conjugate vaccine was introduced into Mali via mass campaigns of 1- to 29-year olds. A prospective, randomised, controlled observer-blind trial measuring the efficacy, safety and immunogenicity of trivalent influenza vaccine (TIV) and the safety and immunogenicity of quadrivalent meningococcal conjugate vaccine (MCV) in pregnant women and their infants up to 6 months of age was conducted in Mali. MCV was used as a comparator vaccine to TIV and allowed for collection of safety and immunogenicity data within this population.

Methods

Third-trimester pregnant Malian women were randomized to receive TIV or MCV. Blood samples were collected from women prior to vaccination, 28 days post-vaccination, at delivery and 3 and 6 months post-delivery and from infants at birth (cord blood) and 3 and 6 months of age. Serogroup A, C, Y and W-specific antibodies were measured by enzyme linked immunosorbent assay in a randomly selected subset of 50 mother-infant pairs where the mother had received MCV.

Results

Percentage of subjects with serogroup A, C, Y and W-specific IgG ≥2µg/mL

	A	C	W	Y
Mother Pre-vaccination	87.8%(43/49)	59.2%(29/49)	32.7%(16./49)	69.4%(34/49)
Mother 28 days post-vaccination	100%(49/49)	92%(46/50)	96%(48/50)	98%(44/47)
Infant at birth	97.9%(47/48)	80.9%(38/47)	91.5%(43/47)	93.6%(44/47)
Infant 3 months of age	72.9%(35/48)	31.9%(15/47)	66%(31/47)	74.5%(35/47)
Infant 6 months of age	29.8%(14/47)	15.2%(7/46)	43.5%(20/46)	63%(29/46)

Conclusions

Maternal immunization with MCV conveyed protective levels of IgG at birth and through 3 months of age in the majority of infants.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0122
ORAL PRESENTATION SESSION 11 - INFECTION AND IMMUNITY

NATURAL ADAPTIVE HUMAN IMMUNITY TO PNEUMOCOCCUS REQUIRES ANTIBODY TO PROTEIN ANTIGENS

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Background

Remarkably, the adaptive immune mechanism through which most individuals are naturally protected against invasive pneumococcal disease (IPD) is unknown. Responses to *S. pneumoniae* (Pnc) colonisation include antibody responses to both capsular and surface protein antigens alongside cellular immune responses. Protection against IPD has long been assumed to be mediated by anti-capsular responses.

Methods

We used human intravenous immunoglobulin (IVIG) to identify the antigen targets for naturally-acquired IgG-mediated immunity to IPD and to identify the relative functional importance of anti-capsular and anti-protein IgG. Studies were performed using *in vitro* assays and murine infection models.

Results

IVIG recognised both Pnccapsule and proteins. The pattern of binding to a series of individual proteins was highly conserved between different geographical sources of pooled human IgG. IVIG caused bacterial aggregation, IgG binding to the bacterial surface and enhanced phagocytosis. Surprisingly, the effect of these processes was increased against unencapsulated *S. pneumoniae* strains. This indicated that the capsule was unlikely to be the dominant antigen mediating these effects. In contrast, IgG binding to Pncwas reduced after trypsin treatment of bacterial surface proteins. Strains of *S. mitis* expressing Pnc capsule or surface proteins were used to deplete IVIG of specific antigens. This demonstrated the role of anti-protein rather than anti-capsular IgG. Critically, the treated IVIG remained able to protect against IPD in a murine passive protection model, confirming the redundancy of anti-capsular IgG in natural protection against IPD.

Conclusions

These results demonstrate that in contrast to vaccine-induced protection, naturally-acquired IgG-dependent immunity to IPD is mediated through recognition of a conserved subset of protein antigens rather than capsular antigen. These results have important implications for identifying individuals at risk of IPD and for future vaccine design.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0391
ORAL PRESENTATION SESSION 11 - INFECTION AND IMMUNITY

A NOVEL PARADIGM FOR IMMUNITY AND VACCINE DEVELOPMENT AGAINST GROUP A STREPTOCOCCUS: PRELIMINARY TESTING OF A UNIQUE FIJIAN SERA BIOBANK

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Background

Group A Streptococcus infections (GAS) cause >500,000 deaths annually but no vaccine is available. The M protein, a highly variable surface protein, is used for typing (223 *emm*-types gathered in 48 *emm*-clusters) and vaccine development. GAS immunity is generally considered to be *emm*-type specific, but protection may correlate with *emm*-clusters rather than with *emm*-types. To test this hypothesis, we investigated a unique collection of paediatric sera.

Methods

Blood samples were collected at three time points from children with GAS infections in Fiji. All GAS isolates were *emm*-typed. We selected patients fulfilling three criteria: infection by *emm*-type belonging to three major *emm*-clusters, pre and post-infection sera availability and no other GAS infections. M protein N-terminal peptide ELISA was used to detect *emm*-type-specific antibody responses following infection using a 3-fold increase threshold between pre- and post-infection sera. Sera were tested against multiple peptides from *emm*-types within the same *emm*-cluster and from different *emm*-clusters (negative controls).

Results

Of 41 patients, 23 had a 3-fold increase in antibody titers against the *emm*-type responsible for their infection (causative *emm*-type). Among these, 12 had an antibody response to

several cluster-related *emm*-types (Figure 1), five to the causative *emm*-type only and six to cluster-related and non-cluster related *emm*-types (Figure 2). Overall, antibody response against cluster-related *emm*-types was higher than against non-cluster related *emm*-types (Figure 3).

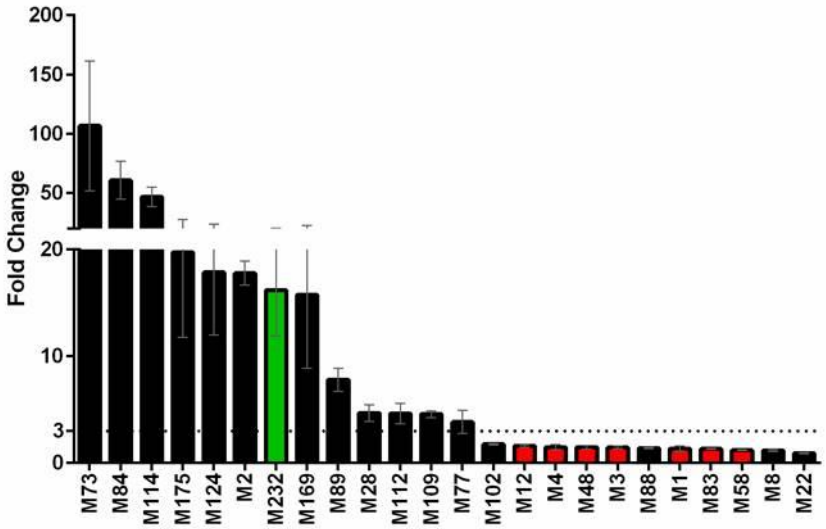


FIGURE 1: Fold change in antibody response between pre-infection and post-infection samples from a Fijian kid who had a GAS infection by M232 (E4 *emm*-cluster). The results appear in green for the causative *emm*-type, in black for the cluster-related *emm*-types and in red for negative controls (non-cluster related *emm*-types). The 3 fold increase is indicated by the dashed line.

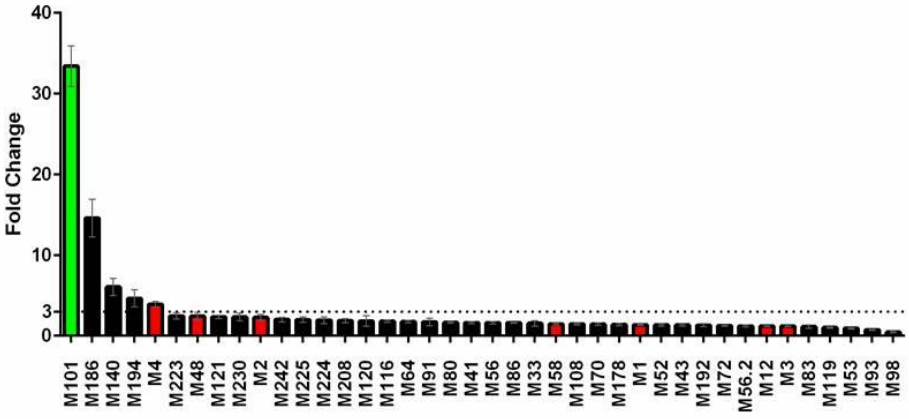
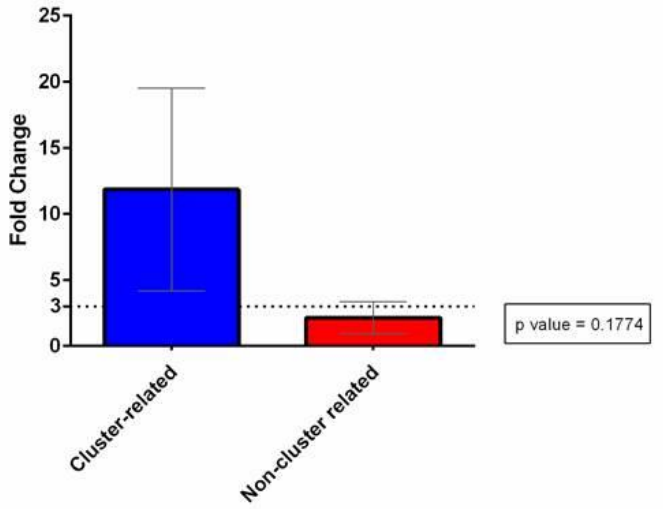


FIGURE 2: Fold change in antibody response between pre-infection and post-infection samples from a Fijian child who had a GAS infection by M101 (D4 *emm*-cluster). The results appear in green for the causative *emm*-type, in black for the other related-cluster *emm*-types and in red for negative controls (non-cluster related *emm*-types). The 3 fold increase is indicated by the dashed line.



Total number of tested strains for each *emm*-cluster	E4	E6	D4
Cluster-related *emm*-types	17	18	32
Non-cluster related *emm*-types	7	6	7

FIGURE 3: Fold increase in antibody titers for 23 GAS infections reported as Mean ± 95% confidence interval. Although not significant, the antibody fold increase for cluster-related *emm*-types (mean = 11.84, 95% CI 4.164-19.52) was higher than for non-cluster related *emm*-types (mean = 2.149, 95% CI 0.9319-3.366).

Conclusions

Some children developed an antibody response broader than the classical type-specific immunity after GAS infection. Overall, antibody responses against cluster-related *emm*-types was higher than against non-cluster related *emm*-types supporting our hypothesis of an *emm*-cluster basis for immunity. Both bactericidal assays and whole M protein ELISAs are being undertaken to further investigate our hypothesis.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0034
ORAL PRESENTATION SESSION 11 - INFECTION AND IMMUNITY

INTERFERON-GAMMA GENETIC POLYMORPHISM AND EXPRESSION IN KAWASAKI

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Background

Kawasaki disease (KD) is a systemic vasculitis of unknown etiology. *IFNG* gene encoding IFN-γ, produced by natural killer cells and T cells, has been suggested to play an important role in the pathogenesis of Kawasaki disease. The aim of this study examined the correlation of gene polymorphisms of the *IFNG* gene and plasma levels of IFN-γ in KD patients and their outcomes.

Methods

A total of 950 subjects (381 KD and 569 controls) were recruited. Three tagging SNPs (rs2069718, rs1861493, rs2069705) were selected for TaqMan allelic discrimination assay. Clinical phenotypes, coronary artery lesions (CAL), coronary artery aneurysms (CAA) and intravenous immunoglobulin (IVIG) treatment outcomes were collected for analysis. Plasma IFN-γ levels were also measured with an enzyme-linked immunosorbent assay.

Results

Polymorphisms of the *IFNG* gene were significantly different between the normal controls and KD patients. The G allele of rs1861493 conferred a better response to intravenous immunoglobulin (IVIG) treatment in KD patients. AA allele frequencies of rs1861493 were also associated with a significantly higher risk of CAA in KD patients. Furthermore, the plasma IFN-γ level was lower in the AA allele than in the GG allele of rs1861493 both before and after IVIG treatment in KD patients.

Conclusions

This study provides the first evidence supporting an association between *IFNG* gene polymorphisms, susceptibility of KD, IVIG responsiveness and plasma IFN-γ levels in KD patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0356
ORAL PRESENTATION SESSION 11 - INFECTION AND IMMUNITY

TLR9 AND TLR10 GENE POLYMORPHISMS ARE ASSOCIATED WITH POST-BRONCHIOLITIS WHEEZING AND PRE-SCHOOL ASTHMA

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Background

Toll-like receptors (TLRs) recognize microbes that contribute to the severity of infection and inflammation. Polymorphisms in TLRs seem to be connected to allergy and asthma. The aim of this exploratory study was to evaluate whether there are associations between *TLR7* rs179008, *TLR8* rs2407992, *TLR9* rs187084 or *TLR10* rs4129009 polymorphisms and viral findings, clinical characteristics, subsequent wheezing or pre-school asthma in infants with bronchiolitis.

Methods

In all, 187 full-term infants were hospitalized for bronchiolitis at age less than 6 months. At the mean age of 1.5 years 129 children, and at the mean age of 6.4 years 135 children attended the control visit. Among the outcome measures were repeated wheezing, atopic dermatitis during the first 1.5 years of life, total serum immunoglobulin E (IgE), and current or previous asthma.

Results

There were no significant associations between the genotypes or allele frequencies of *TLR7* rs179008, *TLR8* rs2407992, *TLR9* rs187084 or *TLR10* rs4129009 polymorphisms and clinical characteristics or severity of bronchiolitis during hospitalization. During the 18 months follow-up, repeated wheezing was more common in children with *TLR9* variant genotype CC (30.5%) than in children with *TLR9* wild genotype TT (12.2%) (p=0.02), aOR 2.73 (95% CI 1.02-7.29). The *TLR10* minor allele G was associated with elevated total serum IgE. At the 6.4 years control visit current asthma was more common (30%) in children who were carriers of the minor allele G in the *TLR10*, compared to those who were homozygous for the major allele A (11%) (p=0.04), aOR 4.30, (95% CI 1.30-14.29).

Conclusions

TLR9 rs187084 gene polymorphism may be associated with post-bronchiolitis wheezing, andpolymorphism in the *TLR10* rs4129009 gene with an increased risk of asthma at preschool-age after bronchiolitis in infancy.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0740
ORAL PRESENTATION SESSION 11 - INFECTION AND IMMUNITY

SEPTICEMIC MELIOIDOSIS INDUCED DNA METHYLATION OF AIM2 AND GBPS WHICH ACTIVATE INFLAMMASOME RESPONSES VIA CASPASE-1-DEPENDENT PATHWAYS

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Background

Melioidosis is a serious infectious disease caused by the Gram negative bacterium *Burkholderia pseudomallei* which has a high mortality rate, especially in septicemic patients. It has been speculated that DNA methylation plays a role in the regulation of inflammatory cytokines during sepsis. However, the patterns and mechanisms of these changes are poorly understood and to date have not been studied in melioidosis. Here, we extended our previous study on whole blood transcriptomes of septicemic melioidosis patients to now analyze the whole blood DNA methylome during acute infection compared with healthy subjects from the endemic region of N.E. Thailand.

Methods

A published data on sepsis melioidosis transcriptome was re-analyzed in depth. The DNA methylation profile was determined using the Infinium HumanMethylation450 BeadChip (450K) (Illumina Inc.). The data was extracted and the initial analysis was performed using GenomeStudio (2010.3) methylation module (1.8.5). Statistical significance was determined using a two tailed Student t-test.

Results

Significant upregulation of a set of genes involved in capase-1-dependent inflammasome activation was found in septicemic whole blood transcriptomes. Of these, *AIM2, GBP6, NLRP3* and *NLRC4* were significantly demethylated near their gene promoters. We also found strong upregulation of Guanylate Binding Protein (GBP) family members that had not been previously reported in melioidosis and we are now investigating their role in infection.

Conclusions

Our findings provide new insights on the changes in DNA methylation during acute bacterial infection in humans which are likely to influence the inflammatory response and the outcome of infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0698
ORAL PRESENTATION SESSION 11 - INFECTION AND IMMUNITY

THE BEFORE-AFTER STUDY OF IMMUNOGLOBULIN PLUS PREDNISOLONE THERAPY IN KAWASAKI DISEASE

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Background: It has been reported that the incidence of coronary lesions can be decreased by the administration of IVIG in combination with PSL as the initial treatment in cases potentially refractory to IVIG. However, adverse reactions associated with steroid administration and the prophylactic effect thereof on large coronary lesions have not been elucidated as of yet. Therefore, in order to determine the external validity, we evaluated the effect and the risk factor of initial treatment in cases potentially refractory to IVIG over the past 10 years at Tokyo Rinkai Hospital.

Methods: Kawasaki Disease patients with a Kobayashi Score (KS) of 5 points or higher were assigned to either IVIG monotherapy group (42 cases) or the PSL combination group (48 cases). The primary endpoint was refractoriness or relapse, while the secondary endpoints were the absence or presence of coronary lesions, adverse reactions and the risk factor of refractory to IVIG.

Result: Regarding the subject backgrounds, the age in months of the subjects in the IVIG monotherapy group and the PSL combination group was 35 months and 44 months, respectively, with the majority being male in both groups, while the mean KS was 6.3 points and 6.8 points, respectively.

In the ratio of refractory and relapse cases in the PSL combination groups compared with the IVIG monotherapy group (Odds ratio: 0.28, $P < 0.05$). No statistically significant differences were observed in the incident of coronary lesions and adverse reactions. The risk factor of refractory to IVIG was total bilirubin 0.9mg/dl or higher.

Conclusion: It was suggested that PSL combination therapy may safely reduce the number of refractory cases. In the future, adding total bilirubin to KS, an evaluation of mPSL combination therapy as a second line therapy in treatment-refractory cases is required.

Clinical Trial Registration (Please input N/A if not registered)

Tokyo Rinkai Hospital 072

ESP16-0258
ORAL PRESENTATION SESSION 12 - IMMUNOPATHOGENESIS 2

PREVALENCE OF CLOSTRIDIUM DIFFICILE AND ASSOCIATED MICROBIOTAL CHANGES IN HOSPITALISED CHILDREN WITH DIARRHOEA IN MERSEYSIDE, UK

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Background

Clostridium difficile infection is an important cause of morbidity and mortality in adults. Frequently found in the paediatric gut, its significance here is less clear. We aimed to review demographics, prevalence of *C. difficile* and microbiotal patterns in diarrhoeal children.

Methods

A total of 196 faecal samples were tested from hospitalised children with diarrhoea (77 children < 2yrs and 119 children 2-16yrs). Demographics were gathered on co-morbidities, current medication and recent antibiotic exposure. Faecal samples were cultured and tested for the presence of *C*. *difficile* antigen (GDH) and toxins A/B. Isolates were characterised using PCR-ribotyping. DNA was extracted from a subset of stools for 16S sequencing.

Results

A total of 19 samples (25%) from <2yr and 13 samples (11%) from >2yr group were culture and antigen positive for *C. difficile*. Of these, 10 (53%) of the <2yr samples and 9 (69%) of the >2yr samples were toxigenic. Most common ribotypes were: 039, 020, 002, 014 and 017. Current proton-pump inhibitor/H2-receptor antagonist use and PEG/JEJ feeding were significantly associated with the presence *of C. difficile* in stools (p=0.02 and p=0.009 respectively). There was no difference in species richness indices (SChao1/SACE) between those with and without *C. difficile*, but increased proportions of proteobacteria and fewer bacteroidetes were seen in children carrying toxigenic *C. difficile* strains. Abundance of Ruminococci, Lachnospiraceae and Klebsiella also correlated with presence of *C. difficile*.

Conclusions

Children with diarrhoea frequently harboured toxigenic isolates of C. *difficile,* but stool microbiota remained diverse. Milieu in children with *C. difficile* differs from that described in adults; suggesting that these differential abundances in the presence of *C. difficile,* rather than simply the presence of *C. difficile* may drive diarrhoeal disease.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0303
ORAL PRESENTATION SESSION 12 - IMMUNOPATHOGENESIS 2

EFFECTS OF PATIENT ISOLATES OF ECHOVIRUS 30 OUTBREAK STRAINS ON THE INTEGRITY OF THE BLOOD-CSF BARRIER

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Background

With an estimated incidence in high income countries of 12 to 19 cases per 100.000 population per year, aseptic/viral meningitis is almost threefold more frequent than bacterial meningitis. Non-polio enteroviruses (NPEV) are the main cause of viral meningitis world-wide with young age as an important epidemiologic factor.

Methods

Using three different patient isolates from the German Echovirus (EV) 30 outbreak in 2013, we investigated the impact on the blood-CSF barrier (BCSFB) in a human *in vitro* model. Via q-PCR, viral titres and replication rates in human plexus epithelial cells (HIBCPP) were determined. Changes in the barrier integrity were evaluated via the measurement of the TEER and the transcellular permeability of dextran. Immunofluorescence and Western blotting were applied to analyze alterations within the expression and localization of tight and adherens junction proteins.

Results

Strain dependent differences on the integrity of the BCSFB could be determined. The barrier function as well as the tight junction protein ZO-1 expression was diminished by the infection with all tested EV30 strains (EV30 wildtype; EV30 13-311; EV30 13-759; EV30 14-397), whereas the tight junction protein Occludin remained intact. The strain EV30 14-397 showed a slower replication rate and less impact on the BCSFB in respect to viability and barrier integrity compared to the other strains.

Conclusions

Different strains of EV30 differ in their cytotoxic properties and influence on the integrity of the BCSFB. These results should be correlated with clinical data in order to be able to differentiate between less and more virulent strains of EV30.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0194
ORAL PRESENTATION SESSION 12 - IMMUNOPATHOGENESIS 2

ENDOGENOUS ALARMINS S100A8/A9 INDUCE MICROBIOLOGICAL TOLERANCE IN NEONATES

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Background

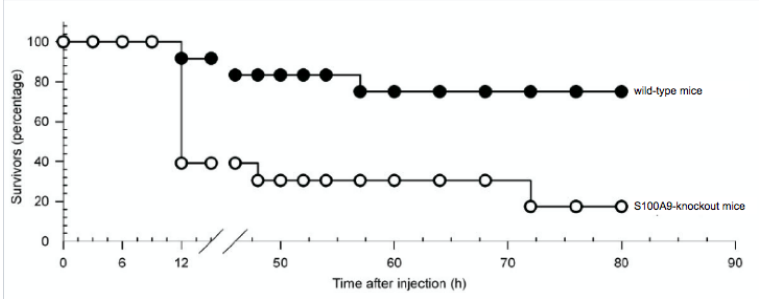
Sepsis still is a leading cause of perinatal mortality. An impaired innate immune response represents a key factor in its pathogenesis. In adult sepsis a secondary stage of immunoparalysis is characterized by hypoinflammation and endotoxin tolerance. Endotoxin tolerance is a well-known phenomenon in phagocytes induced by low-dose endotoxin-stimulation of Toll-like-receptor-4 (TLR4). Recently, the alarmins S100A8 and S100A9 have been identified as endogenous TLR4-ligands. The role of alarmins in neonatal sepsis and their potential to induce microbial tolerance has not been analysed so far.

Methods

S100A8/A9 serum levels were analyzed and effects of S100A8/A9 on phagocytes examined by gene expression and cytokine analysis. Neonatal S100A9 knock out mice were compared to wild-type mice in a neonatal endotoxinemia model.

Results

We show for the first time that the phagocyte-specific alarmins S100A8 and S100A9 similar to exogenous lipopolysaccharide prime phagocytes for a state of hyporesponsiveness to subsequent microbial challenge in a TLR4-dependent manner. Surprisingly, healthy neonates presented with extremely high serum levels of S100A8/S100A9 that decreased to normal adult values within the first week of life. We proved that the massive release of S100A8/S100A9 upon birth is responsible for the induction of microbial hyporesponsiveness in neonatal phagocytes. In the murine model this mechanism resulted in enhanced survival of wild-type pups compared to S100A9-knockout pups suggesting that S100A8 and S100A9 represent important regulators of the inflammatory responsivity of neonates.



Conclusions

Our observations unravel the birth-associated stress-release of endogenous alarmins S100A8/S100A9 as novel regulatory mechanism for inflammatory responses in the neonatal period.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0095
ORAL PRESENTATION SESSION 12 - IMMUNOPATHOGENESIS 2

CORRELATION BETWEEN GROUP B STREPTOCOCCUS (GBS) SEROTYPE-SPECIFIC ANTIBODY-MEDIATED COMPLEMENT C3B-IC3B DEPOSITION AND GBS COLONISATION IN GAMBIAN INFANTS

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Background

Infant colonisation with GBS is a prerequisite for early onset GBS disease (EOGBS). We sought to determine if naturally occurring maternally-derived antibody is associated with reduced infant GBS colonization at birth and three months of age.

Methods

We used a flow cytometric assay to determine antibody-mediated C3b/iC3b deposition against GBS serotypes (ST) Ia, II, III and V in 750 Gambian women and their infants. This assay has been shown to correlate with opsonophagocytic killing. We obtained rectovaginal swabs from mothers in labour and nasopharyngeal and rectal swabs from infants at birth, six days and three months to determine colonizing serotype and bacterial concentration by culture and PCR. We compared ST-specific antibody-mediated C3b/iC3b deposition in cord blood and infant serum to ST-specific maternal and infant colonisation dynamics at birth and 3 months using ANOVA.

Results

When both mother and infant were colonised at birth, C3b/iC3b deposition was significantly lower than in non-colonised mother/infant pairs (STIa (<0.001), STII (p<0.001), STIII (p<0.001) and STV (p<0.001)). Compared to non-colonised mother/infant pairs, colonised pairs had significantly lower C3b/iC3b deposition to STIa (p=0.001), STII (p=0.001), STIII (p<0.001) but not STV (p=1.0). Infants who were persistently colonised with the same serotype from birth to day 60-90 had significantly lower C3b/iC3b deposition than infants who remained non-colonised for STII (p=0.04) and STV (p=0.01). Infants with high concentrations (>75th centile) were less likely to be colonised with STIa (p<0.001), STII (p<0.001), STIII (p=0.01) and STV (p<0.001) than infants with low concentrations (<25th centile).

Conclusions

Higher concentrations of maternally-derived antibodies are associated with a decreased risk of GBS colonisation in infants at birth. Enhancing maternally derived antibody concentrations through vaccination may reduce infant colonisation and reduce the risk of EOGBS.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0225
ORAL PRESENTATION SESSION 12 - IMMUNOPATHOGENESIS 2

B CELL SUBSET ALTERATION DURING ACUTE DENGUE VIRAL INFECTION

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Background

While antibody response plays a major role in dengue-induced immunopathology as well as protection against dengue-viral infection, little is known about the alteration of B cell subsets especially antibody-secreting cells (ASCs) which producing antibodies during the ongoing infection. B cell subsets' alteration and mobilization may dictate their distribution to different target organs during an acute dengue-viral infection.

Methods

Thirty-five confirmed pediatric dengue-infected patients were recruited in this study. Whole blood samples were stained with a combination of fluorochrome-conjugated monoclonal antibodies against cell surface molecules, including CD3, CD14, CD19, CD20, CD21, CD27, CD38, CD45 and various homing molecules. The stained samples were analyzed by flow cytometer. Healthy volunteers were also recruited for a control group.

Results

B cells were divided into 5 subsets based on the expression of CD19, CD20, CD21, CD27 and CD38. High levels of ASCs were observed in dengue-infected patients. Moreover, lower frequencies of naïve and resting memory B cells were observed. However, activated memory and tissue memory B cells showed no different. When comparing between patients categorized as dengue fever and dengue hemorrhagic fever, no difference was observed for any B cell subsets. With respect of organ-homing molecules, marked increases in the frequencies of ASCs expressing CXCR3 and CCR2 were detected.

Conclusions

Alteration of B cell subsets during acute dengue infection were determined by a significant increase in ASCs and marked decreases in naïve and memory cells.However, the alteration of B cell subsets did not show association with disease severity. Furthermore, the result also suggested the mobilization of ASCs to inflamed tissues.

Clinical Trial Registration (Please input N/A if not registered)

Approval by Institution Review Board (IRB) at the Faculty of Medicine Siriraj Hospital (304/2558 (EC4)).

ESP16-0485
ORAL PRESENTATION SESSION 12 - IMMUNOPATHOGENESIS 2

A CASE-CONTROL STUDY INVESTIGATING THE ROLE OF HISTO-BLOOD GROUP ANTIGENS IN TAIWANESE CHILDREN WITH SALMONELLOSIS

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Background

Histo-blood group antigens (HBGAs) including secretor status (determined by FUT2), Lewis antigens (determined by FUT3) and ABO types have been reported to be associated with the susceptibility to enteropathogens including norovirus, rotavirus and *Campylobacter* infections. The relationship of HBGAs and *Salmonella* infections, another common etiology of pediatric acute diarrhea, remains unclear.

Methods

A case-control study was conducted in northern Taiwan from May to December in 2015. The cases were children younger than 18 years old who were hospitalized because of diarrhea with laboratory-confirmed *Salmonella* infection. Healthy Taiwanese children with the HGBAs genotypes determined were used as historical controls of and those with age and sex matched to the cases were included. The distributions of FUT2, FUT3 and ABO genotypes were determined by molecular methods and were compared between cases and controls.

Results

A total of 71 cases and 136 controls were enrolled. Of the cases subjects, 41 (57.7%) cases were male and the mean age was 2.74 years old (range, 0.1 – 11 years). The serotypes of *Salmonella* included *S. enteritis* type B (27, 38.0%), type C (7, 9.9%) and type D (37, 52.1%). Of 207 subjects, secretor and weak-secretor was respectively identified in 157 (75.8%) and 50 (24.2%) subjects. Non-secretor was absent in this cohort. Lewis-positive genotype accounted for 181 (87.4%) subjects. We did not identify significant differences between the cases and controls in terms of the distributions of the secretor genotype (77.9% vs. 71.8%, p=0.330), Lewis-positive genotype (89% vs. 84.5%, p=0.358) and ABO blood types (p=0.698).

Conclusions

The HBGAs including secretor status, Lewis antigens and ABO types was not associated with the susceptibility to salmonellosis in Taiwanese children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

E-Poster Discussion Abstracts

ESP16-0459
E-POSTER DISCUSSION SESSION 1 - EPIDEMIOLOGY AND PUBLIC HEALTH 1 (station 2)

ESTIMATING THE IMPACT OF CHILDHOOD INFLUENZA VACCINATIONS ON THE BURDEN OF INFLUENZA IN THE GENERAL POPULATION IN ENGLAND THROUGH PREDICTIVE MODELLING

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Background

Children experience higher influenza attack rates than adults and are largely responsible for the transmission of influenza in the community. Public Health England (PHE) is undertaking a gradual implementation of the extension of routine influenza vaccination to children through regional and nationwide pilots.

This study estimates the impact of extending routine influenza vaccination to children on influenza burden in the general population in England.

Methods

Weekly rates of influenza-related consultations in General Practices (GP) were modelled using a dynamic Bayesian model informed by the Clinical Practice Research Datalink (CPRD), Datamart laboratory data on A/B viruses, and an age-dependent contact matrix derived from the POLYMOD survey dataset. Given a scenario of vaccine exposure, influenza infection rates were simulated. As a case study, GP consultation rates for influenza-like illness (ILI) and vaccination coverage for the 2010/2011 influenza season (covering 2.67 million people) were calculated to estimate the impact of extending routine vaccination to children <11 years. Two scenarios were compared based on age-specific vaccine coverage rates observed outside (Scenario-1) and within (Scenario-2) PHE pilots.

Results

Table 1 presents influenza incidence rates per 100 people for scenario-1 versus scenario-2, which were 29.6 versus 18.9 for type A and 10.8 versus 3.0 for type B. Extending routine vaccination to children resulted in a 46.1% reduction in infections (36.3% in type A and 71.8% in type B) across the general population. Observed weekly ILI consultation rates from CPRD

were compared to model results for verification.

	Scenario-1 (observed vaccination coverage outside PHE pilot regions)			Scenario-2 (observed vaccination coverage inside pHE pilot regions)			Comparison scenario-1 vs -2	
Age group	Vaccination coverage (%)	Estimated type A incidence per 100	Estimated type B incidence per 100	Vaccination coverage (%)	Estimated type A incidence per 100	Estimated type B incidence per 100	Type A reduction (%)	Type B reduction (%)
0–1 years	1.6	32.1	13.2	42.6	15.0	2.5	53.1	80.7
2–3 years	3.1	49.4	23.1	39.5	24.6	4.4	50.2	80.7
4 years	3.7	73.8	42.3	32.9	43.6	9.6	40.9	76.7
5–10 years	3.9	61.2	36.9	52.5	26.3	6.0	57.0	83.4
11–17 years	4.1	58.2	36.1	4.1	46.4	14.9	20.2	57.8
18–64 years	10.2	27.8	6.2	10.2	18.2	1.7	34.5	73.0
65 and above	71.1	4.8	0.5	71.1	3.1	0.1	36.3	75.0
All age groups	19.7	29.6	10.8	24.9	18.9	3.0	36.3	71.8

Conclusions

Model-based estimations support the conclusion that extending influenza vaccination to children provides additional protection for the general population. Further model extensions will include data from more recent seasons, information on hospitalisations/deaths, and more extensive laboratory data.

Study sponsored by AstraZeneca.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0811
E-POSTER DISCUSSION SESSION 1 - EPIDEMIOLOGY AND PUBLIC HEALTH 1 (station 2)

COST-EFFECTIVENESS EVALUATION OF 10 VERSUS 13 VALENT PNEUMOCOCCAL CONJUGATE VACCINES IN CANADA

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Background

In Canada, the burden of pneumococcal disease has decreased since the introduction of pneumococcal conjugate vaccines (PCVs). Current vaccination programs make use of the 13-valent PCV (PCV-13). Emerging real world effectiveness data have demonstrated comparable benefits for the use of PCV-10, specifically for cross protection to the 19A non-vaccine serotype. It is therefore prudent and timely to compare the health outcomes and economic value of both vaccines in the Canadian context.

Methods

A Markov model1 was adapted with Canadian costs and effectiveness data using current literature and surveillance data. Effectiveness for the vaccine types in PCV-10 and PCV-13 was estimated as 94.7%. Conservative effectiveness estimates for PCV-10 cross protection were 76%, and 71% for the non-vaccine serotypes 6A and 19A, respectively. Herd protection, serotype replacement, and waning effectiveness were included in the analysis. Direct costs and outcomes were discounted by 5% as per Canadian guidelines.

Results

A Canadian birth cohort of 388,729 children with 90% vaccine coverage was modeled over 100 years. This model predicts no difference in deaths but one additional case due to invasive pneumococcal disease (IPD; meningitis, bacteraemia) for PCV-10. PCV-10 offered a greater protection against acute otitis media (AOM) than PCV-13 (cases prevented: 353,382). At price parity, PCV-10 saves treatment costs and prevents additional cases of AOM, thus dominating PCV-13.

Conclusions

This modeling study extrapolates the real world evidence that PCV-10 offers protection comparable to PCV-13 against IPD. The additional cases of AOM prevented provide a benefit beyond that offered by PCV-13. In the event of a 30% price difference, it is predicted that a PCV-10 immunization program would save approximately $29M per Canadian birth cohort in direct costs alone.

1 doi: 10.3111/13696998.2011.622323

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1076
E-POSTER DISCUSSION SESSION 1 - EPIDEMIOLOGY AND PUBLIC HEALTH 1 (station 2)

INVASIVE MENINGOCOCCAL DISEASE (IMD) IN BRAZIL: IMPACT OF MENACWY VERSUS MENC VACCINES EVALUATED BY A DISEASE TRANSMISSION DYNAMIC MODEL

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Background

To evaluate the reduction of Invasive Meningococcal Disease(IMD) as result of the introduction of different strategies of monovalent or tetravalent meningococcal vaccine.

Methods

A disease transmission dynamic model was developed based on a tridimensional compartmental structure. Individuals can evolve as susceptible, asymptomatic carrier of *Neisseria meningitidis* or IMD (C and AWY distinct compartments), vaccinated (mono and/or tetravalent vaccine), or immunized compartments. Model algorithm was developed under a R platform with a MS Excel user interface for inputs and outputs. The baseline vaccination strategy was defined as current routine MenC at 3, 5 and 12 months. Two epidemiologic scenarios were considered: 14% of AWY prevalence among all IMD like at national level and 18% like in Brazilian south region.

Results

In the national prevalence scenario, over 10 years, adding a routine of MenACWY at 9 y.o. reduced by 8% (394 cases) the number of IMD, while similar MenC strategy reduced by 4% (219) the number of IMD, resulting then in 80% more IMD cases avoided with MenACWY. When adding a catch up (10 to 21 years cohorts) to the 9 y.o. routine strategy, 23% (1188) reduction is expected with a MenACWY and 14% (731) with MenC. The same catch-up strategy in the South epidemiologic scenario resulted in reduction of 23% (1530) for MenACWY and 10% IMD cases (686) for MenC.

Conclusions

Meningococcal vaccination in people aged more than 9 years old would reduce the number of IMD, especially when considering mass immunization strategies. This reduction is always higher when a tetravalent vaccine is considered, reaching more than 1500 cases avoided in a situation with high AWY prevalence.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1057
E-POSTER DISCUSSION SESSION 1 - EPIDEMIOLOGY AND PUBLIC HEALTH 1 (station 2)

RISK FACTORS FOR COMPLICATIONS AND POOR TREATMENT OUTCOMES IN CHILDREN WITH TUBERCULOSIS IN SPAIN: A PROSPECTIVE MULTI-CENTER STUDY FROM THE SPANISH PEDIATRIC TB NETWORK

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Background

Children have increased risk of tuberculosis (TB) dissemination and disease severity, and contribute critically on overall TB-associated morbidity and long term sequelae. We aim to describe the risk factors for complications and poor treatment outcomes of pediatric TB cases in Spain.

Methods

We analyzed childhood TB cases enrolled prospectively in the nationwide, multi-center Spanish Pediatric TB Research Network (pTBred). We assessed the incidence of acute complications at diagnosis, complications during antituberculous treatment (including paradoxical reactions), and site specific long-term sequelae. Ethical approval from all the participant centers was obtained. We calculated associated risk factors with multivariable logistic regression models.

Results

Between 2014 and 2015, 340 children with TB disease were enrolled (50% males; median [IQR] age 5.3[2.9-11.4] years). Of them, 34.4% were confirmed TB cases. Overall, the incidence of complications was 16.7% (8.6% at diagnosis, 10.2% during treatment, including 6 children with both), and 4.1% of the children developed long term sequelae. Two children died of TB. The incidence of complications was higher for children <1 year (54.5%, p<0.0001), children born to foreign parents (24%, p=0.002), miliary TB (71.4%, p=0.002), TB meningitis (63.6%, p<0.0001), and skeletal TB cases (100%, p=0.004). Complications were associated with age <1 year (OR 4.8[1.7-13.9], p=0.003), Tuberculin Skin Test induration <5mm (OR 3.1[1-9.7]; p=0.04), bacteriological confirmation (OR 3.3[1.5-7.4], p=0.003) and TB meningitis (OR 4.2[1-18], p=0.04). Long-term sequelae were associated with miliary TB (OR 18[2.1-163], p=0.008) and TB meningitis (OR 15.1[2.7-83.7], p=0.002).

Conclusions

In Spain, the incidence of TB related complications in children remains high, and is strongly associated with early infancy, extrapulmonary disease and enhanced bacteriological confirmation. In our low-burden country, extrapulmonary TB is still responsible of significant long term sequelae and permanent disabilities.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1029
E-POSTER DISCUSSION SESSION 1 - EPIDEMIOLOGY AND PUBLIC HEALTH 1 (station 2)

COLONISATION WITH GRAM-NEGATIVE BACTERIA (GNB) IN INFANTS IN THE NEONATAL UNITS (NNUS) OF THE SOUTH-LONDON NEONATAL NETWORK-THE NEOHIEC STUDY

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Background

Infection is a major issue in the care of hospitalised neonates and its prevention remains a cornerstone of good neonatal care. Multi-resistant Gram-negative bacterial (MRGNB) infections and outbreaks are of particular concern in NNUs across the UK and globally. In order to devise strategies to prevent and control these infections the NeoHIEC Study was undertaken in the south-London neonatal network.

Methods

The NeoHIEC is a large observational cohort study conducted in south-London NNUs aiming to define the epidemiology of neonatal colonisation with MRGNB. During the first 3 months of the study (October-December 2013) samples were collected from 5 NNUs, stored and analysed in batches. All identified GNB were subjected to antibiotic susceptibility testing using BSAC 2014 methodology. MRGNB were defined as isolates resistant to 3 or more antibiotic classes.

Results

782 samples were collected from 421 infants. Overall, 386 GNB were isolated from 297 infants; the majority (349, 90.4%) were *Enterobacteriaceae* with *Klebsiella* spp accounting for 51.3 % (179/349). 19% of the isolates were MRGNB. Median age at the time of colonisation was 35.5 days (range 3-216). Overall resistance to different antibiotics and specific resistance profiles for the most frequent isolates is shown on the table.

		Tobramycin	3rd gen Cephalosporins	Ciprofloxacin	Piptazobactam	Gentamicin	Carbapenems	Colistin
Overall resistance rates to different antibiotics	**Resistant (%)**	46/380 (12)	42/380 (11)	41/383 (11)	21/383 (5)	8/383 (2)	4/380 (1)	3/383 (<1)
	Intermediate (%)	0	0	0	2/383 (<1)	3/383 (<1)	9/380 (2)	0
Resistance rates for the most common *Enterobacteriaceae*	***E. coli* n=112 n (%)**	18 (16)	11 (10)	19 (17)	2 (2)	6 (5)	0	0
	***Klebsiella* spp n=179 n (%)**	24 (13)	20 (11)	20 (11)	9 (5)	1 (<1)	0	0
	***Enterobacter* spp n=58 n (%)**	1 (2)	9 (15)	0	9 (15)	0	3 (5) Intermediate: 6 (10)	0

Conclusions

Hospitalised neonates are frequently colonised with MRGNB of which the majority are Enterobacteriaceae. Resistance to gentamicin, the most commonly used antibiotic against GNB in the UK, remains low overall. More work is required to define transmission of MRGNB within the NNU and through the neonatal network, as well as its relationship with invasive infections.

On behalf of the NeoHIEC Study consortium in south-London, UK

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0169
E-POSTER DISCUSSION SESSION 1 - EPIDEMIOLOGY AND PUBLIC HEALTH 1 (station 2)

MULTICENTER STUDY OF THE INCIDENCE AND RISK OF GROUP B STREPTOCOCCAL COLONIZATION IN NEONATES IN JAPAN

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Background

In Japan, universal screening for group B streptococcal (GBS) colonization in pregnant woman and intrapartum antibiotic prophylaxis (IAP) in positive cases have been recommended to prevent neonatal GBS infection. However, severe GBS infection, especially late-onset disease, remains a leading cause of neonatal infection. Early identification of GBS carriage among neonates is important to prevent and successfully treat GBS infection. The aim of this study was to clarify the incidence and risk of GBS colonization in neonates.

Methods

We conducted a prospective, multicenter study from October 2014 to May 2015 in Japan. Nasopharyngeal and rectal swab samples of 730 neonates were obtained at 1 week and 1 month after birth, and the samples were subjected to GBS identification using our invented real-time PCR method as well as bacterial culture. GBS-positive samples subsequently underwent capsular typing and multilocus sequence typing.

Results

GBS-positive neonates accounted for 8.8% (n=64) by PCR and 6.3% by culture. Of these, 3.2% (n=23) and 5.6% (n=41) were identified at 1 week and 1 month, respectively, after birth. GBS colonization was identified in nasopharyngeal samples in 2.5% and rectal samples in 6.6%. The newborns of GBS-positive mothers were more likely to show GBS colonization ($p<0.01$). Most GBS-positive mothers (n=107) had received IAP. Capsular types V (32%), III (30%), Ib (20%), and Ia (18%) were predominant among the isolates. Three sequence types, ST1, ST335, and ST10, accounted for 79.3% of the isolates. No infants developed invasive GBS disease during the study.

Conclusions

It was concluded that even if GBS-positive mothers receive IAP, the risk of GBS carriage among their neonates is high. A better understanding of the risk of GBS colonization after birth will contribute to the prevention of severe GBS infection.

ESP16-0687
E-POSTER DISCUSSION SESSION 1 - EPIDEMIOLOGY AND PUBLIC HEALTH 1 (station 2)

EPIDEMIOLOGY AND SEVERITY OF RESPIRATORY SYNCYTIAL VIRUS INFECTIONS PRESENTING TO A TERTIARY CHILDREN'S HOSPITAL USING A NOVEL SCORING SYSTEM

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Background

Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infection and bronchiolitis in infants and young children. With the possibility of new RSV vaccines being available in the near future, detailed information concerning the current epidemiology and severity of RSV infections will be essential in determining the impact of any vaccine(s).This study aimed to determine the clinical severity of and epidemiological risk factors in Australian children hospitalised with RSV infection.

Methods

Prospective recruitment of children <2 years of age presenting to a tertiary children's hospital with proven RSV infection was performed in the same epidemic season, with collection of detailed epidemiological data. Applying the "Brisbane RSV Score" to cases, severity was determined and graded based on 3 factors; the length of admission, the need for supplemental feeding and oxygen/ventilator support.

Results

59 children were enrolled with 13 (22%) determined to have severe RSV disease. The majority of infections were in children < 6 months old (54%) and males (56%). Severe RSV disease was more common in infants < 3 months of age with younger infants over 4 times more likely to have severe disease (OR 4.5 (1.2-16.6), p=0.022). Median hospital stay was 49 hours, compared to 187 hours for severe disease. Co-infections with other respiratory viruses occurred in 17 patients (29%) with rhinovirus being most common (n=9; 15%). A family history of atopy was reported in 43 cases (73%) as well as in severe RSV infection (85%).

Conclusions

Severe RSV disease remains a significant burden on children's health care resources. A family history of atopy was common in children hospitalised with RSV infection. Any RSV vaccination strategy would need to protect children early in life to prevent severe RSV disease.

ESP16-0319
E-POSTER DISCUSSION SESSION 2 - HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS & INFECTION CONTROL (station 3)

OUTCOME OF HEALTHCARE-ASSOCIATED INFECTIONS IN PAEDIATRIC AND NEONATAL INTENSIVE CARE UNITS: MULTIVARIATE ANALYSIS OF THE IMPACT OF COHORT CHARACTERISTICS ON 30-DAY MORTALITY

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Background

Healthcare-associated infections are one of the most frequent adverse event affecting children admitted to ICUs. However, few data are currently available on their prevalence and impact in paediatrics. The aim of this study was to analyse the impact of risk factors and AMR on mortality of HAI (CDC definitions) in children admitted to ICU.

Methods

This multicentre, prospective, cohort study was conducted in three tertiary-care paediatric hospitals in Italy and Brazil. All patients aged ≤18 years, admitted to ICU (PICU, NICU or CICU) between 2010 and 2014, with microbiologically-confirmed diagnosis of HAI were included.

Results

Overall, 538 episodes in 454 children were identified. The median age was 7.8 months (IQR 2.1-26.2). 93.3% of patients had an underlying disease. The cumulative incidence was 3.6/100 ICU-admission whereas the rate of infections was 3.6/1,000 ICU-days. The crude rate of mortality was 7% for 7-day and 10.1% for 30-day mortality. In the multivariate analysis, factors independently associated with 30-day mortality were country (Brazil, adjusted-OR: 2.1; 95%CI: 1.2-3.4), BSI (adjusted-OR: 4.5; 95%CI: 1.8-11.4), LRTI (adjusted-OR: 3.1; 95%CI: 1.2-8.1), and MDR infection (adjusted-OR: 1.8; 95%CI: 1.1-3.2).

Conclusions

The overall incidence and mortality of HAI in this cohort is lower than reported in the adult literature. The great majority of children who acquire HAIs have pre-existing underlying disease. Global efforts to reduce HAI in children should focus on BSI prevention in this at risk population.

ESP16-0560
E-POSTER DISCUSSION SESSION 2 - HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS & INFECTION CONTROL (station 3)

ATTRIBUTABLE LENGTH OF STAY FOR PEDIATRIC AND NEONATAL CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTIONS

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Background

Central line-associated bloodstream infections (CLABSIs) are frequent hospital-acquired infections, related with high morbidity and healthcare costs. Little is known about the attributable length of stay (LOS) due to CLABSI in Greek pediatric and neonatal population, the determination of which was the aim of our study.

Methods

A retrospective cohort study was performed, in 2 tertiary pediatric hospitals. Inpatients with a central line in NICUs, PICUs, Hematology/Oncology Units and a Bone Marrow Transplantation Unit (BMTU) during the period 6/2012 – 6/2015 were eligible. Patients with confirmed CLABSI were enrolled on the day of the event and were matched (1:1) to ones without CLABSI (non-CLABSIs) by hospital, unit and LOS prior to study enrolment. Our outcome measure was the LOS after the enrollment day. Baseline demographic, hospitalization and central line characteristics along with factors stating severity of illness were also recorded.

Results

Of 189 children studied, 94 presented a CLABSI. There were no differences between the two groups, regarding baseline clinical and demographic characteristics. In the univariate analysis, more CLABSI patients had been transfused with blood products the 14 days prior to study enrollment (84% CLABSI v 70.5% non-CLABSI, p=0.027). The median (25^{th}-75^{th} percentile) LOS was 37 days (18.5-77) and 22 days (13-48) in patients with CLABSI and non-CLABSI, respectively (p=0.009). Multiple regression analysis, showed that LOS and multiple central lines the 14 days prior to patients' enrollment (p=0.006 & p=0.012, respectively), neutropenia (p=0.002) and CLABSI (p=0.002) were independently associated with higher LOS. The adjusted attributable LOS was found to be 12.4 days.

Conclusions

It was found that CLABSI has a significant impact on LOS indicating the need for the implementation of CLABSI prevention initiatives in Greek pediatric and neonatal population.

ESP16-0429
E-POSTER DISCUSSION SESSION 2 - HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS & INFECTION CONTROL (station 3)

FIRST REPORT OF HOSPITAL-ACQUIRED INFECTIONS WITH USA300 METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS IN JAPANESE PEDIATRIC POPULATION

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Background

The USA300 strain of methicillin-resistant *Staphylococcus aureus* (MRSA) is virulent and isolated in both community and nosocomial setting in the US. In Japan, infections with the USA300 strain are infrequent in community, and nosocomial infections have never been reported. Our aim of study is to identify the USA300 strains in MRSA isolated from hospital.

Methods

MRSA isolates from inpatients were included from June 2012 to April 2015 at Tokyo Metropolitan Children's Medical Center. Isolates were screened for the USA300 strain with genotyping by phage open reading frame typing method and reverse passive latex agglutination assay for Panton Valentine Leucocidin (PVL). Suspected strains were confirmed with the standard USA300 strain of CDC by pulsed-field gel electrophoresis (PFGE). PCR was performed to detect PVL gene and Arginine Catabolic Mobile Element (ACME) gene. Clinical data with the confirmed USA300 strain were reviewed from medical records.

Results

Total of 341 MRSA isolates were identified. Among those, 13 MRSA isolates were suspected and subsequently confirmed as the USA300 strain. All of them were positive for PVL gene and ACME gene. Clinical diseases were identified in 6 patients and the rest were interpreted as colonization. All clinical diseases occurred in neonatology unit. Those infections were 3 catheter related blood stream infections, 1 osteomyelitis, 1 skin abscess and 1 cervical lymphadenitis. All patients were successfully treated with vancomycin without sequelae.

Conclusions

This is the first report that the USA300 strain caused hospital acquired infections in Japanese pediatric population. Further emergence of the virulent strain should be closely monitored.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0282
E-POSTER DISCUSSION SESSION 2 - HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS & INFECTION CONTROL (station 3)

VANCOMYCIN RESISTANT ENTEROCOCCI COLONIZATION IN A NEONATAL INTENSIVE CARE UNIT: WHO WILL BE INFECTED?

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Background

To determine incidence of vancomycin resistan enterococcus (VRE) colonization in our neonatal intensive care unit (NICU) over five-year period, rate of progression to VRE infection and associated risk factors.

Methods

A retrospective analysis of a prospective surveillance for VRE colonization and health care associated infections was made. Contact precautions were taken against colonization, although the application varied over the years due to repairs in the unit.

Results

VRE rectal colonization was detected in 200/1671 neonates (12%) admitted to NICU. It showed great interannual variability from 1.9% to 30.3%. Sytemic VRE infection developed in 6/200 VRE colonized patients (3%) within a median of 9 days (range:3-58 days). The risk factors for VRE infection development identified in the univariate analysis were long hospital stay (≥30 days), necrotizing enterocolitis, surgical procedure, extraventricular drainage, receipt of amphotericin B and receipt of glycopeptides after detection of VRE colonization. Crude in-hospital mortality was higher in neonates who developed a systemic VRE infection ($p<0.001$).

Conclusions

Maintaining physical conditions in the unit favorable for infection control and rational use of antibiotics are essential in control of VRE colonization and resultant infections. Special attention should be directed to VRE colonized babies carrying the risk factors.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0284
E-POSTER DISCUSSION SESSION 2 - HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS & INFECTION CONTROL (station 3)

IMPACT OF VANCOMYCIN-RESISTANT ENTEROCOCCI COLONIZATION IN CRITICALLY ILL PEDIATRIC PATIENTS

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Background

We aimed to determine the frequency of vancomycin-resistant enterococci (VRE) infection occurrence in previously VRE-colonized children in a pediatric intensive care unit (PICU) and to identify associated risk factors.

Methods

Infection control nurses have performed prospective surveillance of health care–associated infections and rectal VRE carriage in PICUs from January 2010-December 2014. This database was reviewed to obtain information about VRE-colonized and subsequently infected patients. A case-control study was performed to identify risk factors associated with VRE infection development in previously VRE-colonized patients.

Results

Out of 1,134 patients admitted to the PICU, 108 (9.5%) were found to be colonized with VRE throughout the study period. Systemic VRE infections developed in 11 VRE-colonized patients (10.2%), and these included primary bloodstream infection (n = 6), urinary tract infection (n = 3), meningitis and bloodstream infection (n = 1), and meningitis (n = 1). Logistic regression analysis indicated long hospital stay (≥30 days) and glycopeptide use after detection of VRE colonization as risk factors for developing VRE infection in VRE-colonized patients (odds ratio [OR], 5.76; 95% confidence interval [CI], 1.6-15.8; *P* = .017 and OR, 12.8; 95% CI, 1.9-26.6; *P* = .012, respectively).

Conclusions

VRE colonization has important consequences in pediatric critically ill patients. Strict infection control measures should be implemented to prevent VRE colonization and thereby VRE infections. Furthermore, irrational antibiotic use and particularly glycopeptide use in VRE-colonized patients should be restricted.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0684
E-POSTER DISCUSSION SESSION 2 - HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS & INFECTION CONTROL (station 3)

TRENDS IN COLONIZATION AND INFECTION DUE TO CARBAPENEM-RESISTANT GRAM-NEGATIVE BACTERIA IN A PEDIATRIC INTENSIVE CARE UNIT. A 35-MONTH STUDY

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Background

Patients in pediatric intensive care units (PICU) are at increased risk for infections caused by resistant bacteria. Our aim was to study rates of colonization and infection caused by carbapenem-resistant (CR) *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii,* during a 35-month period in a PICU.

Methods

Incidence and prevalence of rectum colonization, colonization pressure and incidence of infections caused by the 3 CR bacteria were recorded. The study included 4 periods [retrospectively, 1st: January 2013-January 2014, without active screening cultures (ASC); prospectively, 2nd: February 2014-December 2014, implementation of ASC; 3rd: January 2015-May 2015 with ASC and implementation of infection control measures (ICM) and 4th: June 2015-November 2015 with ASC and enhanced ICM (EICM)]. ASC consisted of rectal swabs taken weekly and cultured on MacConkey agar containing 1mg/l meropenem. ICM included mostly contact precautions. CR bacteria were phenotypically tested for metallo-beta-lactamase and *Klebsiella pneumoniae* carbapenemase (KPC).

Results

During ASC the rolling averages of incidence and prevalence of colonized patients as well as of colonization pressure, at 4-week basis,reduced significantly (p=0.04, p=0.007 and p=0.015 respectively, Figure).

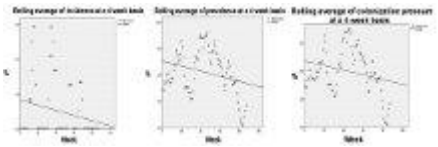

Figure: Incidence, prevalence and colonization pressure

Among newly colonized patients 38.5%, 38.5% and 23% acquired CR *K. pneumoniae,A. baumannii* and *P. aeruginosa,* respectively. Among *K. pneumoniae*, isolated from ASC and clinical samples, 100% were KPC producers during 1st period and 71.4% during the

prospective periods. Despite the reduction in rectum colonization, incidence of infections caused by CR bacteria (mainly by *A. baumannii,* and followed by *P. aeruginosa and K. pneumoniae*) remained constant.

Conclusions

A reduction of rectum colonization was observed after implementation of ASC and EICM. Incidence of infections caused by CR bacteria was not affected suggesting that other factors may play significant role in development of infections in PICU patients.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0812
E-POSTER DISCUSSION SESSION 2 - HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS & INFECTION CONTROL (station 3)

IMPROVEMENT INTERVENTIONS UTILIZING EXISTING RESOURCES FOR REDUCING HEALTHCARE ASSOCIATED INFECTIONS IN NICU: A PROSPECTIVE COHORT STUDY

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Background

Health Care Associated Infections (HAIs) are common cause of mortality among neonates in developing countries. We investigated the impact of a quality improvement (QI) model, within existing resources, on the incidence of (HAIs) in NICU.

Methods

Baseline data (patient days, device days, incidence of HAIs) was collected for 4 months. Simultaneously, various audit tools and care bundles—for monitoring compliance to hand hygiene (HH); availability of alcohol hand rub (AHR) and clean gloves; aseptic non-touch technique (ANTT) for peripheral intravascular (PIV) device insertion and intravenous (IV) fluid preparation; and clean resuscitation practices at birth—were designed and pilot tested. During the next 13 months (intervention phase), QI interventions were introduced in a phased manner. The QI initiatives included education (posters, discussions and teaching sessions), feedback based on video footage, improved availability of AHR and clean gloves, introduction of autoclaved steel tray sets for PIV device insertions and laminar flow for IV fluid preparation. The efficacy of QI initiatives was studied based on Plan-Do-Study-Act (PDSA) cycles. WE studied the *i*ncidence of HAIs before and after implementing QI measures, improvement in compliance to HH, availability of AHR, ANTT and clean resuscitation.

Results

442 neonates were studied over 15,951 patient days. The incidence rate of HAIs (culture positive sepsis and suspected sepsis) decreased from 42.6/1000 patient days in the baseline phase to 15.1/1000 patient days near the end of intervention phase ($p<0.001$). The incidence rate of culture positive sepsis decreased from 14.3 to 4.7 per 1000 patient days ($p<0.001$). Compliance to HH, clean resuscitation and ANTT bundles improved from 32%, 35% and 33% to 71%, 69% and 78%, respectively ($p<0.001$ for all).

Conclusions

QI approach within the existing resources significantly reduced the incidence rate of HAIs

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0846
E-POSTER DISCUSSION SESSION 2 - HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS & INFECTION CONTROL (station 3)

DEVELOPMENT, IMPLEMENTATION AND EVALUATION OF A PAEDIATRIC SEPSIS PROGRAM

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Background and Objective

Paediatric Sepsis is common and on the increase. Use of the American College of Critical Care Medicine (ACCM-PALS) guidelines has been shown to reduce associated morbidity and mortality. The Sepsis Six initiative, initially developed in the adult population, has been shown to improve outcome by increasing adherence to Surviving Sepsis Guidelines. The Great North Children's Hospital identified paediatric sepsis as a quality improvement project as part of the national "Sign up to Safety" Campaign.

Methods

Baseline data was gathered from audits of meningococcaemia and PICU sepsis admissions. Both retrospective audits independently found only 50% patients received antibiotics within the first 60 minutes. A prospective audit of antibiotic delivery in the paediatric emergency department and a hierarchical task analysis of antibiotic delivery to identify processes causing these delays were also undertaken.

A baseline staff survey was distributed throughout the multi-disciplinary team to establish sepsis knowledge and confidence levels. Mean confidence in recognising sepsis was 6.95 with a range from 1-10 (1-no confidence, 10-very confident).

Learning Points Discussion

Early local and regional focus groups were established. The local North East Young People's Advisory Group took an active role in the project. They were all involved in decisions about how to improve current systems in high risk areas and implementation of any changes.

We established a successful collaborative strategy for implementing Paediatric Sepsis guidelines with grassroots engagement.

We developed a paired educational package specifically aimed at targeting identified weaknesses using multi-faceted static and interactive media.

Outcome measures included staff knowledge, confidence and time to treatment and compliance to guidelines.

ESP16-0778
E-POSTER DISCUSSION SESSION 3 - SEVERE INFECTIONS 1 (station 4)

CATHELICIDIN CORRELATES WITH BACTERIAL GENOME COUNT IN CEREBROSPINAL FLUID IN CHILDHOOD BACTERIAL MENINGITIS

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Background

Cathelicidin (LL-37) is an antimicrobial peptide, which contributes to the host defense in bacterial meningitis (BM). Because the number of bacteria in the cerebrospinal fluid (CSF) and the strength of the inflammatory reaction in the central nervous system relate to the adverse outcomes, we investigated to which extent CSF cathelicidin concentrations associate with the CSF bacterial load, and whether the ratio of cathelicidin to bacterial load in CSF predicts the outcome of BM.

Methods

The study comprised 54 children (median age 8 months) with confirmed BM caused by *H.influenzae* (n=30), *S.pneumoniae* (n=20), and *N.meningitidis* (n=4). The data were collected in 1996-2003 during a clinical trial in Latin America, the CSF samples being obtained on admission (CSF1), and 12-24 hours later (CSF2). The bacterial load in CSF was assessed using quantitative real-time polymerase chain reaction (PCR); CSF cathelicidin concentrations were measured by ELISA.

Results

The CSF cathelicidin concentration was associated with the genome count in CSF1 ($n = 43$, rho 0.49, $p < 0.01$) and in CSF2 ($n = 35$, rho 0.41, $p = 0.02$). In CSF1, this relation remained significant when adjusting for CSF white cell count, and the protein and glucose levels. A higher cathelicidin to genome count -ratio in CSF1 related to better audiological outcome ($p = 0.02$).

Conclusions

Overall in BM, higher CSF cathelicidin concentrations associated with higher CSF genome counts. A higher cathelicidin to genome count -ratio reflected milder audiological impairment.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0756
E-POSTER DISCUSSION SESSION 3 - SEVERE INFECTIONS 1 (station 4)

PREDICTORS OF FEVER-RELATED ADMISSIONS TO A PAEDIATRIC ASSESSMENT UNIT (PAU), WARD AND RE-ATTENDANCES IN A SOUTH LONDON EMERGENCY DEPARTMENT. THE CABIN 2 STUDY

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Background

As the rate of severe bacterial infections in children presenting to an emergency department with fever is decreasing, there is a paradoxical increase in acute admissions to paediatric units, but length of stay is short (< 48 hours) highlighting the low-risk nature of the infections encountered.

Methods

Prospective observational study of febrile children attending a large tertiary care ED during the winter of 2014-15. Main outcomes included ward and paediatric assessment unit admissions (PAU), NICE guidelines classification, re-attendance and antibiotic use.

Results

A total of 1097 children attending the children's ED with fever were analysed. Risk factors for PAU admissions were tachycardia (RR=1.1, 95 % CI (1-1.1)), ill-appearance (RR=2.2, 95 % CI (1.2-4.2)), abnormal chest findings (RR=2.1, 95% CI (1.2-4.3)), NICE Amber risk category (RR 1.7 95 % CI (1.2-2.5)). For ward admissions systemic (RR=6.9, 95% CI (2.4-19.8)) or gastrointestinal illness (RR=3.8, 95% (1.4-10.4)) and risk-categorized as NICE Red (RR= 5.9, 95 % CI (2.2-15.3)). 30% of children at triage were incorrectly categorised for NICE risk status. Only 51 children had probable bacterial pneumonia (4.6%), 52 children had a proven UTI (4.2%), with just 2 (0.2%) positive blood cultures out of 485 (44%) children who received an antibiotic. 15 % of all children re-attended by 28 days and were more likely to have been categorised as Amber and had investigations on initial visit.

Conclusions

Risk factors for PAU and ward admissions are different in this setting with high re-attendance rates and very low proportion of confirmed/probable bacterial infections. Implementation studies need to focus on reducing avoidable admissions and antibiotic treatment.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0783
E-POSTER DISCUSSION SESSION 3 - SEVERE INFECTIONS 1 (station 4)

HIGH RATE OF RESPIRATORY VIRAL INFECTION IN CHILDREN WITH INVASIVE PNEUMOCOCCAL DISEASE AND IN HEALTHY CONTROL CHILDREN

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Background

Streptococcus pneumoniae is a commensal pathogen of the human nasopharynx which is a major cause of morbidity-mortality worldwide. It has been reported that respiratory virus could contribute to the development of invasive pneumococcal disease (IPD).

Objective

To assess the rate of respiratory viral infection and *S. pneumoniae* in the nasopharynx in children with IPD and in healthy children

Methods

A prospective case-control study including all children <18 years with IPD assisted by 5 hospitals of Catalonia during January 2014-June 2015. Each case was matched with a healthy control child according to age, sex and date of hospitalization. 16 respiratory virus were detected by a multiplex real-time PCR approach (Anyplex II RV16A). Pneumococcal carriers were detected by a specific real-time PCR.

Results

During the period of study, a total of 64 patients were identified, 50 of them (78.1%) accepted to participate in the study and a matched control was recruited. Average age of patients was 46 months and 61% were male.

Pneumococcal nasopharyngeal carrier was detected in 27 cases (54%) and in 24 controls (48%) p=0.2. A high rate of viral respiratory infection was detected in patients with IPD (55.1%) and in healthy control (44%) p=0.13. Overall, respiratory virus were more frequently detected in pneumococcal carriers vs. non-pneumococcal carriers (60% vs. 38%) p=0.03. This high rate was detected in pneumococcal-carriers cases (69.2%) and pneumococcal-carriers controls (50%) p =0.09.

Conclusions

A high rate of viral respiratory coinfection was detected in pneumococcal nasopharyngeal carriers independently of the health status of the child. Further information would be required to evaluate the role of these associations in the development of IPD.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0550
E-POSTER DISCUSSION SESSION 3 - SEVERE INFECTIONS 1 (station 4)

PREVALENCE OF COMPLICATIONS IN CHILDREN WITH INCOMPLETE KAWASAKI DISEASE

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Background

Incomplete clinical forms of Kawasaki Disease (KD) are associated with a high risk of cardiovascular complications. Objective: To analyze cardiovascular complications, clinical outcomes and treatment by comparing complete KD (cKD) and incomplete KD (iKD) clinical forms.

Methods

Retrospective study of patients under 14 years old with KD admitted to a tertiary Paediatric Hospital from January 2006 to December 2015. We divided patients into cKD and iKD according to diagnostic criteria of the American Heart Association (AHA).

Results

Sixty-two patients were diagnosed with KD: 31 of them (50%) with iKD. Median age was lower in iKD (16 months versus 24 months). Epidemiological, clinical and analytical characteristics are compared in Table 1. Conjunctival injection, lymphadenopathy and polymorphous rash were more frequent in cKD. In relation to laboratory findings, high procalcitonin was the only marker statistically associated with iKD (3,9 ng/ml versus 0,29 ng/ml). Sodium, albumin and transaminases were not statistically analysed because of lack of data. Coronary artery abnormalities were similar in both groups: cKD 16 cases (51,6%) versus iKD 14 cases (45,2%). Four patients developed coronary artery aneurysms, 3 of them in cKD cases. Most patients received intravenous immunoglobulins (IVIG) within the first 7 days of the onset (cKD 84% versus iKD 74%). Nine patients required a second IGIV dose and 5 received steroids (cKD: 3 cases, 9,6%; iKD: 2, 6,4%) Fever disappeared later (24 hours after IGIV) in iKD (35,5% versus 16%) but it was not statistically significant (p >0,05).

Table 1. Epidemiological, clinicals, analytical and echocardiographic characteristics between complete and incomplete Kawasaki disease.			
	Complete Kawasaki Disease (n=31)	Incomplete Kawasaki Disease (n=31)	p value
Epidemiological characteristics			
Age, month; median (range)	24 (3-129)	16 (2-59)	0,158
<12 month; median (range)	4 (3-10)	4 (2-10)	0,892
1- 6 years; median (month), (range)	33,5 (13-60)	31 (13-59)	0,613
Day to diagnosis KD; median (range)	6 (5-12)	6 (2-15)	0,742
Clinical characteristics			
Conjunctival injection n, (%)	30 (96,7)	19 (63,3)	**0,001**
Changes in lips and oral cavities n, (%)	31 (100)	30 (96,7)	0,313
Cervical lymphadenopathy n, (%)	16 (51,6)	6 (19,3)	**0,022**
Polymorphous rash n,(%)	31 (100)	27 (87)	**0,039**
Extremities changes n,(%)	24 (77,4)	13 (41,9)	0,058
Laboratory results			
White blood cell mean (10^3/mmc), ± SD	15.472±6.505	18.488±8.982	0,132
Platelet count mean (10^3/mmc)± SD	442.613±237.255	420.129±141.041	0,672
C-reactive protein mean (mg/L)± SD	115,7±86,7	113,4±78,2	0,972
Procalcitonin mean (ng/ml)± SD	0,29±0,21	3,9±1,9	0,357
Echocardiographic findings			
Coronary artery lesion n,(%)	16 (51,6)	14 (45,2)	0,689
Coronary ectasia n,(%)	14 (45,2)	13 (41,9)	0,611
Coronary aneurysm n,(%)	3 (9,7)	1 (3,2)	0,301
KD: Kawasaki disease. SD: Standard deviation. WBC: White blood cell. CRP: C-reactive protein.			

Conclusions

In our series, iKD diagnosis was not associated with delayed diagnosis, worse clinical outcome or coronary artery abnormalities. Prospective studies with larger sample of KD patients are necessary to prove these results.

ESP16-0660
E-POSTER DISCUSSION SESSION 3 - SEVERE INFECTIONS 1 (station 4)

CHILDHOOD ENCEPHALITIS IN THE UK – EARLY FINDINGS FROM THE UK CHILDHOOD MENINGITIS AND ENCEPHALITIS PROSPECTIVE COHORT STUDY (UK-CHIMES)

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Background

Encephalitis, inflammation of the brain parenchyma, has infective, para-infectious and immune-mediated aetiologies, which need different management approaches. As part of the UK Childhood Meningitis and Encephalitis (UK-ChiMES) study, we are prospectively investigating children with encephalitis to better understand aetiologies and disease burden.

Methods

From 2012, children (<16 years) with suspected meningitis, encephalitis and/or having a lumbar puncture as part of an infection screen have been recruited prospectively into the UK-ChiMES in 30 hospitals. Encephalitis was suspected if there was altered consciousness persisting for >24 hours (including change in personality or behavior) with or without meningeal signs. Patients were classified as having encephalitis if there was evidence of brain inflammation including one or more of: cerebrospinal fluid (CSF) white cell count >4 cells/µL (20 in neonates); neuroimaging or electroencephalography changes consistent with encephalitis.

Results

Of the initial 2468 children recruited to UK-ChiMES, 801 (32%) had suspected encephalitis and of these 452 (56%) had clinically confirmed encephalitis. Causes of encephalitis were identified in 224 (49%): 141 (31%) viral, 59 (13%) bacterial, 24 (5%) immune mediated, 229 (51%) unknown. The commonest viral causes (identified by CSF polymerase chain reaction) were enterovirus n=100 (71%), herpes simplex virus (HSV) type 1 n=11 (8%), parechovirus n=9 (6%) and varicella zoster virus n=4 (3%).

Conclusions

To date, just over half the children presenting with suspected encephalitis had encephalitis confirmed clinically. Viral infection remains the highest proven cause of encephalitis (in one third) with bacterial infection (with associated meningitis) second. Very few cases of HSV type 1 have been identified. The cause remains unknown in half the children. Further analysis will define the outcome, quality of life and health economic data for this important neurological disorder.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0399
E-POSTER DISCUSSION SESSION 3 - SEVERE INFECTIONS 1 (station 4)

COMPARISON OF CLINICAL AND LABORATORY FEATURES IN CHILDHOOD BACTERIAL AND ASEPTIC MENINGITIS – FINDINGS FROM THE UK CHILDHOOD MENINGITIS AND ENCEPHALITIS PROSPECTIVE COHORT STUDY (UK-CHIMES)

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Background

Following the implementation of conjugate vaccine programmes, >80-90% of meningitis in developed countries is aseptic (bacterial culture negative). Early identification of children with viral meningitis could prevent unnecessary hospitalisation and antibiotic management.

Methods

Data were collected from an ongoing prospective cohort study in 30 UK hospitals from December 2012. Inclusion criteria: child <16 years and hospitalisation with suspected meningitis or encephalitis and/or having a lumbar puncture for evaluation of infection. Meningitis was defined as isolation of a pathogen from CSF and/or CSF WBC >4/μL. Clinical and laboratory features were compared for children with bacterial, viral, aseptic meningitis with no pathogen identified, and a non-meningitis illness. T-tests or the Wilcoxon rank-sum test were used to compare continuous variables. Categorical variables were analysed with Pearson Chi-Squared or Fisher's Exact tests.

Results

Of 946 of the first 1000 children recruited, 54 had bacterial, 100 viral, 114 aseptic (of unknown cause) meningitis and 678 did not have meningitis. Infants with bacterial compared with viral meningitis had higher median CSF WBC count (533/μL vs 73/μL, p<0.001) and protein (1.8g/L vs 0.6g/L, p<0.001), lower CSF:plasma glucose ratio (0.29 vs 0.49, p=0.033), and higher blood CRP (115mg/L vs 15mg/L, p<0.001), and were more likely to have vomiting (p=<0.001) and a non-blanching rash (p=0.039). Children >1 year with bacterial compared with viral meningitis had higher median CSF WBC count (705/μL vs 15/μL, p<0.001) and protein (0.7g/L vs 0.5g/L, p=0.036) and higher blood CRP (143mg/L vs 23mg/L, p=0.001), and were more likely to have fever (p=0.041) and vomiting (p=0.012).

Conclusions

Some clinical and laboratory parameters were identified that may differentiate bacterial from viral meningitis. Further analysis could assist in the development and validation of clinical decision rules to optimise management.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0796
E-POSTER DISCUSSION SESSION 3 - SEVERE INFECTIONS 1 (station 4)

BURDEN OF BORDETELLA PERTUSSIS INFECTION IN A REFERENCE CHILDREN CENTRE OF CATALONIA DURING A 5-YEAR PERIOD (2011-2015)

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Background

Whooping cough is a transmissible disease caused by *Bordetella pertussis (Bp)* with high rates of morbidity-mortality. Since 1965, pertussis vaccination has been covered by the public-health system in Catalonia. However, an increase of incidence of pertussis has been reported. To increase protection in infants, a pertussis vaccination program has been extended to all pregnant women since 2014.

Objective
To report the evolution of the Bp disease burden in a reference children's hospital in Catalonia during the period 2011-2015.

Methods

A prospective study was conducted at Hospital Sant Joan de Déu in Barcelona (Spain). Nasopharyngeal samples (NS) were collected from all children <18 years with clinical suspicion of pertussis attended during the study period. Pertussis cases were defined according to clinical criteria and positive pertussis detection by real-time PCR.

Results

A total of 2300 NS samples were received. 482 of them (20.9%) were identified as Bp positive. Globally, 192 episodes (39.8%) occurred in children aged <1 year, 126 episodes (26.1%) in children aged ≥1-<6 years, and 164 episodes (34%) in children-adolescents aged 6-18 years. Positive episodes increased from 107 episodes in 2011 to 185 in 2015. A decrease of cases (from 56 episodes in 2011 to 42 in 2015) was observed in infants <1 year, while an important increase of cases was observed in patients 6-18 years (from 31 episodes in 2011 to 80 in 2015) and in patients ≥1-<6 years of age (from 20 episodes in 2011 to 63 in 2015).

Conclusions

An important increase of pediatric pertussis disease was observed in our geographical area between 2011 and 2015. However, this tendency was not observed in infants <1 year, probably related to the introduction of the pertussis vaccine in pregnant women.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0176
E-POSTER DISCUSSION SESSION 4 - VACCINES 1 (station 5)

ALTERNATIVE VACCINE ADMINISTRATION BY BALLISTIC INJECTIONS: NEEDLE-FREE DERMAL DELIVERY OF THE GLYCOCONJUGUATE MENINGOCOCCAL GROUP Y VACCINE

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Background

Most of the 800 million vaccine injections performed each year are given as liquid antigen formulations that are administered by intramuscular needle-and-syringe injection. There are a number of disadvantages associated with conventional needle administration, including the risk of transmission of blood-borne viruses (such as HIV), the need for large-scale disposal of needles and a requirement for a cold chain for refrigeration of liquid vaccines.
We aimed to investigate the use of dry microparticles for vaccine delivery, using the capsular group Y meningococcal vaccine CRM_{197}-MenY (Novartis Vaccines and Diagnostics).

Methods

Dry-powder formulations of CRM_{197}-MenY for application in needle-free injection were prepared. Formulations were lyophilized, and the stability, physical and chemical properties of the formulation confirmed. Immunogenicity of the needle-free formulation was assessed *in vivo*: mice were immunized with the vaccine in solution subcutaneously (SC), intramuscularly (IM), with or without Alum adjuvant, or with the needle free formulation. Antibody responses were assessed by ELISAs, and by serum bactericidal assay (SBA) with human complement.

Results

The glycoconjugate vaccine MenY-CRM_{197} conjugated onto nanoparticles could be reliably and reproducibly produced. The vaccine was preserved during spray-freeze dry manufacture and did not show physical or chemical signs of degradation after resuspension. The needle free vaccine induced antibody responses as detected by ELISA, but most importantly, this vaccine, which contained no Alum adjuvant, induced functional protective antibody responses *in vivo* of similar magnitude as compared with the conventional vaccine injected by hypodermic needle and syringe and containing Alum adjuvant.

Conclusions

These results demonstrate that needle free vaccination is both technically and immunologically valid, and suggest that this approach could be considered for vaccines in development.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0409
E-POSTER DISCUSSION SESSION 4 - VACCINES 1 (station 5)

ASSESSING THE ONGOING IMPACT OF ROTAVIRUS VACCINATION IN THE UNITED KINGDOM

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Background

The United Kingdom added rotavirus vaccine (Rotarix GlaxoSmithKline) to the national immunisation schedule in July 2013. We reported significant reductions in rates of disease after the first year of vaccination. However several European countries not using rotavirus vaccine reported unprecedentedly low rotavirus incidence in 2014, casting doubt over the causality/magnitude of vaccine effect. We have continued active surveillance to report the epidemiological trends for the two years after vaccine introduction.

Methods

During the 2012-2015 rotavirus seasons, children presenting to our regional paediatric emergency department with gastroenteritis symptoms (>2 loose stools and/or >1 episode of vomiting in the last 24 hours) had stool virology analysis (real-time PCR), severity assessment (Vesikari score) and clinical outcome recorded.

Results

Whilst the number of rotavirus positive samples continued to fall in 2015, the reduction in number of all-cause gastroenteritis attendances and admissions was smaller (table). We found an ongoing shift in genotypes away from wild-type G1P[8] and no detectable rise in rates of intussusception.

	2012	***2013***	**2014**	**2015**
Gastroenteritis attendances	*1464*	*1239*	706	863
(%change postvaccine)			(-43% /-52%)	(-30% /-41%)
Gastroenteritis admissions	*297*	*288*	137	204
(%change postvaccine)			(-52% /-54%)	(-29% /-31%)
Bed days occupied	*506*	*450*	148	217
(%change postvaccine)			(-67% /-71%)	(-52% /-57%)

Proportion of samples rotavirus positive	*54%*	*65%*	36%	30%

Conclusions

In the second year of rotavirus vaccination in the UK, there have been sustained reductions in numbers of hospital attendance and admissions. The magnitude of these effects were lower than those seen in the first year, suggesting that a proportion of the 2014 herd effect may have been due to a low incidence season. Ongoing surveillance will be necessary to demonstrate the true potential of a completely vaccinated preschool cohort.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0717
E-POSTER DISCUSSION SESSION 4 - VACCINES 1 (station 5)

COST-EFFECTIVENESS ANALYSIS OF ROTAVIRUS VACCINATION: IS THERE A BENEFIT IN SWITCHING FROM COHORT TO POPULATION MODELLING?

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Background

Reporting the cost-effectiveness of rotavirus vaccination often occurred with cohort modelling: the vaccination program is compared between a condition without vaccination *versus* a condition where the vaccine has reached its new steady state level in infection spread in the at-risk population. This comparison omits the possibility to evaluate the vaccine uptake scenarios and the impact of indirect herd protection in unvaccinated age-groups at start of the vaccination process.
We investigated the possibility to incorporate them into the cost-effectiveness analysis of the vaccine using a population model instead of a cohort model, during an 8-year observation period.

Methods

The starting data were collected from a previously published cohort model design, measuring the cost-effectiveness of the vaccine at steady state level in the UK. The herd protection data came from published UK data of the 1st year post-vaccination. Subsequent years were simulated by the model. It was expected that the cohort model approach would report better economic data than the population model.

Results

At a price of £15/vaccine dose the cohort model reports a cost-neutral point for the incremental cost-effectiveness ratio (ICER). With the population model including the net herd protection effect of the vaccine at 63%, the ICER result is around £1,439 per quality-adjusted life year (QALY) gained. Without herd effect, the ICER result increases to £5,540 per QALY gained.

Conclusions

Switching from cohort to population model design allows the inclusion of the vaccine herd protection effect during the early years of uptake. Although herd effect could be large in rotavirus vaccination during the first years of introduction, there is no guarantee of obtaining a better ICER result than with a cohort model.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0962
E-POSTER DISCUSSION SESSION 4 - VACCINES 1 (station 5)

PHASE 3 TRIAL OF IMMUNOGENICITY OF BIVALENT rLP2086, A MENINGOCOCCAL SEROGROUP B VACCINE, IN YOUNG ADULTS: BACTERICIDAL ACTIVITY AGAINST A PANEL OF ANTIGENICALLY DIVERSE STRAINS

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Background

Bivalent rLP2086, which targets factor H binding proteins (fHBP), is approved in the US to prevent meningococcal serogroup B (MnB) disease in 10-25-year-olds. Broad protection with bivalent rLP2086 was initially demonstrated in hSBAs with 4 diverse invasive MnB strains expressing fHBPs with sequences different from vaccine antigens. In this pivotal phase 3 trial, broad coverage against MnB disease is further supported by hSBA data with 10 additional MnB test strains representing the diversity of circulating invasive MnB strains (ClinicalTrials.gov: NCT01352845).

Methods

Healthy subjects aged 18-<26 years were randomized to receive bivalent rLP2086 or saline at 0, 2, and 6 months. Immune responses were assessed in hSBAs with 4 primary MnB test strains (primary endpoint; N=1702-1714) and in a population subset (N=273-284) using 10 secondary MnB test strains (secondary endpoint; N=273-284). All strains expressed vaccine-heterologous fHBP.

Results

hSBA responses 1 month after dose 2 and 3 among bivalent rLP2086 recipients against 4 primary MnB test strains as measured by hSBA titers ≥LLOQ were 68.3%-97.4% and 87.4%-99.4%, respectively (Table). hSBA responses to 10 secondary MnB test strains were 51.6%-97.9% and 71.3%-99.3% 1 month after dose 2 and 3, respectively. hSBA GMTs for each

secondary strain increased from 5.1-13.9 at baseline to 20.6-96.3 after dose 3.

Table. hSBA activity elicited by bivalent rLP2086 against a panel of invasive, antigenically diverse meningococcal serogroup B strains

Strain (fHBP Variant)	N	% with hSBA titers ≥LLOQ (1:8 or 1:16)			hSBA GMTs	
		Baseline	After dose 2 *	After dose 3	Baseline	After dose 3
Primary strains						
PMB80 (A22)	1714	33.6	84.7	93.5	12.8	74.3
PMB2001 (A56)	1709	32.2	97.4	99.4	8.8	176.7
PMB2948 (B24)	1702	33.1	86.5	95.1	7.6	49.5
PMB2707 (B44)	1703	11.0	68.3	87.4	4.8	47.6
Secondary strains						
PMB3175 (A29)	283	31.1	96.8	99.3	7.1	96.3
PMB3010 (A06)	275	16.0	77.8	92.0	10.3	69.9
PMB3040 (A07)	277	55.8	97.9	95.7	13.9	60.4
PMB824 (A12)	275	5.0	57.6	71.3	8.4	20.6
PMB1672 (A15)	279	37.3	83.2	91.8	8.0	43.1
PMB1989 (A19)	284	28.8	87.4	95.8	12.1	87.3
PMB1256 (B03)	273	11.2	57.9	86.4	5.1	49.8
PMB866 (B09)	274	23.5	65.3	77.0	6.1	23.3
PMB431 (B15)	276	43.8	86.5	96.7	9.1	49.4
PMB648 (B16)	273	21.9	51.6	78.0	6.2	26.5

*For the secondary strains, subset of subjects; n=90–96.
LLOQ = 1:16 for A06, A12, A19, and A22; 1:8 for A07, A15, A29, A56, B03, B09, B15, B16, B24, and B44.

Conclusions

Bivalent rLP2086 vaccination elicited robust immune responses against diverse MnB strains expressing fHBP variants heterologous to vaccine antigens after 2 and 3 doses. A high proportion of individuals developed protective hSBA titres greater than the correlate of protection (hSBA titre ≥1:4) to 10 additional MnB test strains. Collectively, these phase 3 immunogenicity data support the broad protection afforded by bivalent rLP2086 against MnB disease in young adults. Funded by Pfizer.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov: NCT01352845

ESP16-0426
E-POSTER DISCUSSION SESSION 4 - VACCINES 1 (station 5)

IMMUNOGENICITY AND SAFETY OF GARDASIL 9 IN 16-26 YEAR-OLD MEN: RESULTS OF A DOUBLE-BLIND STUDY CONTROLLED WITH GARDASIL

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Background

The 9-valent HPV vaccine (9vHPV vaccine, Gardasil®9) is comprised of VLPs of the 4 HPV types (Type 6, 11, 16, and 18) contained in GARDASIL® (quadrivalent HPV [qHPV] vaccine), and VLPs of 5 additional oncogenic HPV types (Type 31, 33, 45, 52, and 58). The qHPV vaccine prevents HPV-related anal disease and genital warts in men 16-26 years of age. This study was designed to extend the efficacy findings with qHPV vaccine to 9vHPV vaccine by demonstrating non-inferior HPV 6/11/16/18 antibody response with 9vHPV vaccination compared to qHPV vaccination, in boys/men of 16-26 years of age.

Methods

500 boys/men aged 16-26 years were randomised 1:1 to receive 9vHPV vaccine or qHPV vaccine, at Day 1, Month 2 and Month 6 (3 doses). Antibody responses were evaluated at Month 7 by competitive Luminex Immunoassay. Immunogenicity analyses were performed in the per-protocol population. Adverse events (AEs) were collected from Day 1 to Month 7.

Results

Non-inferiority was demonstrated as the lower bounds of the 95%CI around the GMT ratios (9vHPV/qHPV) at Month 7 were all >0.5: they were 1.23 (95% CI: 1.04-1.45) for HPV6, 0.89 (95% CI: 0.76-1.04) for HPV11, 1.04 (95% CI: 0.89-1.21) for HPV16 and 1.12 (95% CI: 0.91-1.37) for HPV18. Following 9vHPV vaccination, all subjects seroconverted to HPV31/33/45/52/58. The AE profile of the 9vHPV vaccine was generally comparable to that of qHPV vaccine. There were no serious AEs and no discontinuations due to an AE.

Conclusions

The 9vHPV vaccine is generally well tolerated and elicits anti-HPV 6/11/16/18 that are non-inferior to those generated by the qHPV vaccine in 16-26 year-old boys/men. These results support extending the efficacy findings with qHPV vaccine to 9vHPV vaccine in this population.

Clinical Trial Registration (Please input N/A if not registered)

NCT02114385

ESP16-0897
E-POSTER DISCUSSION SESSION 4 - VACCINES 1 (station 5)

SERUM VERSUS SALIVA RV-IGA AS CORRELATE OF PROTECTION FOR ROTAVIRUS VACCINES

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Background

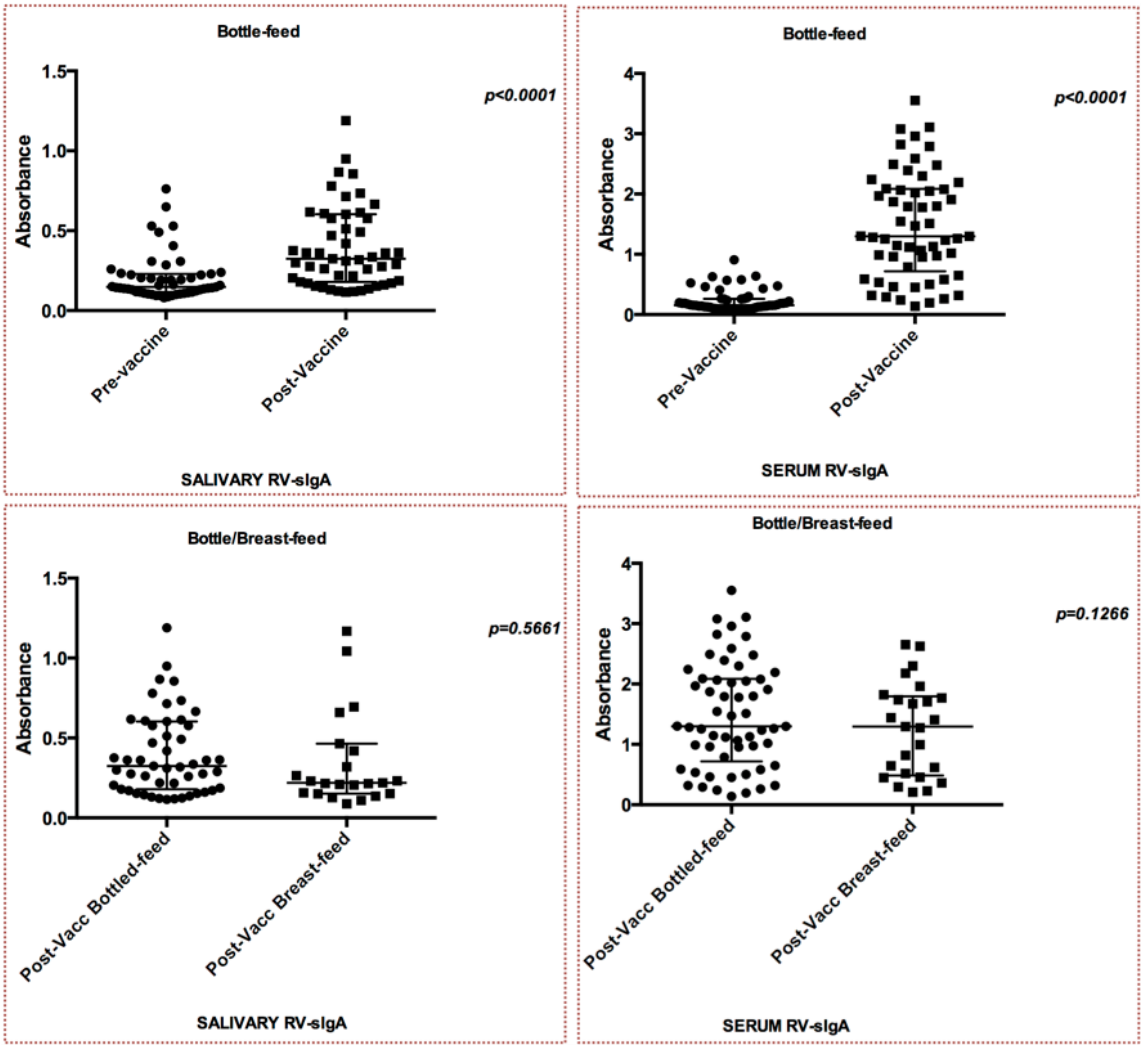
RV-IgA levels constitute the best available correlate of protection for rotavirus vaccine efficacy trials. However, serum IgA levels may not adequately reflect intestinal immunity. We hypothesized that salivary IgA levels could be a better correlate of protection.

Methods

We conducted a prospective comparative study of the serum *versus* saliva humoral response to rotavirus in 82 vaccinated children classified according to their feeding: breast-feeding (*n* = 25) and bottle feeding (*n* = 57). Total RV-IgA levels were measured in serum and saliva at baseline and 40 ± 3 days after 3rd RV vaccine dose using ELISA. To compare serum and saliva RV-IgA values, only bottle-fed children (*n* = 57) were included in the analysis, avoiding interference of maternal RV-IgA antibodies in measurements. To assess this interference, post-vaccination values of bottle-fed and breast-fed children were compared. Serum and salivary RV-IgA levels are expressed as Median (± SD) $OD_{450nm.}$

Results

Serum pre-vaccination values were 0.154 (0.17) and post-vaccination values were 1.300 (0.87), with a conversion rate > 3-fold (*p < 0.0001*). Saliva pre-vaccination values in the same children were 0.148 (0.14) and post-vaccination values were 0.325 (0.44) with a conversion rate of 2-fold (*p < 0.0001)*. No correlation between serum and saliva RV-IgA levels was found (*r = 0.0655*). Comparison of post-vaccination salivary RV-IgA levels between bottle-fed 0.325 (0.44) *versus* and breast-fed children showed no statistically significant differences: 0.325 (0.44) *vs*. 0.219 (0.38) (*p = 0.5661*).



Conclusions

We did not detect correlation between serum and salivary RV-IgA. Salivary RV-IgA levels might still be a correlate of mucosal protection based on compartmentalization of immune system, but this requires further evaluation. Breastfeed does not interfere rotavirus vaccine response according to salivary and serum RV-IgA levels.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0407
E-POSTER DISCUSSION SESSION 4 - VACCINES 1 (station 5)

ANTIBODY RESPONSES AGAINST HAEMOPHILUS INFLUENZAE TYPE B WITH ADMINISTRATION OF DIFFERENT CAPSULAR GROUP C MENINGOCOCCAL CONJUGATE VACCINES: AN OPEN-LABEL RANDOMISED CONTROLLED TRIAL

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Background

A resurgence in *Haemophilus influenzae* type b (Hib) disease in British infants in 2000, attributed to waning herd protection and use of acellular pertussis vaccines, also coincided with the introduction of capsular group C meningococcal vaccines (MenC) containing either diphtheria cross reacting material (CRM) or tetanus toxoid (TT) conjugate proteins.

Methods

An open-label randomised controlled trial was conducted in which 509 2-month old infants received none, one or two doses of MenC-CRM, or one dose of MenC-TT followed by Hib-MenC-TT at 12 months of age. All participants received $DTaP_5$-IPV/Hib-TT at 2, 3 and 4 months of age.

Results

At 5 months of age (post-priming), two doses of MenC-CRM resulted in reduced anti-polyribosylribitol phosphate (PRP) immunoglobulin G (IgG) (GMC 0.309µg/mL; 95%CI 0.218 to 0.439; 61% ≥ 0.15µg/mL, 30% ≥ 1.0µg/mL) compared with one dose of MenC-CRM (0.726; 0.517 to 1.02; 77%, 50%), or MenC-TT (0.765; 0.508 to 1.152; 75%, 51%). Those receiving no MenC had a GMC of 0.509 (0.296 to 0.875; 61%, 42%) which was not significantly different from other groups.

At 12 months of age pre-boost anti-PRP IgG was higher in those receiving MenC-TT than no MenC (0.575; 0.418 to 0.791 vs 0.293; 0.193 to 0.446, p=0.0122).

Following the Hib-MenC-TT booster at 12 months of age, anti-PRP IgG was similar across groups.

Conclusions

Long term protection against Hib following the Hib-MenC-TT booster at 12 months of age is unlikely to be significantly affected if the infant priming dose of MenC is removed from the UK immunisation schedule. The administration of multiple infant doses of MenC-CRM reduced Hib antibody in comparison with single dose schedules.

Clinical Trial Registration (Please input N/A if not registered)

NCT01129518

ESP16-0328
E-POSTER DISCUSSION SESSION 5 - HIV (station 7)

ADIPONECTIN, LEPTIN AND INFLAMMATORY MARKERS IN HIV-ASSOCIATED METABOLIC SYNDROME IN CHILDREN AND ADOLESCENTS

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Background

Metabolic syndrome (MetS) is more common in HIV-infected adults and children than in the general population. Adipocytokines and inflammatory markers may contribute to the pathophysiology of this condition and could be useful parameters for monitoring MetS.

Methods

A cross-sectional study was conducted between October 2013 and March 2014 in the outpatient clinics of two tertiary pediatric referral hospitals. Fifty-four HIV-infected children and adolescents were included. MetS was defined according to the International Diabetes Federation (IDF) and modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria. Measurements included anthropometry, waist circumference, blood pressure, fasting lipids, glucose and insulin, adiponectin, leptin, interleukin-6, vitamin D and C-reactive protein, and clinical lipodystrophy assessment.

Results

Among the total, 3.7% of patients met the IDF criteria for MetS and 7.4% met the NCEP-ATP III criteria. C-reactive protein and leptin levels were significantly higher, and adiponectin level significantly lower in patients with MetS, regardless of the criteria used. Insulin resistance was observed in 40.7% of patients; abnormal QUICK index values were found in 88.9%. Eighteen patients (33.3%) had vitamin D deficiency.

Conclusions

The prevalence of MetS was similar to that observed in larger cohorts of HIV-infected patients in our setting. Adipocytokine dysregulation seems to be related to MetS in HIV-infected children. A high percentage of patients showed insulin resistance, which should be strictly monitored.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0576
E-POSTER DISCUSSION SESSION 5 - HIV (station 7)

LONG-TERM IMMUNE STATUS IN HIV-INFECTED CHILDREN WITH MAINTAINED VIRAL SUPPRESSION

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Background

Little is known about the long-term immune recovery in vertically HIV-infected children treated with prolonged suppressive HAART. We describe the long-term immunological status in HIV-infected children initiating HAART and to assess possible factors associated with immunological recovery.

Methods

HIV-infected children initiating first-line HAART in whom virological suppression was achieved and maintained for more than 5 years were selected out from the Madrid Cohort, from 1997 until January 2015. Inclusion criteria were: perinatal infection, no evidence of previous HAART, achievement of virological suppression (<400 copies/ml) in the first year of HAART initiation, no virological rebound longer than 3 months, follow-up at least 5 years. Immunological recovery was considered CD4 > 800 at the last observation.

Results

57 HIV-infected children were included (46% male, 77% Caucasian, 21% CDC class C) with a median age of 6.7 years (IQR 2.3-10.6) at HAART initiation (PI 67%, NNRTI 33%). 47% had previous exposure to mono or dual NNRI. Median time on HAART was 10.2 years (IQR 6.6-13.4) and undetectable viral load 10 years (IQR: 6.5-10.3). Median nadir CD4 and percentage were 342 and 14% (IQR 155-499; 8-22). Median CD4 and percentage at last observation were 800 cells and 40% (IQR: 654-1050; 34-44%). Absolute CD4 and percentage increased markedly in the first 2 years, stabilizing thereafter. Higher nadir, naïve children and CD4/CD8 > 1 at last visit were associated with immunological recovery. In multivariate analysis, only higher nadir (OR: 1.002 CI 95% 1.000-1.004) and naïve children (OR: 3.4 CI95%: 1.04-11.6) was associated.

Conclusions

In our cohort, long-term immune recovery is observed after 10 years of initiating and maintaining suppressive HAART. A lower nadir CD4 and previous exposure to suboptimal therapy are independently associated with worse long-term immune recovery.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0880
E-POSTER DISCUSSION SESSION 5 - HIV (station 7)

IS LIVER FIBROSIS A SILENT DISEASE IN HIV-INFECTED ADOLESCENTS AND YOUNG ADULTS?

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Background

Effective and long-term combined antirretroviral therapy (cART) has decreased the morbimortality in HIV-infected, but noninfectious conditions continue to occur, including liver fibrosis. This study aims to assess the prevalence of liver fibrosis through liver elastography (FibroScan®), in a cohort of HIV-infected adolescents and young adults in an outpatients clinic in Sao Paulo, Brazil

Methods

This study was approved by the Institutional Ethical Review Board; written informed consent was obtained. A cross-sectional study enrolled 74 HIV-infected adolescents and young adults (10-26 years). Variables examined: age, gender, race, transmission mode, cART use, time of exposure to didanosina, viral load, CD4+T cell count, clinical and laboratory evaluation (hepatosplenomegaly, platelet count, aminotransferases – ALT and AST, Gamma glutamyl transferase, Alkaline Phosphatase). METAVIR stage ≥ F2 defined significant liver fibrosis. Liver parenchyma elasticity indexes ≥7KPa, were considered F≥2.

Results

The median age was 18.5 years (10.4-26.2 years), 71/74 (95.9 %) patients infected by vertical transmission, 67/74 (90.5 %) belonged to the clinical category B and C , 39/74 (52.7 %) had severe immunosuppression. Significant liver fibrosis (> 7kPa) was identified in 11/74 patients (14.9%). There was no statistically significant association between fibrosis and the following factors: time of ART or ddI use, CD4+T cell count (current or nadir) and HIV viral load. From 11 patients with hepatic fibrosis only 1/11 (9 %) had hepatosplenomegaly and increased levels of AST and FA. Decreased platelet counts were identified in 2/11 (18%) and increased gammaGT in 3/11 (27.3%).

Conclusions

Liver fibrosis was identified in 14,9% (11/74) by liver elastography (FibroScan®) of this cohort. The liver fibrosis manifests itself silently, so it should be investigated routinely, avoiding late diagnosis with threatening life complications, such as portal hypertension and esophageal varices.

ESP16-1085
E-POSTER DISCUSSION SESSION 5 - HIV (station 7)

GROWTH IN HIV-INFECTED CHILDREN AND YOUNG PEOPLE FROM DIAGNOSIS TO TRANSFER INTO ADULT CARE, A 4 CENTER AUDIT

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Background

Long term growth and in particular growth data at time of transition to adult care in vertically HIV-infected children is still limited.
We describe growth data from 4 centres in the UK from diagnosis to transition.

Methods

All four centers (Children's Hospital Sheffield, St George's Hospital, Evelina Children's Hospital and Kings College Hospital) report annually to Collaborative HIV Paediatric Study (CHIPS) a multicentre cohort of HIV infected children in the UK and Ireland. Median height and BMI z-scores using the UK growth reference data are described at start of antiretroviral therapy (ART) and at transition to adult care as well as the proportions stunted (height z-score<-2) and BMI z-score <-2 or >2.

Results

296 children with median age at diagnosis of 3.2 years (IQR 0.7,7.6), started ART at a median age of 7.1 years (IQR 2.9,11.5); 140 (47%) were born abroad, median CD4% of 18% (IQR 12, 26) at diagnosis. The mean height and BMI z-score at start of ART were 0.7(SD1.5) and 0.3 (SD1.4) respectively. 21% of children were stunted at start of ART and 5% had BMI <-2 z-scores. 65 (22%) transitioned to adult care with median follow up of 13.4 years (IQR 9.7,16). The median height and BMI z-score in 55 young people with data was -0.75 (SD1) and 0.4 (SD0.9) at transition. 8 (14.5%) young people had a BMI> 25. 5 (9%) were stunted, no BMI s-scores<-2.

Conclusions

Despite the majority of young people transitioning to adult care in our 4 centre cohort with good growth, a fifth are either overweight, underweight or stunted. Poor growth is likely due to long term poor adherence. Weight control is important in young people with higher risk of long-term cardiovascular problems.

ESP16-1095
E-POSTER DISCUSSION SESSION 5 - HIV (station 7)

EPILEPSY IN CHILDREN WITH HIV: AN AUDIT FROM TWO SOUTH AFRICAN REFERRAL HOSPITALS.

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Background

Children infected with HIV are known to be at risk of a wide range of potentially disabling neurological complications. Epilepsy is one of the most common neurological conditions globally, yet there is little recent data on the incidence and outcomes of patients with HIV and epilepsy. The aim of this audit was to assess the prevalence of epilepsy, immune status at presentation and levels of disability in a cohort of children attending two hospital based HIV clinics in order to inform service development.

Methods

All HIV infected children aged 0-16 years attending two referral hospitals in the Eastern Cape, South Africa from 2004-2014 were eligible for inclusion. An electronic anti-retroviral therapy (ART) patient database, used in both hospitals, was searched using key terms to identify epilepsy cases. Supplementary data was collected from hospital notes and HIV clinic files.

Results

Of the 2137 children enrolled in the two clinics, 53 were diagnosed with epilepsy (2.5%) of which 50 (2.3%) had comprehensive records available. Median age at epilepsy diagnosis was 50 months. WHO clinical stage at diagnosis was available for 46 patients, with 3, 6, 26 and 11 presenting at stages 1, 2, 3 and 4, respectively. 40% had a history of central nervous system infection prior to epilepsy diagnosis and 30% had cerebral palsy. 49 of 50 were treated with sodium valporate, without any serious drug reactions.

Conclusions

This audit demonstrates a prevalence of epilepsy in children with HIV of 2.5%, exceeding that in population based studies. Most cases of epilepsy were diagnosed in children with advanced HIV supporting early initiation of ART. High rates of cerebral palsy highlight the complex needs of this group and need to develop a multidisciplinary management approach.

ESP16-1070
E-POSTER DISCUSSION SESSION 5 - HIV (station 7)

THE COHORT OF THE SPANISH PAEDIATRIC HIV NETWORK (CORISPE) AFTER TRANSITION TO ADULT CARE (FARO PROJECT): IMMUNOVIROLOGICAL EVOLUTION OF ADOLESCENTS WITH VERTICALLY ACQUIRED HIV-1 INFECTION

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Background

Few studies have addressed the clinical situation of vertically HIV-1 infected adolescents that have been transfered to Adult Units (AU). The FARO Project from CoRISpe was launched in 2013 to evaluate the clinical, immunological and virological evolution of this population.

Methods

Cross-sectional study that included vertically HIV-infected adolescents registered in CoRISpe that were transferred to AU between 1997-2013. A total of 423/1148 (36.8%) adolescents were transferred to AU, 209 (18.2%) were eligible for our study (58.4% women). We describe their immune and virological characteristics at the time of transition to AU, one year after their transition and at the last registered clinical visit.

Results

During the study period, 174 (83.2%) patients remained under follow-up, 29 (13.9%) were lost and 6 (2.9%) died; the median follow-up time (years) was, respectively, 5.2 [3.3-8.6], 1.8 [0.6-4.9] and 5.2 [2.5-8.6]. Global mean age (years) at transition was 16.9 (1997-2004), 17.8 (2005-2008) and 18.1 (2009-2013) ($p<0.05$). Half (53%) of the patients were transferred to AU from 2009 to 2013.

Globally, the median CD4/mL count increased by 10.6% from the last control in pediatrics (620 [409-868]) until the last registered control in AU (694 [464-972]). Adolescents with undetectable viral load (≤400 copies/mL) in their last control in pediatrics were 36.4% (1997-2004), 45.3% (2005-2008) and 75.7% (2009-2013) ($p<0.01$). After one year of follow-up in AU, the patients with suppressed viremia were, respectively, 56.1%, 57.1% and 85.4% ($p<0.01$). Globally, 77.8% of unsuppressed patients at transition had undetectable viral load in their last registered control ($p=0.05$).

Conclusions

The transition process among vertically HIV-infected adolescents from CoRISpe was usually successful. Immunological and virological outcomes of patients improved over time during follow-up in AU.

ESP16-1077
E-POSTER DISCUSSION SESSION 5 - HIV (station 7)

CHRONIC LUNG DISEASE IN INDIAN CHILDREN WITH VERTICALLY ACQUIRED HIV

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Background

Increased survival of children with vertically-acquired HIV has led to rise in co-morbidities like Chronic Lung disease (CLD). We aimed to characterise this lung disease by determining spirometric lung function and High Resolution CT (HRCT) findings.

Methods

Clinical, anthropometric & spirometric assessments were undertaken in retropositive children aged 5-18yrs, from Indira Gandhi Institute of Child Health, Bengaluru. Lung function was expressed in z-scores based on newly derived coefficient for Indian children aged created from GLI-2012 spirometry equations which were compared with available controls aged 5-12yrs. HRCT's were performed selectively from a wider cohort aged 5-18yrs with clinical or functional suspicion of CLD.

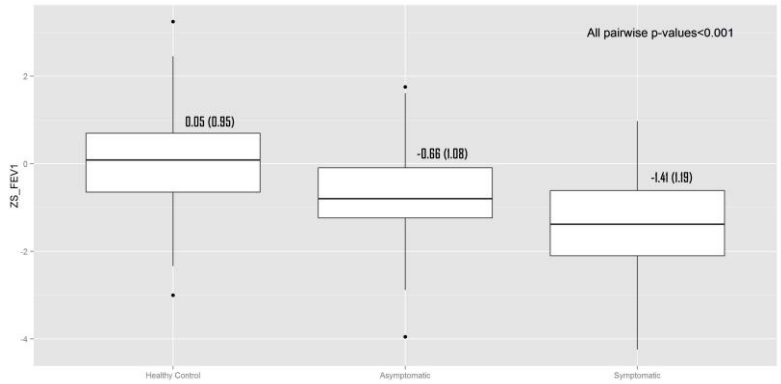
Results

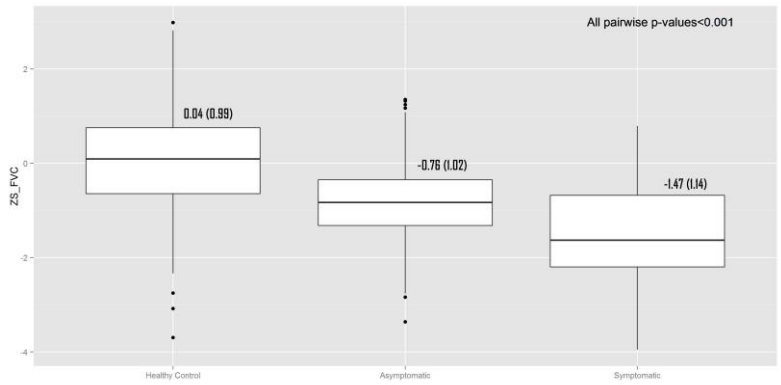
167 from the wider cohort of 455 were selected excluding children above 12 years, technically unacceptable data and those with pulmonary tuberculosis. Of these 65% were boys, 43% were symptomatic (Shortness of breath, cough and chest tightness) and 69% were on ART (Antiretroviral therapy).

Retropositive children were significantly shorter and lighter than the healthy controls by ~ 1 z-score and had significantly lower FEV_1 and FVC by ~1 z-score (~12%) ($p<0.001$) (Table). Significant differences were noted between symptomatic and asymptomatic HIV subjects indicating subclinical disease (Figures). Findings of the 137 HRCTs revealed extensive mixed airway (78%) and parenchymal disease (75%).

	Healthy controls(n=382)	Retropositive(n=167)	Mean diff(95% CI)
Age (years)	9.01(1.93)	10.01(2.09)	1.0(0.64,1.36)
zHeight	0.07(0.90)	-1.37(1.20)	-1.44(-1.64,-1.23)
zWeight	0.13(0.94)	-1.39(0.86)	-1.52(-1.68,-1.35)
zBMI	0.12(0.94)	-0.92(0.62)	-1.04(-1.18,-0.91)
zFEV1	0.05(0.95)	-1.02(1.18)	-1.07(-1.27,-0.86)
zFVC	0.04(0.99)	-1.10(1.13)	-1.14(-1.33,-0.95)
zFEV1/FVC	0.09(0.92)	0.11(0.98)	0.02(-0.15,0.19)

Results: mean(SD)





Conclusions

The proportionally reduced FEV1 & FVC may reflect prior exposure to early insults to the developing lung or a direct consequence of HIV infection. CT findings can provide clues to the pathogenesis of CLD which remains to be elucidated.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0638
E-POSTER DISCUSSION SESSION 5 - HIV (station 7)

CARDIOVASCULAR RISK IN HIV-INFECTED ADOLESCENTS: LONGITUDINAL FOLLOW-UP OF INTIMA MEDIA THICKNESS

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Background

Recent studies have highlighted that HIV-infected children and adolescents show accelerated atherosclerosis and may be at increased risk for cardiovascular disease. We evaluated the progression of carotid intima-media thickness (IMT) in HIV-infected children and adolescents and uninfected controls over 4 years as a marker of cardiovascular risk.

Methods

IMT was measured in a cohort of vertically HIV-infected children and uninfected controls at baseline and after a 4-year follow-up period. Cardiovascular risk factors, clinical and immunovirological data were extracted from medical records, patient interview and clinical examination.

Results

To date, 47 HIV-infected subjects and 12 controls have completed the follow-up and were included in the analysis. Mean age was 16.5±4.6 years vs 18±4.7 (P=0.2), 66% were female. All HIV-infected youths were on ART, and 78% had undetectable viral load. Median CD4 nadir was 362 cell/mm^3 [190-642]. Median CD4 T-cell count was 720cell/ mm^3 [617-992]. Twelve (29%) cases vs 1 control (8%) were smokers (P=0.07). Progression of IMT was increased in HIV-infected subjects, with a delta/year of 0.003 vs 0.0006mm/y (P=0.042). No association was found between smoking habits and IMT progression (delta: smokers 0.003mm/y vs non-smokers 0.003mm/y, P=0.43) and no difference was found between patients with detectable vs undetectable viral load (delta: 0.003 vs 0.002, P=0.5).

Conclusions

Despite the reduced sample size that limits the interpretation of results, our findings suggest that HIV-infected adolescents present faster progression of carotid atherosclerosis, compared to uninfected controls, despite being on ART and most of them virologically suppressed. IMT measurement might be a useful marker to address cardiovascular risk since childhood, in order to achieve an early diagnosis of patients at risk. There is a need to implement cardiovascular preventive measures since childhood in vertically HIV-infected patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0486
E-POSTER DISCUSSION SESSION 6 - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS (station 8)

SECULAR TREND OF ADENOVIRUS INFECTION IN SOUTHERN TAIWAN FROM 2010 TO 2015

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Background

Human adenovirus (HAdV) is one of the most common causes of respiratory tract infections. In Taiwan, HAdV infection is noted year round with sporadic outbreaks. In this study, we analyzed the secular trend of HAdV serotype epidemiology and clinical manifestations.

Methods

Patients with HAdV infection at National Cheng Kung University Hospital from Jan. 2010 to Feb. 2015 were enrolled. HAdV infection was defined by isolation of adenovirus from throat swabs or nasopharyngeal aspirates. Demographic data, clinical manifestations, outcome and deposition were analyzed prospectively.

Results

Among 1711 cases, 97.0 % were children with a median age of 4.0 years. Adult patients were prone to have more co-detection of bacteria (7.5% vs. 1.1%), underlying disease (49.1% vs. 6.9%), lower respiratory tract infections (54.7% vs. 24.2%), need for hospitalization (71.7% vs. 29.8%), and intensive care (6.6% vs. 1.9%) compared with children ($P< 0.05$). The baseline HAdV-positive rate during whole study period was 5.5%, except two episodes of the epidemic. First episode started from late 2010, extending to 2011 and other was in 2014. Patients in epidemic 2011 had more pneumonia (5.3% vs. 1.9%), gastro-enterocolitis (9.2% vs. 5.7%), oxygen demand (5.0% vs. 1.5%), hemodynamic instability (2.1% vs. 0.4%) and longer hospitalization days (6.2±6.3, 4.8±5.2) compared those in epidemic 2014. HAdV genotype 1 (23.6%), 3 (41.0%) and 7 (17.7%) were the most common genotypes. Genotype 3 was the major genotype in epidemic 2011 (63.4%), while genotype 1 was more prevalent in epidemic 2014 (30.2%). Genotype 7 HAdV in epidemic 2010 is associated with more pneumonia cases (21.4% vs. 3.0%, $P<0.05$) than in epidemic 2014.

Conclusions

The HAdV infections occurred year-round. Circulation of different genotypes resulted in different clinical manifestations and disease severity

ESP16-0612
E-POSTER DISCUSSION SESSION 6 - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS (station 8)

CLINICAL CHARACTERISTICS AND COMPLICATIONS OF ROTAVIRUS ACUTE GASTROENTERITIS IN HOSPITALISED CHILDREN IN EAST LONDON: A RETROSPECTIVE CASE-CONTROL STUDY

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Background

Rotavirus infection is the main cause of acute gastroenteritis in children. Less well recognized is the association of rotavirus-infection with neurological complications such as seizures and encephalopathy. The aim of this study was to investigate presentation and complications of rotavirus gastroenteritis compared to non-rotavirus gastroenteritis in children, in the era before the introduction of rotavirus vaccine, focusing specifically on the neurological manifestations.

Methods

This is a retrospective, case-control and hospital-based study conducted at three hospitals in East London. Data were collected from 50 patients aged 1 month to 16 years diagnosed with acute gastroenteritis between 1 June 2011 and 31 December 2013, in whom stool virology investigations confirmed presence of rotavirus by PCR. They were matched by age, gender and month of presentation to 66 children with rotavirus negative gastroenteritis.

Results

Children with rotavirus gastroenteritis suffered more often from metabolic acidosis, and fever and were more likely to require hospitalisation compared to children with non-rotavirus gastroenteritis (7.30 vs 7.37, P=0.01, 37/50 (74%) vs 30/66 (46%), P=0.005 and 38/41 (93%) vs 44/60 (73%), P=0.02, respectively). Neurological complications were the most common extra-intestinal manifestations of rotavirus infection. Seizures (n=5, 10%) and encephalopathy (n=3, 6%) were reported in previously healthy children presenting with rotavirus gastroenteritis.

Conclusions

Rotavirus causes more severe gastroenteritis than other enteric pathogens. Rotavirus infection is often associated with neurological complications such as afebrile and febrile seizures and encephalopathy in previously healthy children. Therefore, it is important to consider rotavirus infection in the differential diagnosis of a child with encephalopathy or encephalitis, particularly if associated with a diarrhoeal disease. Rotavirus vaccination may reduce the risk of hospitalisation due to seizures. Additional studies are required to test this hypothesis in a UK cohort.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0221
E-POSTER DISCUSSION SESSION 6 - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS (station 8)

CHARACTERIZATION OF PRIMARY AND SECONDARY DENGUE IN CHILDREN IN SINGAPORE

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Background

Dengue is a mosquito-borne viral disease endemic in Singapore. The aim of our study was to look at the difference in the epidemiology, presentation, trend in daily platelet counts and outcome of primary and secondary dengue in children in Singapore.

Methods

Retrospective study of 290 paediatric dengue admissions in KK Women's and Children's Hospital (KKH), Singapore, from January 2008 - December 2010. Two study groups were compared: primary dengue (PD) and secondary dengue (SD).

Results

A total of 290 paediatric patients were included (216 PD cases and 74 SD cases). There were 174 boys (60%) and median age was 12 years (IQR 8.4 -14 years). There was no difference in age or gender between the 2 groups. The SD group had a higher rate of overseas-acquired dengue (OR 3.0, 95% CI 1.7-5.2), dengue haemorrhagic fever /dengue shock syndrome (OR 4.8, 95% CI 2.7-8.5) and severe dengue (OR 3.6, 95% CI 1.6 – 8.4). For complications, the SD group had a higher rate of blood product transfusion (OR 6.1, 95% CI 2.2 – 17.2), transaminitis (OR: 2.6, 95% CI 1.5 – 4.7), pleural effusion (OR 3.6, 95% CI 1.3 – 9.7) and ascites (OR 7.4, 95% CI 2.2 – 24.4). There was no difference in the complication rates of hypotension or haemorrhagic manifestation between the 2 groups.

Figure 1 and 2 shows the graph of the mean daily platelet (PLT) counts according to the day of illness and complications for PD and SD respectively.

Figure 1

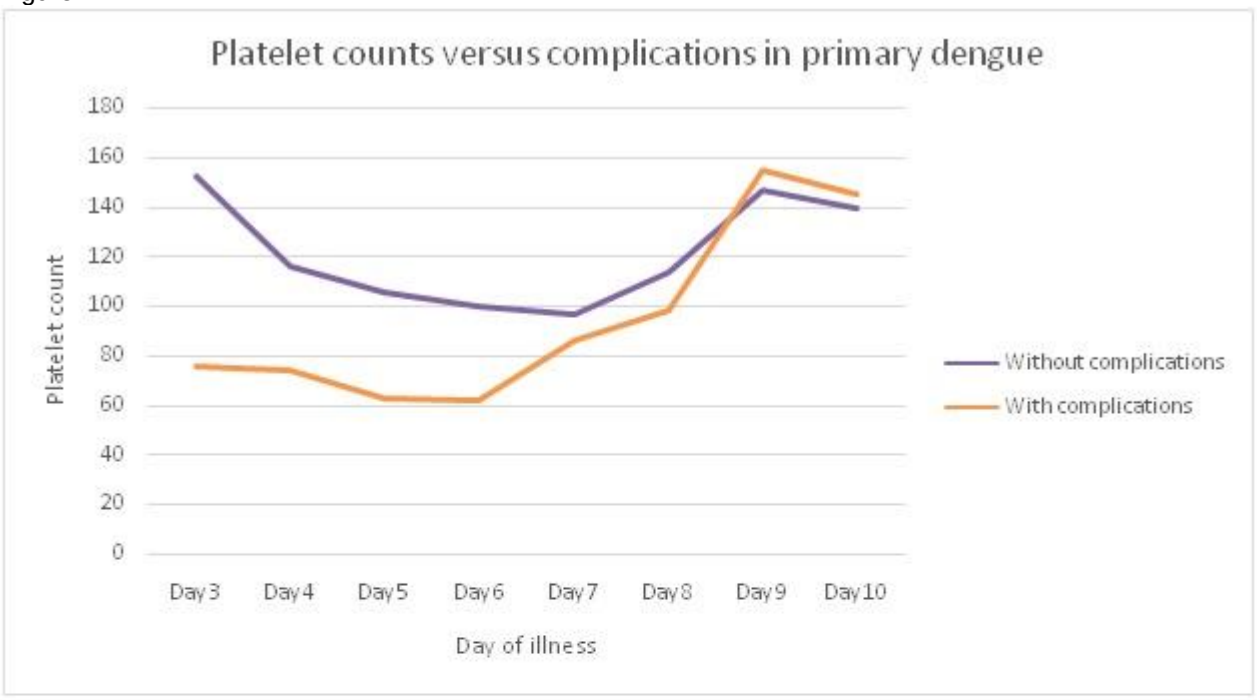
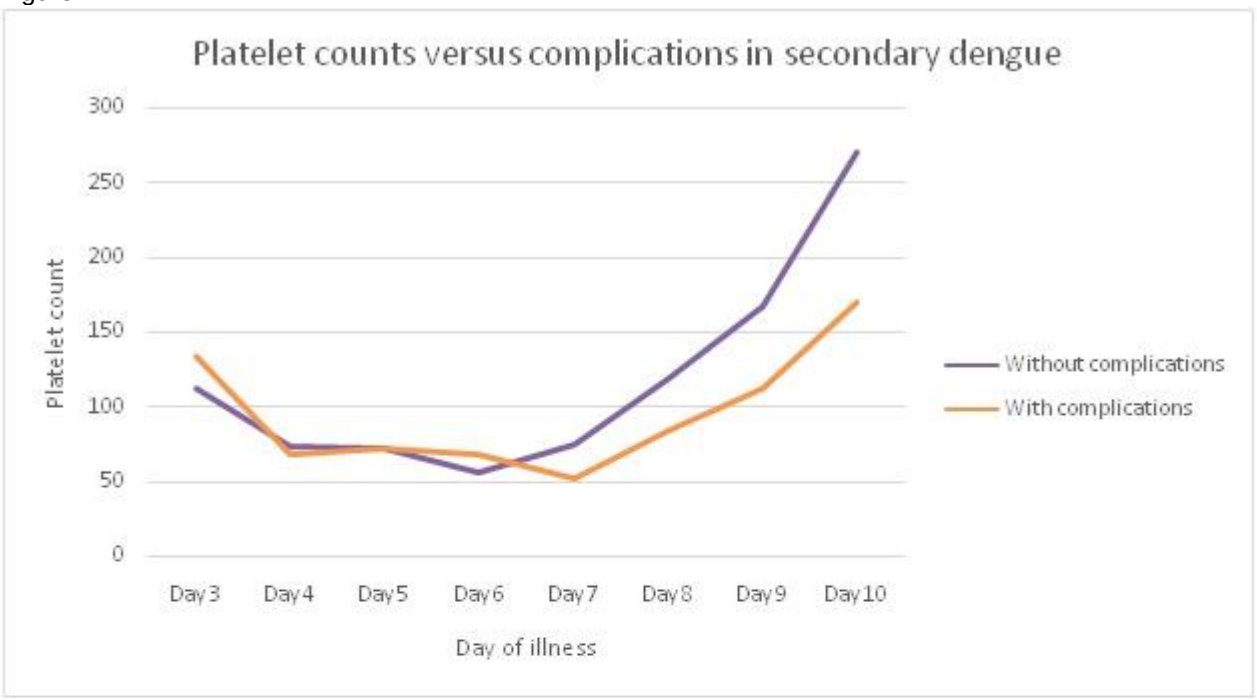

Platelet counts versus complications in primary dengue
180
160
140
120
100
80
60
40
20
0
Platelet count
Day 3
Day 4
Day 5
Day 6
Day 7
Day 8
Day 9
Day 10
Day of illness
Without complications
With complications

Figure 2



Conclusions

SD, when compared with PD, was associated with lower mean daily PLT counts, especially with complications, and higher rates of severe dengue. This may aid paediatricians in predicting and treating complications of dengue early in children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0823
E-POSTER DISCUSSION SESSION 6 - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS (station 8)

DIAGNOSIS AND TREATMENT OF PAEDIATRIC ACUTE PHARYNGITIS – IS THERE ANY BENEFIT ON TEN-DAY COURSE OF ANTIBIOTICS?

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Background

In group A streptococcal (GAS) pharyngitis a ten-day course of amoxicillinis is recommended. However, short-course treatments seem to be equally effective. The aim of this study was to evaluate the management of GAS pharyngitis including prescription regimens.

Methods

Retrospective analysis of all cases of GAS pharyngitis admitted to a paediatric emergency department (ED) in 2014. Recurrent pharyngitis was excluded. Short-course (up to 7days) and long-course treatment (10 days) groups were compared.

Results

We included 1190 cases of GAS pharyngitis. The median age was 5.6 years. A rapid antigen detection test (RADT) was performed in 830 cases (70%), positive in 97%. Amoxicillin was the most prescribed antibiotic (93%) - median duration of 7days. Ten-day course therapy was prescribed in 30% of the cases. One child had peritonsillar abscess. There were no differences between short and long-course treatment groups regarding age (p=0.49), gender (p=0.48), complications and return to the ER with a new episode of pharyngitis (p=0.55).

Conclusions

The RADT was frequently used. The antibiotic of choice was amoxicillin, but a 10-day course was only prescribed in 30% of the cases, in disagreement with national guidelines. In our analysis there seems to be no benefit with long-course treatments with amoxicillin.

ESP16-0826
E-POSTER DISCUSSION SESSION 6 - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS (station 8)

HIGH SALIVARY LEVELS OF EPIDERMAL GROWTH FACTOR (EGF) IN ROTAVIRUS INFECTED PATIENTS

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[2]Translational Pediatrics and Infectious Diseases- Department of Pediatrics- Department of P ediatrics, Hospital Clínico Universitario de Santiago de Compostela, Santiago de Compostela, Spain
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Background

In a previous whole transcriptome analysis of rotavirus-infected patients, a large increased expression of IFI27 gene (23.75 fold change) was found compared to control group (*unpublished data*). This gene encodes a protein of unknown function, linked to epidermal proliferation and related to the epidermal growth factor (EGF) protein. This salivary polypeptide plays an important role in maintaining oro-esophageal and gastric tissue integrity.

We aimed to determine salivary EGF levels in rotavirus infected patients to elucidate its eventual relationship with IFI27 increased expression and a EGF-mediated mucosal protection in rotavirus infection.

Methods

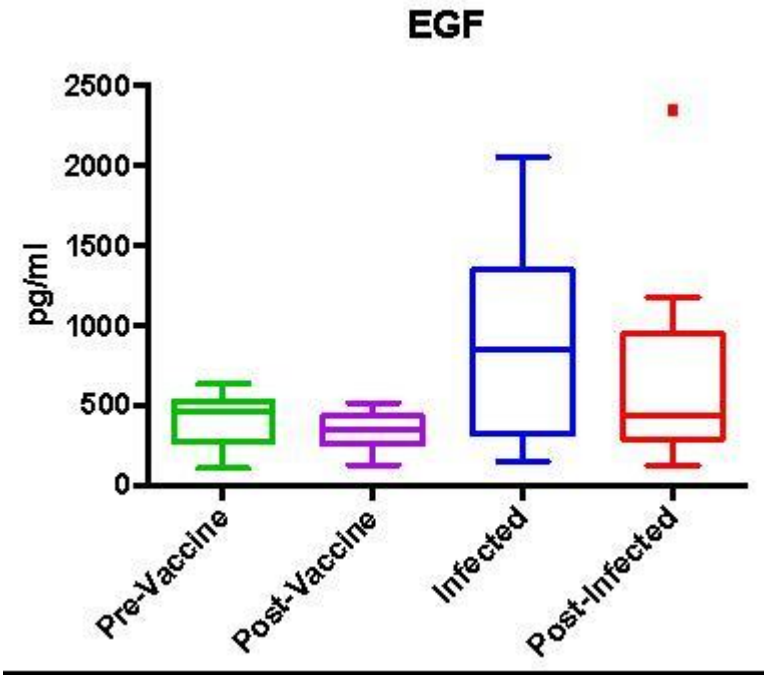
We conducted a prospective comparative study of saliva samples from 27 infants infected with (sampled at recruitment during hospital admission and at convalescence - i.e. at least 3 months after recovery) and from 36 rotavirus vaccinated patients (baseline and 40±3 days after 3rd vaccine dose)

EGF salivary levels were determined in a multiplex assay with other chemokines by Luminex (Millipore) Saliva samples were obtained by elution from an oral swab in 500 µl of PBS, ultra-centrifuged to remove mucin and epithelial cells and stored at -30 ºC prior analysis.

Results

Median (SD) EGF salivary concentration (pg/ml) was 843.8 (6862) in rotavirus-infected group at acute phase and 435.3(1239) at convalescence time, while it was 458.5 (156.1) at baseline

in vaccines and 343.1 (119) after vaccination



(*p=0.0008*).

Conclusions

During the acute phase of natural rotavirus infection the salivary levels of EGF are significantly increased. This increase could be linked to the previously found increased systemic expression of IFI27 gene and might lead to mucosal protection after rotavirus induced epithelial injuries. Vaccination of children with rotavirus vaccine does not induce EGF salivary increase. These findings could be applied in future treatment after rotavirus infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0205
E-POSTER DISCUSSION SESSION 6 - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS (station 8)

IMPACT OF ROTAVIRUS VACCINE ON BURDEN AND SEVERITY OF ROTAVIRUS GASTROENTERITIS IN HOSPITALIZED PEDIATRIC PATIENTS: SINGLE CENTER PROSPECTIVE STUDY IN A TERTIARY HOSPITAL IN JEDDAH.

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Background

In Jeddah, previous studies showed RV prevalence around 40% in pediatric inpatients with a maximum level during cooler months. Currently, there is no data on impact of rotavirus vaccine (RVV) on RV-gastroenteritis (RV-GE) in Saudi Arabia. Therefore this study was conducted to assess impact of RVV on burden and severity of RV-GE, 3 years after introduction of RVV in Saudi immunization program in January, 2013.

Methods

This study included all under 5-year GE cases admitted to Hai Al-Jameah hospital, one of tertiary hospitals in Jeddah, from October-December, 2015. All included GE-cases had RV antigen detection in stool by immunochromatographic assay, complete data collection including RVV status and severity assessment (Vesikari score) on initial admission.

Results

During study period, 151 total GE cases in children <5 years were hospitalized with only 5 (3.3%) RV-GE confirmed cases. Median age of patients was 12 months. All RV-GE cases didn't receive RVV and had severe GE. Among other 146 GE cases, 65 cases (44.5%) didn't receive RVV and 45 cases (30.8%) had severe GE. Severe GE was significantly more in RV-GE than in other all-cause GE (p=003). During same period of this study, 95 RV-GE out of 541 total GE cases (17.6%) were hospitalized in 2012, so, hospitalization-rate for all-cause GE and RV-GE in children <5 years, decreased significantly (odds ratio: 6.2, 95% CI: 2.8-15.8, p<0.001) in 2015 RV season.

Conclusions

RRV was protective especially against severe RV-GE. The burden of RV-GE was reduced significantly in vaccinated and even in unvaccinated under 5 years children possibly by good RVV herd effect, 3 years after introduction of Saudi RRV program. Further improvement in RVV coverage rate may make RV-GE a disease of the past in Saudi children.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0362
E-POSTER DISCUSSION SESSION 6 - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS (station 8)

URINARY TRACT INFECTIONS IN CHILDREN: EPIDEMIOLOGY, CLINICAL PROFILE, MICROBIAL SPECTRUM AND ITS ANTIBACTERIAL SENSITIVITY PATTERN

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Background

Urinary tract infections (UTI) are a common bacterial infection in children. The diagnosis of UTI is often clinically missed in children due to non-specific symptoms. Rapid evaluation and treatment of UTI is very crucial to prevent renal parenchymal damage and chronic renal failure. This prospective observational study was conducted to evaluate epidemiology, clinical profile, microbial spectrum and its antibacterial sensitivity pattern in urinary tract infections in children.

Methods

This study included children aged 0-14 years presented with UTI in Children Hospital, S.P.Medical College, Bikaner, during 2014-2015. The diagnosis of UTI is based on positive culture of properly collected urine sample in a symptomatic child before starting antibiotics. Antibacterial sensitivity pattern of cultured microbial was noted. Data were analysed by student *t*-test.

Results

During study period, 468 children presented with culture proven UTI in which proportion of boys and girls was 25.21% and 74.78% respectively. Below one year age boys (13.67%) were predominantly affected than girls (4.05%), while after one year age girls (70.73%) preceded to boys (11.53%) ($p<0.01$). The common clinical manifestations were fever (90.17%), vomiting (81.20%), abdominal pain (76.92%), and poor weight gain (35.90%). The risk of UTI is higher in children with protein energy malnutrition and chronic diarrhea. The most prevalent cause of UTI was *E.coli* (58.12%), *Enterobacter* (15.12%), *Proteus* (11.11%) and *Klebsiella* (8.12%). *E.coli* was highly sensitive to nitrofurantoin (84.72%), levofloxacin (78.56%) and amikacin (68.62%) but highly resistant to cotrimoxazole (81.81%), ampicillin (76.19%), ceftriaxone (68.78%) and nalidixic acid (54.68%).

Conclusions

UTI was commonly seen in girls (boys in <1 year age); clinical presentation was nonspecific; *E.coli* was most prevalent microbial with highest sensitivity to nitrofurantoin and levofloxacin.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0601
E-POSTER DISCUSSION SESSION 7 - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP (station 9)

PAEDIATRIC RESULTS FROM THE GLOBAL POINT PREVALENCE SURVEY OF ANTIMICROBIAL CONSUMPTION AND RESISTANCE (GLOBAL-PPS) IN 335 HOSPITALS WORLDWIDE

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Background

The Global Point Prevalence Survey (Global-PPS), conducted in February-September 2015, monitored antimicrobial prescribing and resistance in 335 hospitals (H) from 53 countries (C): Europe (214H;24C), Africa (12H;5C), Asia (57H;16C), South-America (19H;3C), North-America (24H;3C), Oceania (9H;2C) using a standardized and validated method (www.global-pps.com). bioMérieux provided unrestricted funding support.

Methods

We extracted data on children 1 month to 17 year. Mandatory data included age, gender, weight, antimicrobial agent, dose, reason and indication for treatment or prophylaxis, prescription based on biomarker; and microbiology data based on targeted treatment. Mandatory quality indicators of antimicrobial use included reason to treat and stop/review date recorded in the notes, existence and compliance to local guidelines; and duration of surgical prophylaxis. Denominator included children admitted on paediatric wards. Data were entered online using a web-based system for data-entry, validation and reporting.

Results

6,867 antimicrobials were administered to 4,759 children. Antimicrobial prevalence was 40.8%, varying between continents (highest in Africa:56.3%) and countries (highest in Bahrain:100%). 22.8% of antibiotics were for hospital acquired infections (highest in South-America:32.7%). Ceftriaxone was most frequently recorded (14.5%). Meropenem represented 3.6% (highest in South-America:5.0%). Six percent of children got a targeted treatment, among which 28.0% (highest in Asia:48.5%) received an antibiotic targeting a multidrug resistant organism. ESBL-producing Enterobacteriaceae were most reported (highest in Asia:15.3%). A stop/review date was frequently missing (36.8%). Guideline compliance was lowest in Africa (66.4%).

Conclusions

The Global-PPS provided quantifiable outcome measures to assess and compare quantity and quality of antimicrobial prescribing and resistance in hospitalized children worldwide. Antimicrobialprevalence and resistance rates were high, especially in Asia and South-

America. These data serve to identify targets for quality improvement of antimicrobial prescribing, the development of local guidelines, education and practice changes.

ESP16-0864
E-POSTER DISCUSSION SESSION 7 - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP (station 9)

ANTIBIOTICS USE IN CHILDREN PRESENTING TO THE EMERGENCY DEPARTMENT AT LOW RISK OF SERIOUS INFECTIONS: PROSPECTIVE OBSERVATIONAL STUDY AND AUDIT OF COMPLIANCE WITH NATIONAL GUIDELINES

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Background

To evaluate the judicious use of antibiotics in children presenting to the paediatric emergency department, and to assess compliance with guidelines for antibiotics prescribing.

Methods

Prospective observational cohort study of children (<16 years) presenting to the paediatric emergency department of Sheffield children's hospital, Sheffield, UK, between November 2014 – April 2015. Compliance with local recommendations for type and duration of antibiotics prescribed to children being discharged home were evaluated. For children with a discharge diagnosis of tonsillitis and otitis media a retrospective audit (March – April 2015) was performed looking at adherence with clinical indications for antibiotics.

Results

390/2,214 (18%) children with fever ≥ 37.8 ^{o}C, and 1,372/9,109 (15%) of children with a discharge diagnosis of an infectious illness had antibiotics prescribed. Type and duration of antibiotics were compliant with guidelines in > 90% for any indication.

Antibiotics were prescribed in 382/597 (64%) of children with tonsillitis and 178/468 (38%) of children with otitis media. Only 5/217 children with tonsillitis reviewed in the audit had Centor score 4, of whom 4 were given antibiotics. 121/217 (56%) were given antibiotics with Centor score <4.

Age <1year (p-value 0.84), bilateral otitis media (p-value 0.74), previous medical history including ENT risk factors (p-value 0.06), unwell appearing (p-value 0.1) were not significantly associated with antibiotics prescribing in otitis media. 27/55 (49%) of children receiving antibiotics for otitis media did not have any of these features.

Conclusions

A considerable proportion of children at low risk of serious infections have antibiotics prescribed on discharge from the emergency department. Type and duration of antibiotics mostly followed local prescribing recommendations. The paediatric emergency department offers opportunities for improved antibiotic stewardship, in particular in children with upper airway infections.

ESP16-0681
E-POSTER DISCUSSION SESSION 7 - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP (station 9)

CARBAPENEMASE PRODUCTION AMONG ENTEROBACTERIACEAE CANNOT BE ESTIMATED FROM SURVEILLANCE OF ROUTINE ANTIMICROBIAL SUSCEPTIBILITY TESTING DATA

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Background

Accurate data on the prevalence of antimicrobial resistance in selected pathogens is needed. While carbapenemase-production is associated with higher rates of treatment failure, many carpabenemase-producing *Enterobacteriaceae* (CPE) are phenotypically susceptible to carbapenems, such as imipenem or meropenem. However, resistance to other beta-lactams has been associated with carbapenemase-production. We aimed to investigate the proportion of specific *Enterobacteriaceae*, for which presence or absence of a carbapenemase could be reliably determined based on reported susceptibility to other beta-lactams.

Methods

The study used antimicrobial susceptibility testing (AST) data from 19 centres in 12 European countries on bloodstream isolates of *E. coli*, *Enterobacter* spp. and *K. pneumoniae* collected as part of the Antibiotic Resistance and Prescribing in European Children (ARPEC) project. We analyzed the range of beta-lactams tested in the different centres, and used these results to identify AST profiles potentially indicative of CPEs categorized as (i) probable; (ii) possible; (iii) unlikely; (iv) uninterpretable or (v) no AST data reported.

Results

In total, 685 isolates were included (380 *E. coli*, 122 *Enterobacter spp* and 183 *K. pneumoniae*), of which 17 (3%) were reported to be imipenem or meropenem-resistant. Most isolates had beta-lactam AST profiles that made expression of a carbapenemase unlikely (392/685, 57%). Conversely, only 2% (14/685) were considered as probable CPEs. A large proportion of isolates had reported beta-lactam AST profiles that indicated possible CPEs (152/685, 22%) or were uninterpretable (124/685, 18%). Only 3 isolates (<1%) had no reported AST data.

Conclusions

Although the proportion of ARPEC carbapenem-resistent enterobacteriaceal isolates was low, available beta-lactam AST data were insufficient to reliably estimate CPE prevalence for 40% of all reported isolates. Prevalence of CPEs may be underestimated when surveillance relies purely on reporting of routine clinical AST data.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0850
E-POSTER DISCUSSION SESSION 7 - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP (station 9)

SURVEILLANCE OF PAEDIATRIC STERILE SITE ISOLATES IN A TEACHING HOSPITAL

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Background

To assess local antimicrobial resistance, we reviewed all our local antibiotic susceptibility patterns from bacterial cultures of normally sterile sites in children.

Methods

We extracted data on all positive blood, cerebrospinal fluid (CSF) and urine bacterial cultures from children below 18 years of age between 11/07/2012 and 28/03/2015 with routine antibiotic sensitivity results (disc diffusion using BSAC methodology). Duplicate organisms from the same patient, route and day were excluded.

St Mary's is a large metropolitan hospital with a paediatric emergency department, general and haematology (including bone marrow transplant) inpatient care, paediatric intensive care and a level 2 neonatal unit.

Results

There were 1208 isolates from 1188 samples, with 990 patient identifiers.

CSF isolates

	Age				
Organism	**<3m**	**3m - 1y**	**1 - 5y**	**≥5y**	**Total**
Gram Positive	14	1	1	4	20
Enterococcus sp.	1				1
Beta-haemolytic strep. Group B	1				1
Streptococcus pneumoniae			1		1
Probable contaminants	12	1	0	4	17
Gram Negative	5	1	0	0	6
Escherichia coli	1				1
Haemophilus sp.	1				1
Pseudomonas sp.	2				2
Acinetobacter sp.	1	1			2
Total	**19**	**2**	**1**	**4**	**26**

Urine isolates

	Age				
Organism	**<3m**	**3m - 1y**	**1 - 5y**	**≥5y**	**Total**
Gram Negative	182 (84%)	107 (86%)	315 (79%)	80 (73%)	684 (81%)
Escherichia coli	131 (61%)	71 (57%)	228 (57%)	49 (45%)	479 (56%)
Other Enterobacteriaceae	41 (19%)	33 (26%)	48 (12%)	29 (27%)	151 (18%)
Pseudomonas aeruginosa	6 (3%)	3 (2%)	22 (6%)	1 (1%)	32 (4%)
Environmental gram negative	4 (2%)		17 (4%)	1 (1%)	22 (3%)
Gram Positive	34 (16%)	18 (14%)	83 (21%)	29 (27%)	164 (19%)
Enterococcus sp.	29 (13%)	15 (12%)	42 (11%)	20 (18%)	106 (13%)
Staphylococcus aureus	2 (1%)	1 (1%)	14 (4%)	2 (2%)	19 (2%)
Group B Streptococcus	1		6 (2%)	4 (4%)	11 (1%)
Group A Streptococcus			2 (1%)		2
Probable contaminants	2 (1%)	2 (2%)	19 (5%)	3 (3%)	26 (3%)
Total	**216**	**125**	**398**	**109**	**848**

CSF and urine samples in infants under 3 months are not stratified due to small numbers of inpatients.

Blood isolates

	Age					
	<3m		**3m - 1y**	**1 - 5y**	**≥5y**	**Total**
Organism	Hospital	Community				
Gram Positive	41 (93%)	42 (78%)	39 (93%)	76 (90%)	72 (65%)	270 (81%)
Coagulase-negative staphylococcus	19 (43%)	26 (48%)	20 (48%)	38 (45%)	40 (36%)	143 (43%)
Viridans Streptococci	2 (5%)	4 (7%)	7 (17%)	6 (7%)	10 (9%)	29 (9%)
Staphylococcus aureus	9 (20%)	2 (4%)	1 (2%)	6 (7%)	8 (7%)	26 (8%)
Streptococcus pneumoniae			4 (10%)	9 (11%)	1 (1%)	14 (4%)
Group B Streptococcus	8 (18%)	8 (15%)				16 (5%)
Enterococcus sp.			2 (5%)	1 (1%)	2 (2%)	5 (1%)
Actinomycetes		1 (2%)		2 (2%)	2 (2%)	5 (1%)
Group A Streptococcus				2 (2%)		2 (1%)
Group C/G Streptococcus			1 (2%)	1 (1%)		2 (1%)
Gram positive probable contaminants	3 (7%)	1 (2%)	4 (10%)	11 (13%)	9 (8%)	28 (8%)
Gram Negative	3 (7%)	12 (22%)	3 (7%)	8 (10%)	37 (34%)	63 (19%)
Enterobacteriaceae	3 (7%)	11 (20%)		4 (5%)	5 (5%)	23 (7%)
Pseudomonas aeruginosa				1 (1%)	18 (16%)	19 (6%)
Haemophilus influenzae		1 (2%)		2 (2%)		3 (1%)
Neisseria sp.				1 (1%)	1 (1%)	2 (1%)
Salmonella sp.					2 (2%)	2 (1%)
Kingella kingae			1 (2%)			1
Moraxella sp.			1 (2%)			1
Campylobacter sp.					1 (1%)	1
Environmental gram negative			1 (2%)		10 (9%)	11 (3%)
Anaerobic					1 (1%)	1
Total	**44**	**54**	**42**	**84**	**110**	**334**

7% of *Staphylococcus aureus* isolates (3/45) were methicillin resistant, all from urine. 19% of Group A *Streptococcus* and *Staphylococcus aureus* isolates (9/48) were resistant to both erythromycin and clindamycin.

7% of *Streptococcus pneumoniae* isolates (1/15) were penicillin resistant. 4% of enterococcal isolates (4/108, 4 not tested) were resistant to vancomycin.

8% of Gram negative organisms (62/753) were found to be resistant to gentamicin. No carbapenemase producing organisms were identified among 654 Enterobacteriaceae. 12% Of *E. coli* isolates (58/495) were resistant to co-amoxiclav, 9% resistant to gentamicin (45/495) and 11% (72/495) resistant to cefotaxime or cephalexin. 6% (30/495) were resistant to both gentamicin and cefotaxime or cephalexin.

Conclusions

The prevalence of resistant organisms is surprisingly low in this metropolitan paediatric population. Data on local resistance patterns aid local prescribing guidelines. In the absence of any late onset *Listeria* cases we have restricted empirical use of amoxicillin to infants below one month of age.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1033
E-POSTER DISCUSSION SESSION 7 - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP (station 9)

EFFECT OF CLINICAL PATHWAYS TOOLS ON ANTIBIOTIC PRESCRIPTIONS FOR ACUTE OTITIS MEDIA IN AN ITALIAN EMERGENCY DEPARTMENT

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Background

Italian pediatric antimicrobial prescription rates are among the highest in Europe. Identifying effective stewardship activities is essential. This study evaluates the impact of clinical pathways tools (CP) on antibiotic prescribing for acute otitis media (AOM) in children presenting to a large Italian emergency department (ED).

Methods

We collected data at the Department of Woman and Child Health in Padua from children 2 months-15 years diagnosed with AOM from 15 October 2014 through 15 January 2015 (pre-intervention period) and from 15 October 2015 through 15 January 2016 (post-intervention period). The intervention consisted of implementation of a CP for the diagnosis and judicious treatment of AOM, along with education and training to adhere to the CP. The CP summarizes national and international guidelines for the diagnosis and treatment of AOM. We assessed differences in pre- and post-intervention antibiotic prescription appropriateness, including delay in prescription and spectrum of first-line antimicrobial therapy, using chi squared goodness of fit tests.

Results

177 clinic visits were associated with AOM pre-intervention and 143 post-intervention. From pre- to post-intervention, there was an increase in: 1) delayed antimicrobial prescription (20.9%vs 32.9%, $p<0.01$) and 2) use of narrow spectrum first line therapy (amoxicillin) versus broad spectrum (amoxicillin-clavulanate, cephalosporins or macrolides) (32.9% vs. 52.1%, $p=0.02$). Broad spectrum agents were used mostly for perforated AOM or patients with antibiotic use in the previous 30 days. Overall prescription of antibiotics for AOM decreased from 79.1% to 67.1%. ($p=0.02$).

Conclusions

Our clinical pathway was associated with reductions in overall and broad spectrum antibiotic prescription for AOM, as well as with increased delayed antibiotic prescription in the short term in a large Italian ED, indicating its promise for antimicrobial stewardship in this setting.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0316
E-POSTER DISCUSSION SESSION 7 - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP (station 9)

SPECIFIC GENE DELETION BY DUO-SELECTION WITH THE TELA/B-SACB CASSETTE IN ACINETOBACTER BAUMANNII

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Background

A specific gene knock-out for verifying its regulatory role *per se* in antibiotics resistance is difficult for the pan-drug resistant *Acinetobacter baumannii* (PDRAB), because of the rarely remained selectable antibiotics markers *in vitro*.

Methods

A tellurite-resistant (*sacB*+, *xylE*+) suicide vector (pMo130-Tel^R) was used to specifically delete the adeRS operon by two-step homologous crossover in *Acinetobacter baumannii*. Tellurite resistance was used to select the first crossover to successfully introduce the *telA/B-sacB* cassette flanked with adeR and adeS homology arms into the bacterial chromosome. Final deletion of the adeRS gene could then be selected by looping-out the *sacB* containing gene cassette in the second recombination.

Results

The adeRS deleted *Acinetobacter baumannii* strain (ABΔadeRS) grew well as its parental strain. The mutant strain exhibited 0.52-fold, 0.61-fold, 0.54-fold and 0.86-fold decreased expression of *adeA*, *adeb*, *adeF* and *adeI* gene, respectively. Phenotype microarray comparison between the ABΔadeRS mutant strain and its parental strain disclosed different resistance to high concentrations of

5,7-Dichloro-8-hydroxyquinoline, phleomycin, puromycin, iodonitro tetrazolium violet, chlorpromazine, and oleandomycin. Resistance to phleomycin was reversible by complementing the ABΔadeRS strain with the authentic AdeRS operon.

Conclusions

Specific gene deletion by duo-selection with the *telA/B-sacB* cassette could be applied to PDRABisolates for further elucidating the drug resistance mechanism of a specific gene.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0317
E-POSTER DISCUSSION SESSION 7 - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP (station 9)

MULTIDRUG-RESISTANT HEALTHCARE-ASSOCIATED INFECTIONS IN NEONATES AND CHILDREN ADMITTED TO INTENSIVE CARE UNITS: EPIDEMIOLOGY AND IMPACT OF RISK FACTORS

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Background

Children admitted to ICU are at high risk of developing MDR-HAI. However, the real estimate of MDR impact in children, especially of carbapenem-resistant Enterobacteriaceae (CRE), is hampered by the paucity of published data. Our aim was to evaluate epidemiology, risk factors and clinical impact of MDR-HAI (CDC definitions) in children admitted to ICU.

Methods

This multicentre, prospective, cohort study was conducted in three tertiary-care paediatric hospitals in Italy and Brazil. All patients aged ≤18 years, admitted to ICU (PICU, NICU or CICU) between 2010 and 2014, with microbiologically-confirmed diagnosis of HAI were included.

Results

538 episodes in 454 children were identified (median age 7.8 months, IQR 2.1-26.2). 93.3% of patients had an underlying disease. BSI were the leading cause (45.3%), followed by LRTI (27.7%), UTI (15.8%) and SSI (5.9%). 566 microorganisms were isolated. The most frequent strains were Enterobacteriaceae (30.9%), followed by *Pseudomonas aeruginosa* (19.4%) and *Staphylococcus aureus* (11.1%). The percentage of MDR isolates was 45%. Among the Enterobacteriaceae, 45% were ESBL-positive whereas 2% were carbapenem-resistant. 56% of *S. aureus* were methicillin-resistant. No vancomycin-resistant Enterococci were isolated. In the multivariate analysis, factors independently associated with a MDR-HAI were country (Brazil, adjusted-OR 2.5; 95%CI: 1.5-4.2),use of 3rd-generation cephalosporins (adjusted-OR: 2.3; 95%CI: 1.1-4.8), use of carbapenems (adjusted-OR: 1.8; 95%CI: 1.05-3.2), previous surgery (adjusted-OR: 1.5; 95%CI: 1.01-2.4) and colonization by a MDR strain (adjusted-OR: 1.9; 95%CI: 1.2-3.1).

Conclusions

Children significantly differ from adults in HAI distribution, with BSI representing the leading pattern. Despite the increasing rates of CRE among adults worldwide, their prevalence

remains relatively uncommon in children. European and global surveillance programmes should be emphasized in order to define the risk factors for CRE acquisition and the best treatment strategies.

ESP16-0142
E-POSTER DISCUSSION SESSION 8 - TB & MYCOBACTERIAL INFECTIONS / ANTIMICROBIAL USE (station 10)

PERFORMANCE OF TUBERCULIN SKIN TEST AND QUANTIFERON-TB GOLD IN-TUBE® FOR THE DIAGNOSIS OF TUBERCULOSIS INFECTION AND DISEASE IN IMMUNOCOMPETENT CHILDREN AGED <5 YEARS

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Background

The evidence to define the optimal diagnostic approach in children aged <5 years at risk of tuberculosis (TB) is scarce. We aimed to evaluate the performance of the combined use of tuberculin skin test (TST) and QuantiFERON-TB Gold In-Tube® (QFT-GIT, Cellestis, Australia) for the diagnosis of TB infection and disease in immunocompetent children aged <5 years.

Methods

Prospective observational study. Children aged 0-5 years at risk of TB were evaluated with both TST and QFT-GIT in two referral TB Units in Barcelona. Results of both tests and their agreement were assessed, and also compared with baseline variables, reason for study and final diagnosis.

Results

507 TST/QFT-GIT pairs were conducted in 385 children, mainly after TB contact and because of new-entrant screening. Median (IQR) follow-up time after assessment was 36 (21-48) months. Agreement between tests according to reason for study, BCG vaccination status and final diagnosis is shown in Table 1. Overall, agreement was moderate (κ=0.46), but good in children studied for contact with a TB case (κ=0.67) and in BCG-unvaccinated patients (κ=0.70). The highest rate of discordant results occurred in new-entrant screening and in BCG-vaccinated children; most children in both groups were considered uninfected. Age correlated with TST (r=0.54, p=0.001) and QFT-GIT (r=0.51, p=0.001) results in latent infection cases, but not in disease ones. Indeterminate results were more frequent in younger children (9 *vs.* 28 months, p=0.001), mainly due to low response to mit

		n (%)	n, excluding indet. QTF-GIT	Agreement proportion (%)	κ (SE)
Reason for study	Clinical and/or radiological suspicion	37 (7)	34	71	0.45 (0.12)
	Contact tracing	379 (75)	366	93	0.67 (0.06)
	New-entrant screening	91 (18)	89	42	0.12 (0.04)
BCG vaccination	No	380 (75)	366	93	0.70 (0.05)
	Yes	88 (17)	109	47	0.15 (0.04)
Diagnosis	Uninfected	397 (78)	385	82	0.06 (0.05)
	TB infection	66 (13)	61	79	0.59 (0.09)
	TB disease	44 (9)	43	84	0.59 (0.14)
	Microbiologically confirmed	18 (41)	17	94	0.64 (0.33)
Overall		507 (100)	489	82	0.46 (0.05)

κ (SE), Cohen's kappa coefficient (standard error)

ogen.

Conclusions

In native BCG-unvaccinated children with a TB contact, concordance between TST and QFT-GIT was good. QFT-GIT added specificity in the new-entrant screening of BCG-vaccinated children. In the latter, a dual test strategy may be indicated.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0543
E-POSTER DISCUSSION SESSION 8 - TB & MYCOBACTERIAL INFECTIONS / ANTIMICROBIAL USE (station 10)

MULTIFOCAL BCG OSTEOMYELITIS COMPLICATING BCG VACCINATION IN A CHILD WITH SUSPECTED MENDELIAN SUSCEPTIBILITY TO MYCOBACTERIAL DISEASE: A CASE REPORT.

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Title of Case(s)

Multifocal BCG osteomyelitis complicating BCG vaccination in a child with suspected Mendelian Susceptibility to Mycobacterial Disease: a case report.

Background

BCG is a live attenuated vaccine that can rarely cause disseminated disease in immunocompromised hosts.

Case Presentation Summary

A previously healthy 9 month old boy presented with a 6 week history of left elbow swelling and pain. He underwent a joint wash-out twice, with negative culture results, and received several courses of antibiotics with no improvement of symptoms.

On examination, he had swelling of the left elbow with two discharging sinuses, sublaxation of proximal radio-ulnar joint and a collection within the olecranon fossa (Figures 1 and 2).

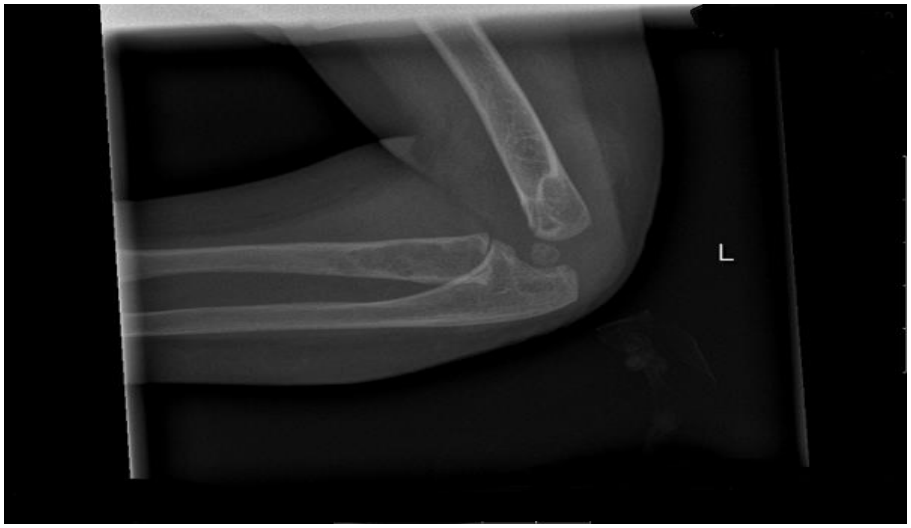

Figure 1

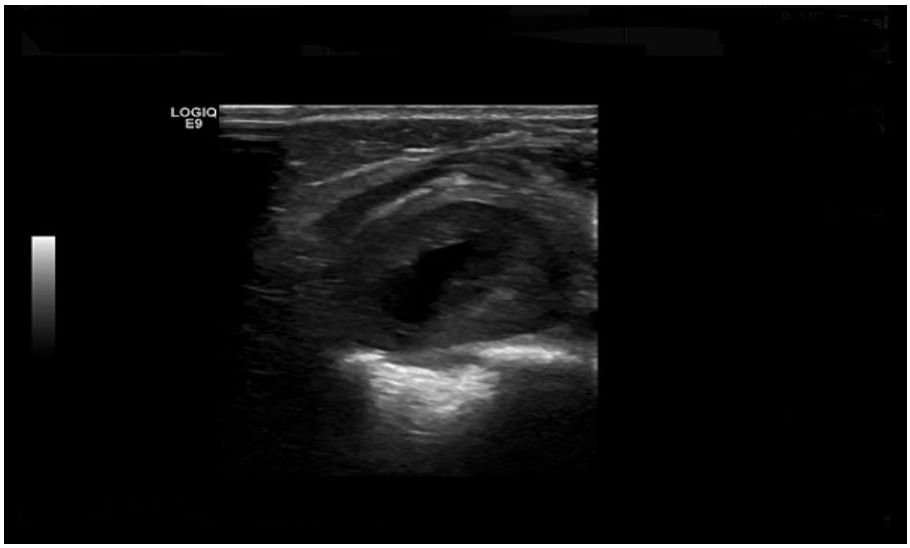

Figure 2

A Mantoux test was positive (16mm) but TB Elispot negative. A broad range PCR-electrospray ionization mass spectrometry analysis of bone/joint specimens using the Iridica (Abbott) system revealed *Mycobacterium tuberculosis* complex.

He was treated initially with isoniazid, rifampin, ethambutol and pyrazinamide. *Mycobacterium bovis* (BCG) was isolated on culture and pyrazinamide was stopped. Three months into treatment, he relapsed with a lytic lesion in the distal radius, and his regimen changed to isoniazid, rifampicin, ethambutol and ciprofloxacin. Immune testing showed low IFN-γ production *in vitro* by T-cells and subcutaneous IFN-γ treatment was commenced thrice weekly, with good response.

Learning Points/Discussion

BCG osteomyelitis is a rare complication of vaccination. Mendelian Susceptibility to Mycobacterial Disease (MSMD) encompasses a range of defects that predispose to atypical mycobacteria, including defects in the IFN-γ/IL-12 axis. 18 MSMD disorders have been described, but about half of all patients remain undiagnosed.

Novel diagnostic methods, using PCR/mass spectrometry in combination with traditional culture, may allow more rapid identification of unusual organisms in recalcitrant cases of osteomyelitis. Recombinant IFN-γ treatment should be considered in patients with suspected MSMD.

ESP16-0595
E-POSTER DISCUSSION SESSION 8 - TB & MYCOBACTERIAL INFECTIONS / ANTIMICROBIAL USE (station 10)

NUCLEIC ACID AMPLIFICATION TEST FOR RAPID DETECTION NONTUBERCULOUS MYCOBACTERIAL LYMPHADENITIS USING FINE NEEDLE ASPIRATES IN CHILDREN

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Background

Diagnosis of Nontuberculous mycobacterial (NTM) lymphadenitis is clinical, histological and microbiological. Microbiological diagnosis of NTM lymphadenitis is commonly based on molecular identification of the specimen after the pathogens have grown in cultures. However these techniques can take as long as 12 weeks before a result is obtained. Rapid techniques of specimen identification may help in appropriate and timely treatment.The aim of the study was to assess the diagnosis accuracy of this test to reduce the diagnostic time.

Methods

From 2011 to 2015, children <14 years old with suspected mycobacterial lymphadenitis were included. All samples obtained by fine needle aspiration (FNA) were cultured on Coletsos solid medium and Bactec MGIT 960 liquid medium (Becton Dickinson, Maryland USA)**.** We have used a commercial nucleic acid amplification tests (NAAT), GenoType ® Mycobacterium CM/ASassay.

Results

17 patients were included (64% female). Median age at diagnosis was 27 months (IQR 19.5-29). Submandibular lymph nodes were the most commonly area affected (74%). Tuberculin skin test showed an induration 0 mm in 59% and between 5-10 mm in 41% of the patients. Histological examination showed granulomatous lymphadenitis in 13 patients (76%).

Mycobacteria study was conducted with 15 of 17 patients. The results of mycobacteria study were positive by culture 6 (40%), NAAT 8 (53%) and combining culture and NAAT 12 (80%). All isolates (6) from culture were identified as *M. lentiflavum.* No clinical differences in the follow-up between patients with MNT identified by culture versus NAAT from FNA were observed.

Conclusions

Themycobacteria study is used for the diagnosis of children with lymphadenitis. NAAT from direct samples is a good additional assay to conventional tests, and also the results of NAAT are available sooner than results of culture.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0955
E-POSTER DISCUSSION SESSION 8 - TB & MYCOBACTERIAL INFECTIONS / ANTIMICROBIAL USE (station 10)

MYCOBACTERIUM LENTIFLAVUM AND MYCOBACTERIUM AVIUM CERVICOFACIAL LYMPHADENITIS IN SPAIN: A COMPARATIVE MULTICENTER STUDY

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[16]Hospital de Móstoles, Pediatrics, Móstoles, Spain
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Background

Mycobacterium avium and *Mycobacterium lentiflavum* are frequently isolated in previously healthy children with nontuberculousmycobacterial lymphadenitis in Spain. We compared the clinical features, outcome and geographical distribution of cervicofacial lymphadenitis caused by both species of mycobacteria.

Methods

Ongoing retrospective-prospective, multi-center observational study including Institutions within Red Española de Tuberculosis Pediátrica (Spain, pTBred). Patients aged 0-18 years with microbiologically culture or PCR-confirmed *M.avium* and *M.lentiflavum* cervicofacial lymphadenitis were eligible. Epidemiological, clinical and treatment data were collected through Redcap software (http://www.project-redcap.org/).

Results

A total of 86 patients were included (45 *M.lentiflavum*, 41 *M.avium*), 47% vs 44% males ($p>0.05$). Children with *M. lentiflavum* lymphadenitis were younger (mean±SD age: 26.7±15 vs 37.6±18 months; $p=0.02$) and more often presented with preauricular nodes involvement (29% vs 12%; $p=0.06$).

No differences were observed in mean±SD time from onset of symptoms to diagnosis (4.9±3.9 vs 3.6±3.3 weeks), TST induration (6.5±5.4 vs 5.1±4.5 mm), bilateral involvement (7% vs 9%), recurrences (14% vs 4.4%), fistula formation (22% vs 13%), need of surgery (65% vs 75%) or antibiotic treatment duration in cases in which this was prescribed (12±11 vs 14±8 weeks) ($p>0.05$ in all cases).

Mycobacterial isolations showed geographical differences ($p=0.01$), *M.lentiflavum* being more frequently identified in Madrid than in other regions (88% vs 11%), whereas the prevalence of *M. avium* was similar (56% vs 44%).

Conclusions

- Compared to *M.avium*, children with *M.lentiflavum* cervicofacial lymphadenitis were younger and showed more often preauricular node involvement.

- Clinical course was similar for both species of mycobacteria.

- *M.lentiflavum* was more frequently identified in Madrid, suggesting endemicity in this region.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0247
E-POSTER DISCUSSION SESSION 8 - TB & MYCOBACTERIAL INFECTIONS / ANTIMICROBIAL USE (station 10)

IN UTERO EXPOSURE TO MYCOBACTERIUM TUBERCULOSIS: ISONIAZID PROPHYLAXIS IN AN EXTREMELY LOW-BIRTH-WEIGHT INFANT

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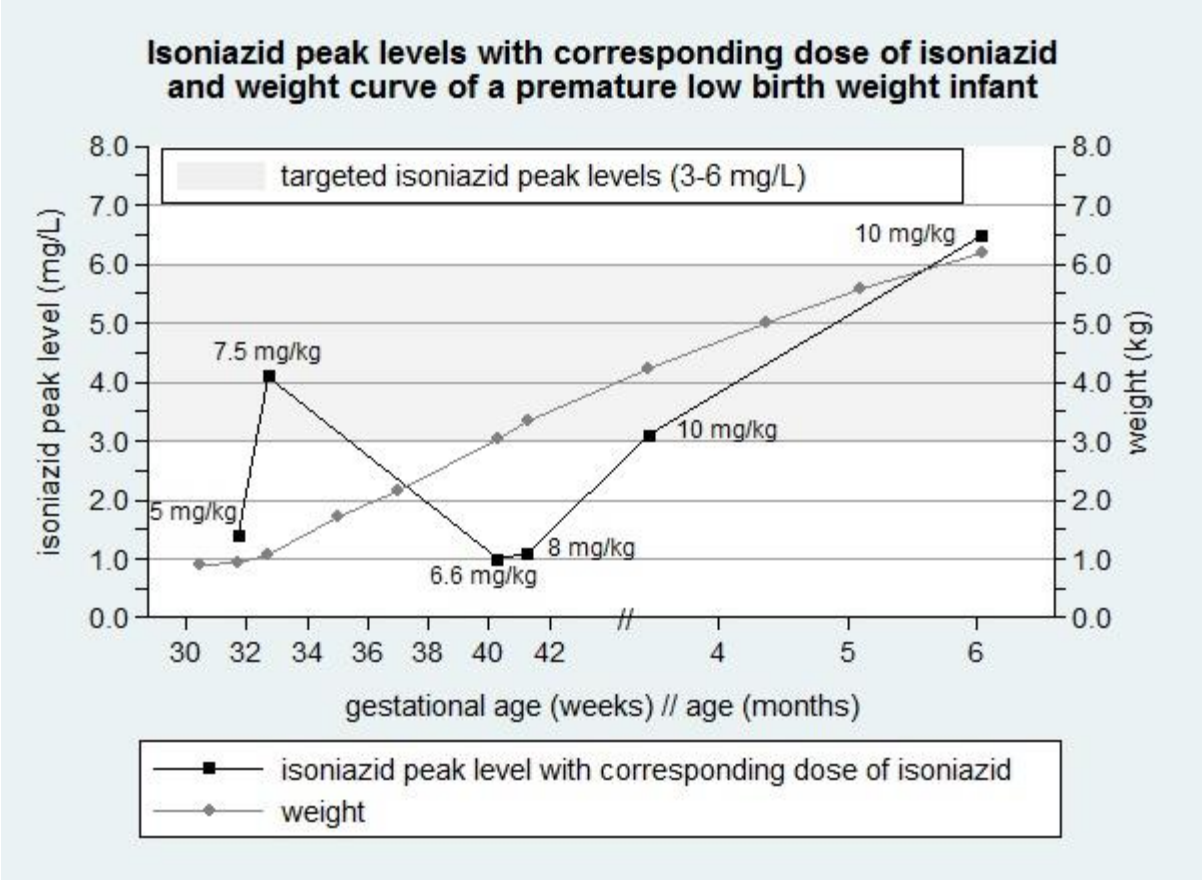
Title of Case(s)

***In utero* exposure to *Mycobacterium tuberculosis*: Isoniazid prophylaxis in an extremely low-birth-weight infant**

Background

Cases of *in utero* exposure to *Mycobacterium tuberculosis* are rare in Switzerland. Limited data are available on isoniazid dose (IZD) in preterm low birth-weight infants. Hereby we report our experience in dosing of isoniazid in this setting.

Case Presentation Summary



A female infant was born by caesarian section at 30 weeks of gestation with a birth-weight of 890g. The mother had been diagnosed with smear positive pulmonary tuberculosis 4 weeks earlier and the infant had intrauterine growth restriction. Evaluation showed no signs of congenital tuberculosis, in particular no fever, lymphadenopathy or hepatosplenomegaly. The infant had minor signs of respiratory distress and required nasal continuous positive airway pressure ventilation for one week. The maternal placenta and the infant's gastric aspirates were PCR and culture negative for *Mycobacterium tuberculosis.*
Oral preventive treatment with isoniazid (5mg/kg) and pyridoxine (1mg/kg) was started. The 2-hours isoniazid peak concentration (Cmax) was 1.4mg/L, and subsequently the isoniazid dose was increased to 7.5mg/kg, resulting in a Cmax of 4.1mg/L. At the age of 40 weeks of gestation the isoniazid dose was 6.6mg/kg resulting in a Cmax of 1.0mg/L. A further increase of the isoniazid dose to 10mg/kg resulted in a Cmax of 3.1mg/L. At the age of six months Cmax was 6.5mg/L, tuberculin skin test and the interferon-γ release assay were negative and isoniazid treatment was discontinued.

Learning Points/Discussion

Both isoniazid dose and postnatal age influenced Cmax. Our case suggests that isoniazid doses above 5mg/kg are needed to achieve therapeutic drug concentrations of 3 to 6mg/L. This is in accordance to dose recommendations for infants and children. Determination of isoniazid Cmax is useful for optimal dosing in preterm low-birth-weight infants.

ESP16-0196
E-POSTER DISCUSSION SESSION 8 - TB & MYCOBACTERIAL INFECTIONS / ANTIMICROBIAL USE (station 10)

CHARACTERISTICS AND OUTCOMES OF PAEDIATRIC OUTPATIENT PARENTERAL ANTIMICROBIAL THERAPY IN A TERTIARY ACADEMIC HOSPITAL

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Background

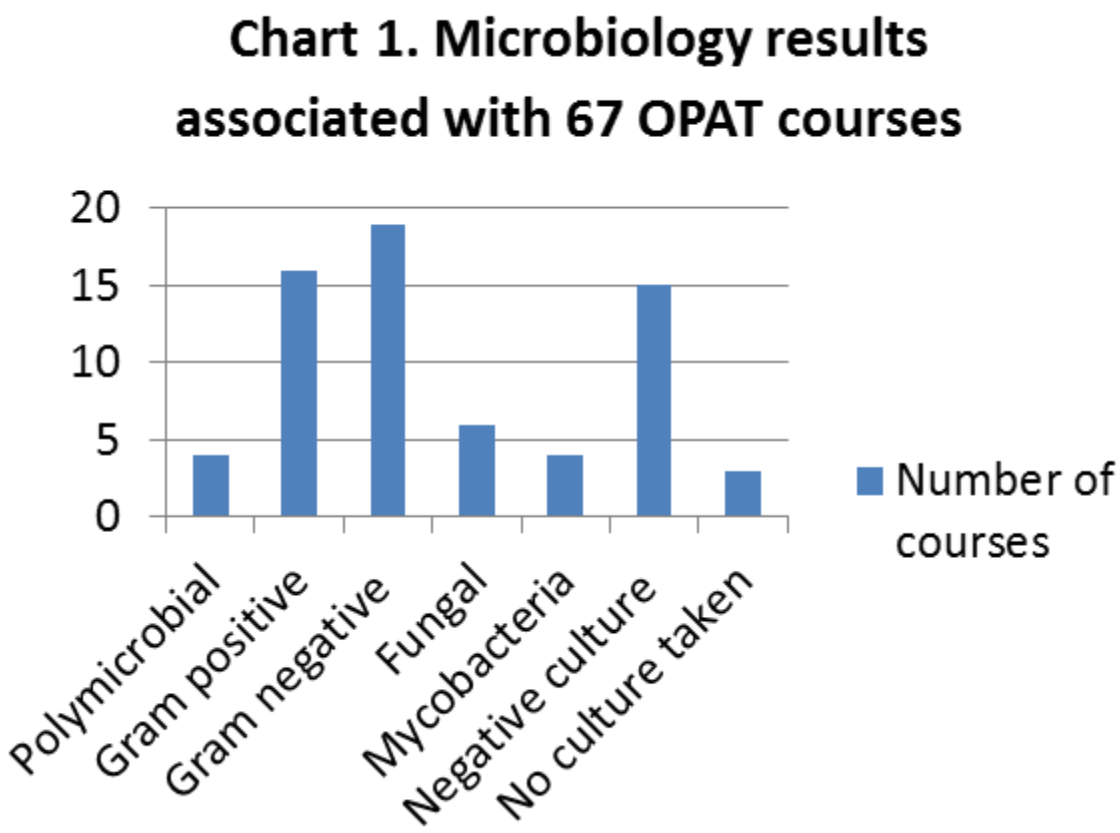
Paediatric outpatient parenteral antimicrobial therapy (p-OPAT) has numerous benefits, but is time consuming, requiring education, close monitoring and communication with the child and family. There is little data on the unique challenges and outcomes of p-OPAT. Our hospital p-OPAT service was implemented in 2013.

Methods

We conducted a prospective observational study of all patients who received p-OPAT in National University Hospital, Singapore, between 1 May 2013 to 31 December 2015. The p-OPAT patient database systematically records details of episodes from initiation to cessation, including indications, antimicrobial management, and outcomes. Data was analysed to evaluate the characteristics and outcomes of OPAT courses administered.

Results

60 children (34 male, 26 female) received 67 OPAT courses (total 1407 OPAT days). Median age was 9.8 years (range 7 days to 30.6 years). Mean duration of therapy was 21.0 days (range 2-177 days). 6 OPAT courses were not completed. OPAT was used most commonly to treat bone and joint infections (26%) and bloodstream infections (23%). 49 OPAT courses (73.1%) had positive culture results (Chart 1). The most frequently used antibiotics were ceftriaxone (31.4%) and ceftazidime (11.4%). Most frequent antifungal used was fluconazole (57.1%). 43 courses (64.2%) were administered via peripherally inserted central catheter. 21 courses (31.3%) resulted in 25 complications; readmissions for fever (5) and catheter (17) or antimicrobial (3) associated adverse effects. Infection outcomes were 63 cures (94%), 3 treatment failures and 1 lost to follow up. 43 courses (64.2%) achieved complete success with cure, no complications or readmissions.



Conclusions

One third of p-OPAT courses resulted in complications, comparable with previously published rates. A favourable infection cure rate of 94.0% was achieved. Patient and family satisfaction should be surveyed to ensure acceptability of the p-OPAT service.

ESP16-0583
E-POSTER DISCUSSION SESSION 8 - TB & MYCOBACTERIAL INFECTIONS / ANTIMICROBIAL USE (station 10)

SAFETY OF SYSTEMIC GENTAMICIN TREATMENT IN NEONATAL SEPSIS

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Background

Gentamicin is used empirically in neonatal sepsis. In neonatal intensive care units gentamicin use is guided by protocols because of its narrow therapeutic window and the potential risk of oto- and nephrotoxicity. We aimed to determine if the current gentamicin prescribing practices on the Neonatal and Paediatric Intensive Care Unit (NPICU) at Mater Dei Hospital, Malta result in safe trough levels.

Methods

All neonates on gentamicin were recruited in the study carried out on NPICU from 2013-2015. Gentamicin at 5mg/kg was administered every 24 or 36 hours in neonates </≥32 weeks gestation, respectively with trough levels being taken prior the third dose. Participants were stratified according to birth weight as follows: <1.5kg, 1.5-<3kg and ≥3kg. A gentamicin concentration of ≥2mg/l was taken as indicative of potential toxicity. Group differences were analysed using a z-test.

Results

A total of 115 neonates were recruited, with 119 trough gentamicin levels taken before the 3rd dose. 90% (107/119) had trough levels <2mg/l). Of the 41 babies with a birth weight ≥3kg (mean gestation 38.7 weeks), 38 (93%; 95% Confidence Intervals [CI]: 85-100%) had gentamicin trough levels <2mg/l. Safe levels were recorded in 53/61 (87%; 95%CI: 82-98%) of neonates weighing 1.5-<3kg (mean gestation 35.9 weeks). In comparison 13/17 (76%; 95%CI: 56-96%) of neonates weighing ≤1.5kg had gentamicin levels below the threshold of toxicity. Differences in the proportion of neonates with gentamicin levels <2mg/l were not significant between the groups.

Conclusions

The current gentamicin prescription practices in neonatal sepsis result in safe gentamicin trough levels. The trend towards high gentamicin trough levels in neonates weighing ≤1.5kg suggests the need for more frequent monitoring of trough gentamicin levels in this group.

ESP16-0080
E-POSTER DISCUSSION SESSION 8 - TB & MYCOBACTERIAL INFECTIONS / ANTIMICROBIAL USE (station 10)

A RANDOMIZED CONTROLLED TRIAL ON THE EFFECTIVENESS OF ORAL ZINC SUPPLEMENTATION IN AUGMENTING TUBERCULIN SKIN TEST RESPONSE AMONG MALNOURISHED CHILDREN WITH PULMONARY TUBERCULOSIS INFECTION

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Background

Tuberculin skin test is central in diagnosing Tuberculosis, especially in malnourished children who are prone to false-negative skin test results. Zinc supplementation plays a role in the generation and functioning of the immune system and correct false negative tuberculin skin test reactions by correcting Zinc deficiency, commonly seen in malnourished children with Tuberculosis.

Methods

It is community-based, double blind, placebo-controlled, randomized study. Fifty malnourished children aged 2-7 years old with BMI of z-score below -2 were included. Participants were randomly divided by into two groups. One group was given 5 ml oral glucose water, once a day, for two weeks. The other group was given Zinc syrup (20 mg elemental zinc sulfate) 5 ml, once a day, for two weeks. After two weeks, the investigator injected Tuberculin (5TU in 0.1 ml) on the proximal volar surface of the forearm of each participant. A health worker read the tuberculin skin test result in a blinded manner, 48-72 hours after administration. A 5 mm induration was considered positive.

Results

Out of the 50 participants, 47 patients came back for Tuberculin skin test reading. Twenty-one (45%) had positive tuberculin skin test response, 15 (65.2%) patients belonging to Zinc group and 6 (25%) belonging to placebo group. In terms of induration size, those belonging to Zinc group had more significant induration (7± 5.9mm) as compared to those in the placebo group (2.2±4.2). Based on Mantel Haenzel test, there is significant difference in the outcome response between the Zinc and placebo group with p value set at < 0.05.

Conclusions

Oral Zinc supplementation enhances the tuberculin skin test response as seen by higher positive responders and bigger mean induration size as compared to placebo.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0300
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

IMMUNE MEMORY AGAINST HEPATITIS B PERSISTS IN ADOLESCENTS PREVIOUSLY VACCINATED WITH 4 DOSES OF HEXAVALENT DTPA-HBV-IPV/HIB VACCINE IN ROUTINE CLINICAL PRACTICE

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Background

Hepatitis B virus (HBV) vaccination strategies predominantly focus on infants and children. As HBV exposure can increase during adolescence, it is important that protection, in terms of antibody persistence and ability to mount an anamnestic response, is maintained. We evaluated long-term HBV immune memory in adolescents, primed and boosted with DTPa-HBV-IPV/Hib vaccine (*Infanrix hexa*™; GSK Vaccines).

Methods

Open phase IV study at 12 centres in Germany [NCT02052661]. Adolescents aged 12-13 years, vaccinated with 4 DTPa-HBV-IPV/Hib doses in the first two years of life, received a single challenge dose of monovalent paediatric HBV vaccine (*Engerix*™-B Kinder; GSK Vaccines). Anti-HBs antibodies were measured pre- and 1-month post-vaccination using a ChemiLuminescence ImmunoAssay (seroprotective concentration ≥10mIU/ml). Post-challenge adverse events (AE) were monitored.

Results

300 subjects (mean age: 12.3 years) were vaccinated. Of 293 subjects in the ATP immunogenicity cohort, 60.5% had pre-challenge anti-HBs antibodies ≥10mIU/ml. 1-month post-challenge, 97.6% had anti-HBs antibodies ≥10mIU/ml (≥100mIU/ml in 94.1%). Anti-HBs antibody geometric mean concentrations rose 150-fold from 22.4 to 3502.6mIU/ml. 87 subjects had undetectable pre-challenge anti-HBs antibodies; of which 80 (92.0%) responded to the challenge dose. Overall anamnestic responses were seen in 96.5% subjects.

Pain (44%) and fatigue (24.3%) were the most frequent solicited local and general AEs, respectively. During 31-days post-vaccination, 14.7% subjects recorded ≥1 unsolicited AE; 2 subjects reported vaccine-unrelated serious AEs.

Conclusions

As previously observed in monovalent HBV vaccine-primed adolescents,[1] primary and booster vaccination with DTPa-HBV-IPV/Hib in routine clinical practice induces long-term seroprotection against HBV and immune memory as demonstrated by the strong response to HBV challenge in 12-13 year-old adolescents.

[1]Behre U, et al Hum Vaccin Immunother 2012;8:813-8.

Clinical Trial Registration (Please input N/A if not registered)

NCT02052661

ESP16-0361
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

CONCOMITANT ADMINISTRATION OF A FULLY LIQUID, READY-TO-USE HEXAVALENT VACCINE DTaP-IPV-HB-Hib WITH A MENINGOCOCCAL ACWY VACCINE IN TODDLERS

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Background

To study the immune response to all antigens included in this hexavalent vaccine when co-administered with MenACWY vaccine.

Methods

Phase III, open-label, randomized, multi-centre study (HXM01C) in Finland. At 12 months of age, 312 infants previously primed at 2-3-4 months with hexavalent vaccine (Hexyon/Hexaxim/Hexacima) with or without MenC vaccine (NeisVac-C) (used as strata) were randomized as follows: 104 infants had hexavalent co-administered with MenACWY vaccine (Nimenrix), 105 had only hexavalent vaccine and 103 had only MenACWY vaccine. Antibody response were descriptively assessed at 13 months of age for all hexavalent and MenACWY antigens. Persistence to all hexavalent antigens was described at 12 months. Safety profile was described.

Results

Summary of Post-Booster Response Rate to All Hexavalent Vaccine Antigens (Per Protocol Set)	Hexavalent + MenACWY N=87	Hexavalent only N=91
Anti-D (% ≥0.1 IU/mL) [95% CI]	100% [95.8;100.0]	100% [96.0;100.0]
Anti-T (% ≥0.1 IU/mL) [95% CI]	100% [95.8;100.0]	100% [96.0;100.0]
Anti-PT (% Vaccine response §) [95% CI]	98.8% [93.6;100.0]	98.8% [93.7;100.0]
Anti-FHA (% Vaccine response §) [95% CI]	100% [95.8;100.0]	100% [95.9;100.0]
Anti-HBs (%≥10 mIU/mL) [95% CI]	98.9% [93.8;100.0]	98.9% [94.0;100.0]
Anti-IPV1 (% ≥8 (1/dil)) [95% CI]	98.9% [93.8;100.0]	98.9% [94.0;100.0]
Anti-IPV2 (% ≥8 (1/dil)) [95% CI]	100% [95.8;100.0]	100% [96.0;100.0]
Anti-IPV3 (% ≥8 (1/dil)) [95% CI]	100% [95.8;100.0]	100% [96.0;100.0]
Anti-PRP (% ≥1.0 µg/mL) [95% CI]	97.7% [91.9;99.7]	100% [96.0;100.0]
§ Vaccine response: If pre-vaccination (pre-dose 1) antibody concentration <8 EU/mL, then the post-vaccination antibody concentration should be ≥8 EU/mL. Otherwise, post-vaccination antibody concentration should be ≥ pre-immunisation level (pre-dose 1)		

Summary of Post-Vaccination Rate for All the Men ACWY Vaccine Antigens (Per Protocol Set)	Hexavalent + MenACWY N=87	MenACWY only N=94
Anti-MenA (% ≥8 (1/dil)) [95% CI]	100% [95.8;100.0]	100% [96.2;100.0]
Anti-MenC (% ≥8 (1/dil)) [95% CI]	98.9% [93.8;100.0]	95.7% [89.5;98.8]
Anti-MenW (% ≥8 (1/dil)) [95% CI]	100% [95.8;100.0]	98.9% [94.2;100.0]
Anti-MenY (% ≥8 (1/dil)) [95% CI]	100% [95.8;100.0]	100% [96.2;100.0]

At 12 months of age, no notable differences in terms of antibody persistence for any hexavalent vaccine antigen whether MenC vaccine was co-administered or not during primary series, except for tetanus.

Safety profile of the hexavalent vaccine was generally comparable whether co-administered or not with MenACWY vaccine. No related SAE reported.

Conclusions

Co-administration of hexavalent vaccine with MenACWY vaccine did not affect the immune response to either vaccine. Prior receipt of meningococcal serogroup C conjugate vaccine during infancy did not preclude the use of a MenACWY vaccine for booster vaccination. Adequate antibody levels at 12 months of age and robust post booster responses. All vaccines were well tolerated. Hexavalent safety profile consistent with established product profile. Study sponsored by Sanofi Pasteur MSD.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov identifier NCT01839175, EudraCT Number 2012-005547-24

ESP16-0453
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

IMPACT OF ROTAVIRUS SPECIFIC MATERNAL ANTIBODIES ON VACCINE TAKE TO RV3-BB NEONATAL ROTAVIRUS VACCINE IN NEW ZEALAND

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Background

Passively acquired maternal antibodies may contribute to the reduced oral rotavirus vaccine efficacy observed in developing countries. This study aimed to investigate the effect of rotavirus specific maternal antibodies on vaccine take of an oral neonatal rotavirus vaccine, RV3-BB, within a Phase IIa clinical trial conducted at Dunedin Hospital, New Zealand.

Methods

Rotavirus specific IgA levels in colostrum and breast milk samples collected ~4 weeks, ~20 weeks and ~28 weeks after birth and rotavirus specific IgG and SNA levels in cord blood were measured. Participants were randomised to receive the first dose of vaccine at 0–5 days after birth (neonatal schedule) and at 8 weeks (infant schedule). Breast feeding was with-held for 30 minutes before and after vaccine administration. The primary objective was to determine the relationship between rotavirus specific IgA in breast milk and vaccine take (serum immune response or stool shedding of vaccine virus after any dose) after three doses in the neonatal and infant schedule.

Results

42 (79%) of 53 infants received 3 doses of RV3-BB rotavirus vaccine. IgA responses were identified in 76% and 74% of infants in the neonatal and infant groups but there was no evidence of an association between colostral or breast milk IgA at birth or at 4 weeks and vaccine take after three doses of RV3-BB, or after one dose (neonatal schedule). There was no evidence of an association between cord IgG or SNA level and vaccine take.

Conclusions

The level of colostral or breast milk IgA and placental IgG and SNA did not affect vaccine take to three doses of RV3-BB Rotavirus Vaccine. The impact of maternal antibodies on the sub-optimal vaccine performance in regions with high rotavirus disease burden warrants further investigation.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0536
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

CYTOKINE PROFILE AFTER A TDAP BOOSTER SHOT IN HIV-INFECTED AND IN HEALTHY ADOLESCENTS

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Background

Pertussis cases have increased worldwide and knowledge on immune response and cytokine profile after adult Tdap vaccine is scarce. This study evaluated the cellular response through cytokine profile after Tdap in HIV-infected and in healthy adolescents.

Methods

After written informed consent, HIV-infected (HIV) and healthy adolescents (Control) who received three whole-cell DTP vaccine (DTwP) plus two booster doses and had CD4 cell counts>200 received a Tdap dose. Blood samples were collected immediately before and 28 days after vaccine. *In vitro* culture was performed with whole blood stimulated with tetanus toxoid, *Bordetella pertussis* or medium. Supernatants were collected after 7 days, kept frozen and subsequently assayed for cytokines secretion by xMAP-Luminex platform.

Results

HIV group median age was 19.3y and Control group, 15.1y; median CD4+ T cells were 694.2 and 1030.9, respectively (p=0.061). The cellular immune response was more intense on day 28 in the Control group when compared to HIV. For *pertussis,* cytokines (pg/mL) were: **IFN-gamma** (HIV, 161.0xControl, 1247.9; p=0.008**), IL-17A** (HIV, 1.9xControl, 16.3; p=0.045), **IL-21** (HIV 1.3xControl 8.1 p=0.002) **IL-4** (HIV, 0.1xControl, 1.4 p=0.002) **TNF-alpha** (HIV, 88.4xControl, 285.4; p=0.006). For tetanus, differences were observed for **IL-21** (HIV, 0.3xControl, 2.3; p=0.004), **IL-4** (HIV, 0.3xControl, 2.3; p=0.006), **IL-6** (HIV, 3116.0xControl, 3915.8; p=0.045), **TNF-alpha** (HIV, 510.7xControl, 3075.1; p=0.017). All pre- and post-Tdap cytokine levels were higher in the Control group, the only exception being **IL-6** on day 0 for *pertussis.*

Conclusions

Cellular immune response of HIV-infected adolescents to Tdap is less intense than Control group. Moreover, Control adolescents showed a more appropriate immune response to *B. pertussis* and tetanus: a better Th1 and Th17 response for the former and aTh2 response, for the latter; both antigens elicited high TNF-alpha responses.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0342
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

IMMUNOGENICITY/SAFETY OF DTaP-BACKBONED VACCINES IN A HEXAVALENT/PENTAVALENT/HEXAVALENT SEQUENTIAL SCHEDULE AT 2, 4, 6 MONTHS OF AGE IN EUROPEAN INFANTS

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Background

Assess immunogenicity and safety of a fully liquid, ready-to-use, hexavalent DTaP-IPV-HB-Hib vaccine (Hexaxim®/Hexacima®/Hexyon®) administered in a sequential schedule with Pentavalent DTaP-IPV/Hib (Pentavac®/Pentaxim®) in infants who received HepB at birth.

Methods

Phase III, open, multicenter study in Spain. Infants received DTaP-IPV-HB-Hib (N=265) at 2, 6 month, DTaP-IPV/Hib at 4 month, after HepB at birth; and 13-valent pneumococcal conjugate, rotavirus and meningococcal C vaccines as per local recommendations. Blood samples were collected pre-Dose 1, 1-month post-dose 3 and analyzed via validated serological assays. Immunogenicity was described for all antigens contained in the DTaP-backboned vaccines, and RotaTeq®. Safety was assessed via study site observation and parental monitoring/reporting of solicited/unsolicited adverse events.

Results

High immune responses were observed for the antigens contained in the DTaP-backboned vaccines.

Summary of seroprotection/seroconversion/vaccine response rates for study vaccines – Per-protocol analysis

		Hexa/Penta/Hexa (N=236)		
		n/M	**%**	**(95% CI)**
Anti-D (IU/mL)	**≥ 0.01 IU/mL**	211/211	100.0	(98.3; 100)
Anti-T (IU/mL)	**≥ 0.01 IU/mL**	205/205	100.0	(98.2; 100)
Anti-PT (EU/mL)	**Vaccine response***	183/184	99.5	(97.0; 100)
	Seroconversion †	165/184	89.7	(84.3; 93.7)
Anti-FHA (EU/mL)	**Vaccine response***	178/178	100.0	(97.9; 100)

	Seroconversion †	170/178	95.5	(91.3; 98.0)
Anti-Polio 1 (1/dil)	**≥ 8 (1/dil)**	196/196	100.0	(98.1; 100)
Anti-Polio 2 (1/dil)	**≥ 8 (1/dil)**	202/203	99.5	(97.3; 100)
Anti-Polio 3 (1/dil)	**≥ 8 (1/dil)**	205/205	100.0	(98.2; 100)
Anti-Hep B (mIU/mL)$	**≥ 10 mIU/mL**	223/225	99.1	(96.8; 99.9)
Anti-PRP (µg/mL)	**≥ 0.15 µg/mL**	226/226	100.0	(98.4; 100)

* Vaccine response: anti-PT or anti-FHA Ab concentrations (EU/mL) ≥ 4 x LLOQ if pre-vaccination concentration was <4 x LLOQ, or ≥ pre-vaccination concentration if pre-vaccination concentrations ≥ 4 x LLOQ
† Seroconversion (anti-PT, anti-FHA): anti-PT and anti-FHA ≥ 4-fold Ab concentrations increase from V01 (2 month) to V04 (7 month)
$ All subjects received hepatitisB vaccine at birth - Hexa/Penta/Hexa: DTaP-IPV-HB-Hib (2, 6 month); Pentavac (4 month)

One month after the 3-dose primary series, the anti-rotavirus GMC was 279 EU/mL and GMC ratio (V04/V01) was 66.6.

No safety concern was observed. No death or adverse event leading to study discontinuation was reported during the study.

Conclusions

DTaP-IPV-HB-Hib in a sequential schedule with DTaP-IPV/Hib elicits protective responses against 6 targeted diseases, with no safety concern.

Clinical Trial Registration (Please input N/A if not registered)

EudraCT#:2012-001055-39; UTN:U1111-1122-2329

ESP16-0724
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

RETROSPECTIVE MULTICENTER MATCHED CASE-CONTROL STUDY ON THE RISK FACTORS OF NARCOLEPSY IN GERMANY

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Background

Following the 2009 influenza A/H1N1/v pandemic and mass vaccination campaign an association between H1N1 vaccination and narcolepsy was confirmed in several epidemiological studies. In Germany, a retrospective multicenter matched case-control study was initiated to identify risk factors of narcolepsy and to quantify the detected risks.

Methods

Patients with excessive daytime sleepiness who had been referred to a sleep center between 1 April 2009 and 31 December 2012 for a multiple sleep latency test (MSLT) were eligible. Details regarding the sleep disorder were retrospectively recorded by the sleep centers. Information on medical history including vaccination status was obtained via standardized interviews with the patients. Case reports were validated by two experts for narcolepsy according to the criteria defined by the Brighton Collaboration blinded to the patients' vaccination status. Confirmed cases of narcolepsy were matched with population-based controls by year of birth, gender, and place of residence (first two digits of zip code).

Results

A total of 103 validated cases of narcolepsy (44 males, 59 females) were matched with 264 population-based controls (94 males, 170 females). Median age was 18.8 years (range: 6.0−55.1) in cases and 17.3 years (range: 5.3−55.2) in controls. At the date of referral to MSLT, 48 cases and 137 controls were under 18 years of age.

In individuals who had been immunized with pandemic influenza A/H1N1/v vaccine prior to symptoms onset, an significantly increased odds ratio (OR) of narcolepsy was detected when compared to non-vaccinated individuals [OR 3.9 (95% confidence interval: 1.8−8.5)] Besides H1N1 vaccination, no other risk factors were identified.

Conclusions

These findings support a significantly increased risk to develop narcolepsy following H1N1 vaccination.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0770
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

SAFETY AND IMMUNOGENICITY OF AN INACTIVATED QUADRIVALENT INFLUENZA VACCINE MANUFACTURED BY AN OPTIMIZED PROCESS: A 2014/2015, PHASE III, RANDOMIZED, DOUBLE-BLIND STUDY IN CHILDREN AND ADULTS

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Background

GSK Vaccines has investigated an optimized monovalent bulk manufacturing process for its inactivated quadrivalent subvirion influenza vaccine (IIV4, made in Dresden), to harmonise process conditions for different influenza strains and obtain a simplified and robust manufacturing process. This multi-center study assessed safety and immunogenicity of IIV4 manufactured by the investigational (IIV4-IP) vs the licensed process (IIV4-LP) in subjects aged 6 months (m) to 49 years (y).

Methods

Subjects were sequentially enrolled in 3 age cohorts (18-49y/3-17y/6-35m) and randomized 1:1 to receive IIV4-IP or IIV4-LP as 1 (9-49y and primed 6m-8y) or 2 doses (unprimed 6m-8y, 28 days apart). Main objectives: (1) demonstrate immunogenic non-inferiority of IIV4-IP vs IIV4-LP for each vaccine strain 28 days post-vaccination series (criterion: upper limit [UL] of 95% confidence interval [CI] of haemagglutination inhibition geometric mean titre ratio [IIV4-LP/IIV4-IP] ≤1.5) (6-35m/3-17y); (2) demonstrate the absence of significant increase in fever ≥38°C with IIV4-IP vs IIV4-LP recipients within the 7 days post-vaccination (criterion: 95%CI UL for relative risk of fever ≥38ºC [IIV4-IP/IIV4-LP] ≤2.0) (6-35m); (3) demonstrate an acceptable reactogenicity/safety profile (6-35m/3-17y/18-49y).

Results

Total vaccinated cohorts included 466/474 (6-35m), 410/411 (3-17y) and 60/60 (18-49y) IIV4-IP vs IIV4-LP recipients, respectively. IIV4-IP was shown to be immunogenically non-inferior to IIV4-LP for each vaccine strain in 6-35m and 3-17y (Table). Fever ≥38ºC (post-dose 1 or 2) occurred in 15.6% (IIV4-IP) vs 14.7% (IIV4-LP) 6-35m vaccinnees, with a relative risk of 1.06 (95%CI: 0.75, 1.50). Both IIV4s had similar, acceptable reactogenicity/safety profiles in all 3 cohorts.

Table. Immunogenic non-inferiority of IIV4-IP vs IIV4-LP (6-35m and 3-17y ATP immunogenicity cohorts)

Vaccine strain	6-35m			3-17y		
	GMT		GMT ratio* (95% CI)	GMT		GMT ratio* (95% CI)
	IIV4-IP (N=432)	IIV4-LP (N=427)		IIV4-IP (N=403)	IIV4-LP (N=402)	
Flu A/H1N1	98.0	105.3	1.07 (0.90; **1.28**)	707.3	684.9	0.97 (0.85; **1.11**)
Flu A/H3N2	47.7	56.3	1.18 (1.00; **1.39**)	160.6	168.8	1.05 (0.94; **1.18**)
Flu B/Yamagata	99.2	106.4	1.07 (0.91; **1.27**)	496.0	509.4	1.03 (0.91; **1.16**)
Flu B/Victoria	32.2	37.7	1.17 (0.99; **1.38**)	240.8	250.4	1.04 (0.90; **1.21**)

m, month-olds; y, year-olds; ATP, according-to-protocol; CI, confidence interval; GMT, geometric mean titre adjusted for baseline, 28 days post-vaccination series; N, number of subjects included in ATP immunogenicity cohorts; *IIV4-LP/IIV4-IP. Bolded values indicate upper limit of 95% CI of GMT ratio ≤1.5 (criterion for immunogenic non-inferiority of IIV4-IP vs IIV4-LP).

Conclusions

IIV4-IP was immunogenically non-inferior to IIV4-LP, without significant increase in fever. IIV4-IP had the same acceptable safety profile as IIV4-LP in children and adults. These results support IIV4 manufacture through the optimized process.

Funding: GlaxoSmithKline Biologicals SA

Clinical Trial Registration (Please input N/A if not registered)

NCT02207413

ESP16-0708
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) IN A CHILD AFTER MEASLES-MUMPS-RUBELLA-VARICELLA (MMRV) VACCINATION

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Title of Case(s)

Acute respiratory distress syndrome (ARDS) in a child after measles-mumps-rubella-varicella (MMRV) vaccination

Background

Measles infection is associated with significant morbidity and mortality in childhood. Implemented vaccination strategies coupled with sustained vaccination coverage reduce risk of infection. Pneumonitis and ARDS due to vaccine measles strain after MMRV has never been reported before.

Case Presentation Summary

A 22-month-old full-term male (no history of previous hospitalisations/severe infections) was admitted in our Hospital due to 3-day fever up to 40^{o}C and generalized erythematous popular eruption. Vaccination with MMRV 9 days earlier was reported. Upon admission (day 1, D1), he was at good clinical condition, with rhinitis, pharyngitis and conjunctivitis. At D5, the patient presented with progressive respiratory distress and was transferred to the ICU. He was feblile, on stridor with intercostal retractions and swollen tonsils. Repeated chest X-rays revealed pneumonia of the middle and lower right lobe and progressive ARDS. Due to severe hypoxia/hypercapnia the patient was intubated. He was treated with intravenous meropenem-vancomycin and inhaled bronchodilators. Due to clinical deterioration he further received IVIG and acyclovir and was supported with human albumin, FFP and RBC infusions. The child was clinically improved at D22.

Measles vaccine strain was isolated in throat swabs, bronchial excretions and urine (real-time-PCR). Serology tests were positive for IgM and IgG measles antibodies. BAL tests were negative for pneumonocystis carinii, EBV and CMV. Blood cultures were negative. Immunoglobulin profile and cellular immunity will be evaluated (3 months after infection) and presented to confirm clinical perception of an immunocompetent child.**Learning Points/Discussion**

Pneumonitis and ARDS due to a vaccine measles strain after MMRV has never been demonstrated before. This case illustrates the necessity of ongoing surveillance after MMRV vaccination.

ESP16-0456
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

IMMUNOGENICITY OF A BOOSTER DOSE OF THE DTPw-HBV/Hib VACCINE AND SECOND DOSE OF MEASLES VACCINE CO-ADMINISTERED IN HIV-INFECTED, HIV-EXPOSED-UNINFECTED AND HIV-UNEXPOSED-UNINFECTED TODDLERS IN SOUTH AFRICA

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Background

Previously we assessed the effect of HIV status on the immunogenicity of the 10-valent pneumococcal conjugate vaccine, PHiD-CV (GSK Vaccines), and showed that a 3-dose primary series (6, 10, 14 weeks of age [w]) of DTPw-HBV/Hib vaccine (GSK Vaccines) and a first dose of measles vaccine (Sanofi Pasteur) given at 9 months of age (m) were immunogenic in HIV-infected (HIV+), HIV-exposed-uninfected (HEU) and HIV-unexposed-uninfected (HUU) children. In the same study we assessed the immune responses to a DTPw-HBV/Hib booster dose and a second measles vaccine dose.

Methods

In this phase III, open-label, single-centre, controlled trial in South Africa, HIV+, HEU and HUU infants received 3 or 4 doses of PHiD-CV (6w, [10w,] 14w and 9-10m) co-administered with DTPw-HBV/Hib (6w, 10w, 14w) and measles vaccine (9-10m). At 15-18m they received a booster dose of DTPw-HBV/Hib co-administered with a second dose of measles vaccine. Immune responses to the DTPw-HBV/Hib and measles vaccines were measured by ELISA (DTPw, Hib, measles) or a chemiluminescence immunoassay (HBV). HIV+ infants received triple antiretroviral therapy (ART) per national guidelines (start ART in all HIV+ infants <12m upon HIV confirmation).

Results

The total vaccinated cohort comprised 484 children.
Seroprotection/seropositivity/seroconversion rates for antibodies against DTPw-HBV/Hib and measles antigens were 97.3%-100.0% (except HB: 91.4% [HIV+]; 93.6% [HEU]). Antibody

geometric mean concentrations (GMCs) for DTPw-HBV/Hib and measles were similar among study groups, except those for *Bordetella pertussis* and Hib PRP, which tended to be lower in HIV+ children (Table).

Table. Geometric mean concentrations (with 95% CIs) for antibodies against DTPw-HBV/Hib antigens (ATP cohort for immunogenicity at 15-18m*) and measles antigens (ATP cohort for immunogenicity) 1 month after vaccination**

Antigen	HIV+	HEU	HUU
DTPw-HBV/Hib vaccine	N=59	N=81	N=270
Diphtheria toxoid (IU/mL)	9.6 (7.9; 11.6)	11.7 (10.3; 13.3)	11.6 (10.7; 12.6)
Tetanus toxoid (IU/mL)	14.4 (12.2; 17.1)	14.6 (12.6; 17.0)	17.8 (16.6; 19.1)
***Bordetella pertussis* (EL.U/mL)**	161.0 (131.9; 196.6)	227.0 (202.9; 254.0)	256.2 (242.0; 271.1)
HBs (mIU/mL)	1871.0 (892.9; 3920.7)	2507.4 (1500.7; 4189.4)	3822.5 (2966.0; 4926.3)
Hib PRP (µg/mL)	50.1 (33.3; 75.4)	71.2 (55.0; 92.2)	100.6 (86.7; 116.7)
Measles vaccine	N#=55	N#=75	N#=252
Measles (mIU/mL)	3268.3 (2435.5; 4385.9)	4140.9 (3345.2; 5125.9)	3447.9 (3063.0; 3881.1)

ATP, according-to-protocol; CI, confidence interval; m, months of age; HIV+, HIV-infected children; HEU, HIV-exposed-uninfected children; HUU, HIV-unexposed-uninfected children; N, maximum number of children with available results; N#, number of subjects who received 2 doses of measles vaccines, with results available for pre-vaccination and 1 month post-vaccination timepoints; HBs, hepatitis B surface antigen; Hib PRP, *Haemophilus influenzae* type b polyribosyl-ribitol phosphate.

*Included all evaluable children (complying with protocol-defined procedures and intervals between vaccine doses/blood samples, including between DTPw-HBV/Hib booster and post-booster blood sample) with DTPw-HBV/Hib immunogenicity results available.
**Included all evaluable children (complying with protocol-defined procedures and intervals between PHiD-CV doses/blood samples) with immunogenicity results available.

Conclusions

A DTPw-HBV/Hib booster dose and a second dose of measles vaccine co-administered in HIV+ children were immunogenic, eliciting similar seroprotection/seropositivity/seroconversion rates. A trend for lower antibody GMCs for *Bordetella pertussis* and Hib PRP compared to HUU children was observed.

Funding: GlaxoSmithKline Biologicals SA

Clinical Trial Registration (Please input N/A if not registered)

NCT00829010

ESP16-0186
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

CD4/CD8 RATIO AS A PREDICTOR OF VACCINE RESPONSE IN HIV INFECTED CHILDREN

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Background

Vaccine immunogenicity has been shown to be hampered in HIV-infected children. Chronic immune activation, which correlates with the CD4/CD8 ratio, may potentially impair cellular and humoral responses to vaccines. To date, no clinical biomarkers have been validated as immunologic predictors of vaccine response during childhood in HIV infection

Methods

The role of CD4/CD8 ratio as a predictor of response was specifically addressed using retrospective data from the Spanish Cohort of HIV-infected children (CoRISpeS). Children with available data on immunization records and response to vaccines were included. Clinical and immunovirological variables were analyzed in relation to the specific serologic response obtained after completing the immunization schedule.

Results

A total of 125 children (mean age 12.7 years [9.3-17], 62% female, 93.5% on ART) meet the inclusion criteria. At baseline, 62.6% had completed the immunization schedule and were included in the analysis (incomplete immunization 23.4%, unknown 13%). Mean CD4/CD8 ratio was 1.03 [0.68-1.4], and 52% had a CD4/CD8 ratio >1. Patients with no protective antibody titers against measles, rubella, tetanus and diphteria showed lower CD4/CD8 ratio compared with their counterparts (all $p<0.05$). This association remained significant after adjustment by age, sex and CD4 counts. No association was found between the CD4/CD8 ratio (nor the CD4 counts or CD4 nadir) and the response to HVB or HVA vaccine, polio or whooping cought vaccines. However, suppressed patients showed more frequently protective titers against HVB ($p= 0.015$)

Conclusions

If further confirmed, the CD4/CD8 ratio might be a useful marker to predict the immune response to immunizations among pediatric HIV-infected populations. Its association to vaccine response was shown to be independent of age, and superior compared to the prognostic value of the CD4, CD8, CD4 nadir or virological situation.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0091
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

EARLY IMPACT OF UNIVERSAL SINGLE DOSE VARICELLA VACCINE ON HOSPITALIZATION IN TURKEY (VARICOMP STUDY 2008-2015)

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Background

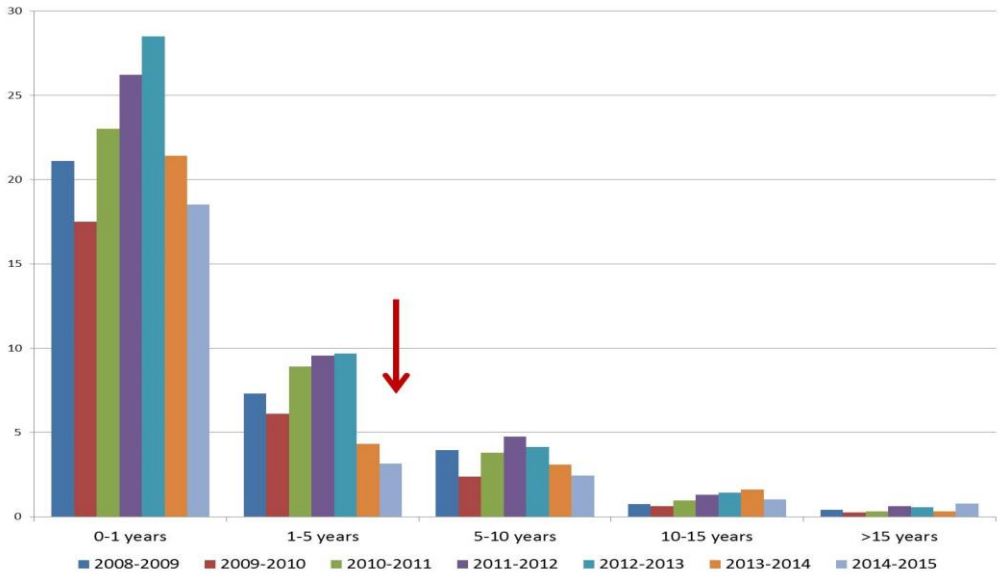
VARICOMP is an ongoing study, which aims to evaluate pediatric varicella-related hospitalization in Turkey since October 2008. Single dose varicella vaccine at 12 month of age was introduced to the National Immunization Program in February 2013 and varicella vaccination coverage is 95% in children 12 to 36 months of age. The aim of this study was to evaluate early impact (2.5 years) of universal varicella vaccination on the incidence of varicella related hospitalization.

Methods

Medical records of children requiring hospitalization due to varicella from 30 health care centers in 14 cities (representing 50% of the childhood population in Turkey) have been evaluated from October 2008- October 2015 and performed comparsion between the prevaccine era (October 2008-February 2013) and post-vaccine era (February 2013 and October 2015).

Results

3266 children (72% previously healthy) were hospitalized for varicella over the 7-year period. The incidence of varicella related hospitalization among children aged between 1-5 years was significantly lower (4.3 and 3.1 per 100.000 children) at 2013-2014 and 2014-2015 (post vaccine era) comparing the previous 5 years (varies 6.1 to 9.7 per 100.000 children). Incidence of varicella related hospitalization was similar among other age groups including; below 1 years, 5-10 years, 10-15 years and >15 years between pre- and post-vaccine era (Figure).



Conclusions

The incidence of varicella related hospitalization in children 1-5 years old declined after the routine use of single dose varicella vaccine in Turkey. After 2.5 years of routine single dose immunization, we did not observe herd protection for other age groups. Our routine hospital based surveillance until 2018, could help us to evaluate the potential effect of single dose vaccine or requiring booster dose of varicella vaccine at pre-school children.

Clinical Trial Registration (Please input N/A if not registered)

NCT01887496

ESP16-0466
E-POSTER DISCUSSION SESSION 9 - VACCINES 2 (station 2)

THE EFFECTIVENESS AND SAFETY OF ROTAVIRUS VACCINATION AFTER INTRODUCTION IN THE NATIONAL SCHEDULE IN FIJI

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Background

In 2006-7 rotavirus (RV) caused almost 40% of hospitalized non-bloody diarrhoea in children under 5 years in Suva, Fiji. In October 2012 RV vaccination was introduced into the national schedule, given in two doses at 6 and 14 weeks of age. This study reports RV surveillance, using WHO RV surveillance protocols, in two clinical settings that was undertaken to investigate RV vaccine's effectiveness in Fiji.

Methods

Children, under 5 years, were enrolled when they presented with non-bloody diarrhoea as inpatients of the tertiary hospital (Colonial War Memorial Hospital, Suva), and as both inpatients and outpatients at a secondary hospital (Savusavu Health Centre). Stools were tested for RV antigen and RV positive samples had viral genotype determined by PCR. National intussusception surveillance was established in January 2013.

Results

Among Suva inpatients the RV positivity rate fell from 38% to 14%, (pre- versus post-vaccine introduction) yielding an incidence rate ratio of 0.40 (95%CI: 0.31-0.51, p<0.001). In Savusavu RV positivity fell from 16% to 0% among outpatients and from 5% to 1% among inpatients following vaccine introduction. Intussusception occurred in 25 vaccine eligible children between January 2013 and November 2015. Among the eleven of known vaccination status, intussusception occurred a median of 104 days (IQR 90-127 days) following the first dose of RV vaccine and none occurred within 21 days.

Conclusions

Fiji is the first low- or middle-income country in the Asia-Pacific region with evidence of RV vaccine effectiveness. Ongoing surveillance may reveal a greater impact as a larger proportion of under 5 year olds become vaccinated. Among the eleven cases of intussusception where the vaccine history was known, none were temporally associated with RV vaccination.

ESP16-0625
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

ANTIBIOTIC USE IN CHILDREN – A CROSS-NATIONAL ANALYSIS OF 6 COUNTRIES

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Background

Antibiotic overuse is a major public health problem. Despite global recognition of potential adverse results associated with overuse of antibiotics, limited pediatric data suggest that marked variability in the use of these medications across countries persist. We aimed to describe the rates of pediatric antibiotic use across three continents.

Methods

Cross-national analysis of 7 pediatric cohorts in 6 countries (Germany, Italy, Korea, Norway, Spain and the US) was performed for the years 2008-2012. Antibiotic Dispensings were identified and grouped into subclasses. We calculated the rates of antimicrobial prescriptions per person-year specific to each age group, comparing the rates across different countries.

Results

A total of 74,744,302 person-years from all participating centers were included in the analysis. Infants in South Korea had the highest rate of antimicrobial consumption, with 3.41 prescribed courses per child-year during the first two years of life. This compares with 1.6 in Lazio, Italy, 1.4 in Pedianet, Italy, 1.5 in Spain, 1.1 in the U.S., 1.0 in Germany, and 0.5 courses per child-year in Norway. 64.8% of antimicrobial prescriptions in Norway were for first-line penicillins, compared to 38.2% in Germany, 31.8% in the US, 27.7% in Spain, 25.1% in the Italian Pedianet population but only 9.8% of prescriptions in South Korea and 8% in the Italian Lazio population.

Conclusions

We found substantial differences of up to 7.5-fold in pediatric antimicrobial use across several industrialized countries from Europe, Asia and North America. These data reinforce the need to develop strategies to decrease the unnecessary use of antimicrobials.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0133
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

IL-28B AS A PRE-TREATMENT PREDICTOR OF THERAPY EFFECTIVENESS IN CHILDREN WITH CHRONIC HEPATITIS C.

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Background

Hepatitis C in children is mostly mild or asymptomatic but can lead to liver cirrhosis and hepatocellular carcinoma. Therapy consists of pegylated interferon and ribavirin. Early Viral Response (ERV) isassociated with therapy effectiveness and is defined as an undetectable HCV RNA (cERV) or a greater than $2\log_{10}$ decline in HCV RNA (pERV) at week 12 of treatment. Polymorphism of IL28B (rs12979860) is thought to be a realiable pre-treatment predictor of virologic response, particularly in adults infected with genotype 1HCV. The importance of this factor in children remains unknown. The aim of the study was to assess the relationship between the polymorphism of IL28B and ERV in HCV infected children treated with PEG-INF+RIBA.

Methods

The study included 12 children chronically infected with HCV (10 vertically infected) aged 6,5-17,3 years. Genotype (GT) 1HCV was present in 9 (75%), GT 4HCV in 2 (16.6%), GT 3HCV in 1 (8.4%). Polymorphism of IL-28B was as follows: CC, CT, TT.

Results

Polymorphism CC was detected in 9/12 (75%), CT in 2/12 (16.7%), TT in 1/12 (8.3%). High baseline viral load (>600000IU/ml) was revealed in 10/12 (83%) children. cERV was present in 7/12 (58.4%) - among them 100% were CC, pERV was attained in 3 (25%): 2 with CC, 1-CT, decline of HCV RNA $<2\log_{10}$ was in 2 (16.6%): CT and TT.

Conclusions

Theundetectable HCV RNA at week 12 of treatment was observed only in children with favourable IL28B: CC.

Clinical Trial Registration (Please input N/A if not registered)

n/a

ESP16-0387
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

SUCCESSFUL IMPLEMENTATION OF PAEDIATRIC OUTPATIENT PARENTERAL ANTIMICROBIAL THERAPY (P-OPAT) SERVICE AT BRISTOL CHILDREN'S HOSPITAL, UK: OUTCOME ANALYSIS AND OPPORTUNITIES FOR ANTIMICROBIAL STEWARDSHIP

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Background

Use of outpatient parenteral antimicrobial therapy (OPAT) in paediatrics is increasing but data evaluating characteristics and outcomes of p-OPAT is lacking. Also, there is a paucity of data on stability of antimicrobials/antivirals administered over 24 hours via elastomeric devices.

We undertook an audit: to describe the quality outcomes of our p-OPAT programme.

Methods

A p-OPAT service was introduced at Bristol Children's Hospital in November 2014. Data on patient demographics, diagnoses, microbiology, antimicrobial therapy, duration, outcome, and complications were sourced from a prospectively collected database and from patient medical records. Standardized BSAC definitions were used to collect p-OPAT and patient infection outcomes.

Results

There were 101 patients over 13 months (November 2014 - December 2015) resulting in 1320 bed-days saved and estimated £328,000 cost-saving. Most common indications were sepsis (28%), osteoarticular (26%), central nervous system (10%), respiratory (8%) and urinary tract (8%) infections. The commonest microorganisms isolated were *S.aureus (9%), E.coli (9%),* group A *streptococcus (6%) and meningococcus (5%)*. The most frequently used antibiotics were ceftriaxone (87%), piperacillin-tazobactam (2.6%), teicoplanin (2.6%) and flucloxacillin (1.7%). Stability data showed flucloxacillin, piperacillin-tazobactam, temocillin, acyclovir, vancomycin and meropenem to be stable in elastomeric devices, but not ceftazidime.

Conclusions

All patients attended for weekly review and laboratory monitoring. During this period, there were no re-admissions and rate of line-associated complications was extremely low (3%). Two patients experienced antibiotic-associated adverse events. All patients completed OPAT therapy. There were no treatment failures and 22% of the patients improved. Overall p-OPAT cure rate was 78%. Our experience demonstrates that p-OPAT can deliver safe, cost-effective, and high-quality care when managing children on parenteral antibiotics at home.

ESP16-0901
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

EVOLUTION OF ACUTE INFECTION BY MYCOPLASMA PNEUMONIAE, CHLAMYDIA PNEUMONIAE OR CHLAMYDIA TRACHOMATIS AMONG CHILDREN WITH NON-SEVERE COMMUNITY-ACQUIRED PNEUMONIA TREATED WITH AMOXICILLIN

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Background

Atypical bacteria are treatable causative agents of childhood community-acquired pneumonia(CAP). However, there is no conclusive evidence that a child with CAP should receive empirical antibiotic to treat those agents. We assessed if there is an association between clinical failure and acute infection by these bacteria.

Methods

Patients aged 2-59 months with non-severe CAP (respiratory findings plus radiographic pulmonary infiltrate/consolidation) received amoxicillin and were prospectively followed-up. Acute and convalescent blood samples were collected. Acute infection by *M. pneumoniae* (specific IgM antibodies), by *C. pneumoniae* or *C. trachomatis* (specific IgM antibodies and/or IgG/IgA titer change) was investigated. Outcomes were assessed at 2,5, and 14 days after initiation of therapy. Treatment failure included development of danger signs, persistence of fever, tachypnoea, or death.

Results

The study group comprised 787 children; 86(10.9%) had acute *M. pneumoniae* infection. *C. pneumoniae* acute infection was found in 79(10.8%) of 733 and by *C. trachomatis* was found in 3(10.7%) of 28 cases under 6-months-old. Overall, 147(20.1%) of 731 cases had acute infection by at least one bacterium. Among patients with or without treatment failure at 2 days, acute *M. pneumoniae* infection (11.7% *vs.* 10.7%;P=0.7), acute *C. pneumoniae* infection (8.5% *vs.* 11.3%;P=0.3) and acute *C. trachomatis* infection (16.7% *vs.* 9.1%;P=0.5) were found. Acute infection by one of these bacteria was found in 18.4% *vs.* 20.5%(P=0.6). No significant differences between the groups were found in regard to treatment failure at 5 and at 14 days evaluation. None died. Amoxicillin was substituted in 3.5% *vs.* 2.7% of the patients with or without acute infection by one of these bacteria (P=0.6).

Conclusions

It is not necessary to give empirical antibiotic to treat infection by atypical bacteria among children between 2-59-months of age with non-severe CAP.

ESP16-0904
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

ANTIBIOTICS IN NEONATAL SEPSIS: CURRENT USES AND FUTURE TRENDS (ON BEHALF OF TEDDY NETWORK)

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Background and Objective

Up to 90% neonates are exposed to at least one antibiotic during their stay in NICUs. Drugs tailored for neonates are needed. With reference to medicines currently used for neonatal sepsis, we report the MA status and the existing/ongoing studies supporting their use.

Methods

Guidelines and scientific publications were used as sources to identify antibiotics for neonatal sepsis treatment.
TEDDY European Paediatric Medicines Database provided information on the EMA and nationally approved drugs (in UK and Italy). Completed and ongoing clinical studies were searched consulting EPARs and clinical trial registries (http://www.clinicaltrial.gov/, www.clinicaltrialsregister.eu). Additionally, we searched Head of Agencies (HMA) database.

Learning Points Discussion

Our data demonstrate that

- none of the antibiotic approved by the EMA is indicated for neonatal sepsis;

- 3/40 antibiotics currently used in NICUs are licensed for neonatal sepsis, 4 are approved for neonatal indications but sepsis is not specified, 5 include a dosage without a neonatal indication; Benzyl penicillin is licensed for prevention but not for treatment, while Cefuroxime is licensed for neonatal infections but not for neonatal sepsis;

- of the 3 approved drugs, only gentamicin has paediatric clinical pharmacology; the 5 drugs for which a dosage is indicated do not have any PK study;

- a total of 12 neonatal studies are reported in the HMA database, 5 are PK and 3 comparative (of the 22 studies in the clinical trial databases, 11 are interventional and 1 observational), globally including more than 5500 newborns. No study includes a novel molecule.

All the antibiotics used in NICUs for neonatal sepsis are off-patent and the majority is used ‘off-label’. The most intensive studied drug is gentamicin in association with other antibiotics, while meropenem is the most studied antibiotic as single therapy (as detailed in tables).

ESP16-0974
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

COMPARASION OF CARBAPENEM VERSUS AMIKACIN ANTIMICROBIAL THERAPY FOR PEDIATRIC ACUTE PYELONEPHRITIS CAUSED BY EXTENDED-SPECTRUM B-LACTAMASE PRODUCING ENTEROBACTERIACEAE

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Background

Acute pyelonephritis(APN) related to extended-spectrum β-lactamase (ESBL) producing Enterobacteriaceae is usually tended to be treated with carbapenems, even in vitro amikacin susceptibility is determined. However, widespread and inappropriate usage of carbapenems may lead to carbapenem resistance even in the community. The aim of this study was to compare the efficacy of amikacin versus carbapenem antibiotics for pediatric APN caused by ESBL producing Enterobacteriaceae.

Methods

Episodes of pediatric APN caused by ESBL-producing Enterobacteriaceae and treated with either carbapenem or amikacin between January 2014 to May 2015 were evaluated retrospectively. We evaluated microbiological cure, clinical achievement and relapse rate in two groups.

Results

Thirty seven patients were evaluated. The median age of the patients was 2,5 ± 4 years (0,1-13 years). Twenty eight (75,7%) cases were caused by *Escherichia coli* and 9 (24,3%) cases were caused by *Klebsiella pneumonia*. All were susceptible to both carbapenem and amikacin in vitro. Sixteen patients (43,2%) received carbapenems and 21 (56,8%) received amikacin (6 intramuscular or 15 intravenous). Seventeen cases (45,9%) had an underlying urologic disease. One patient (2,7%) had nosocomial infection, 36 patients (97,3%) had community onset infection. There were no statistically significant difference regarding microbiological cure, clinical achievement and relapse rate between the two groups.

Conclusions

A narrow spectrum amikacin can be an effective alternative to carbapenems for the treatment of APN caused by ESBL producing Enterobacteriaceae if the species is susceptible in vitro.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0487
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

SUCCESSFUL INTRODUCTION OF AN OUTPATIENT PARENTERAL ANTIMICROBIAL THERAPY (OPAT) PROGRAMME IN A LARGE UK PAEDIATRIC HOSPITAL

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Background

An OPAT service at was launched at Alder Hey Children's Hospital in November 2014 to facilitate safe and efficient discharge of patients from the hospital into the community across the Northwest.

Methods

Prospective audit using the BSAC p-OPAT (British Society of Antimicrobial Chemotherapy Paediatric Out-patient Parenteral Antimicrobial Therapy) database including data from January 1st to December 31st, 2015.

Results

Two hundred and thirteen patients were admitted to the OPAT service leading to 1749 bed-days saved for the trust. Seventy-four patients avoided admission. The most common conditions were: bronchiectasis/chronic respiratory tract infection (15.5%), bacteraemia (15%), pre-septal cellulitis (15%) and respiratory tract infection (11.2%). While more complex infections were less common they accounted for longer antibiotic courses, such as cerebral abscess (5 patients – 170 days of intravenous therapy) and endocarditis (3 patients - 75 days of intravenous therapy).

Using the BSAC outcomes definitions, we reported a 90% infection cure rate with a further 6.5% showing clinical improvement. OPAT outcomes were: success in 87% and partial success in 8.5%. The remaining patients (n=6) were classified as OPAT failures due to worsening of infection, drug reactions or inability to re-establish lost vascular access.

Feedback from children and parents showed overall satisfaction with the OPAT service. Completed feedback questionnaires (n=30) rated the support and care as satisfactory or better in all cases, with over 83% rating the service as excellent.

Conclusions

We report a positive financial and clinical impact of a new paediatric OPAT service. The service expansion will focus on the involvement of new patient groups (oncology, general surgery) and the increase use of elastomeric devices allowing for an increase number of patients to be treated in their home environment.

ESP16-0797
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

PROCALCITONIN TO STOP ANTIBIOTIC TREATMENT IN SEVERE BRONCHIOLITIS ADMITTED IN A PAEDIATRIC INTENSIVE CARE UNIT; PROSAB STUDY

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Background

Our group reported a 30% of confirmed bacterial coinfections in children with severe bronchiolitis. Despite the utility of procalcitonin(PCT) as a biomarker for the detection of these cases, some antibiotic treatments could be unnecessarily prolonged in severely-ill children in whom antibiotics were started due to a suspected superinfection. PCT-guided antibiotic stewardship has been effective and safe in adults with severe infections in ICU settings, but the data for children is very scarce.

Methods

The objective of this study was to analyze the antibiotic stewardship practices and their safety in children < 2-year-old with severe bronchiolitis after implementing a PCT-guided decision protocol (2012-2013). We compared these results with those of a period before the implementation of this protocol (2010-2012). During the pre-implementation period, antibiotics were discontinued when the recommended duration according to each type of suspected bacterial infection was accomplished in patients who develop clinically well. After the implementation, antibiotics were discontinued if PCT fell >50% or to a level of <0.5 ng/ml. The setting of the study was the Paediatric Intensive Care Unit of the Hospital Sant Joan de Déu (Barcelona).

Results

81 children of the post-implementation period were included. 245 of the pre-implementation period. Both periods were comparable in patients' epidemiologic characteristics, severity and viral etiology. Patients were markedly less exposed to antibiotics in the post-implementation period (mean days of antibiotic treatment 6.4 (SD:1.0) Vs 8.4 days (SD:4.1); p<0.01) with no adverse effects detected (no differences in length of PICU stay, nor relapses, nor mortality).

Conclusions

PCT-guided protocol was implemented in our PICU for antibiotic management practices in children with severe bronchiolitis and it reduced the total exposure to antibiotic treatment. No adverse outcomes were detected in comparison to the pre-implementation period.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0063
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

NON-ANTIMICROBIAL EFFECTS OF ANTIBIOTICS: RIFAMPIN INDUCES NITRIC OXIDE-MEDIATED INCREASED EXPRESSION OF microRNA-155

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Background

Rifampin, a potent antibiotic agent and a major drug in the treatment of tuberculosis,has immunomodulatory effects. We have previously shown that rifampin increased significantly nitric oxide (NO) production and inducible NO synthase transcription induced by cytokines in human epithelial cells. We also reported that microRNA-155 (miR-155), one of the main miRNAs implicated in inflammation and cancer, is upregulated by NO. We now investigated the effect of rifampin on miR-155 expression.

Methods

Human lung epithelial A549 cells were incubated with cytokines (tumor necrosis factor-α, interleukine-1β, and interferon-γ) alone or together with rifampin, and with rifampin in the presence or absence of the nitric oxide synthase inhibitor L-NAME, for 24h. RNA was isolated and subjected to RT-PCR analysis for miR-155 expression. Nitric oxide concentrations were determined in cells' supernatants by the spectrophotometric Griess reaction.

Results

Incubation of cells with cytokines upregulated miR-155 expression by 5.9 ±0.1 fold and the addition of rifampin further increased the expression to 9.1±1 ($p<0.03$). The ability of rifampin to augment miR-155 was abolished when NO production was inhibited by the addition of L-NAME; the relative expressions of miR-155 with cytokines and L-NAME and cytokines with rifampin and L-NAME were 7.1±0.5 and 6.9±0.4, respectively. The effect of NO on miR-155 expression was mediated by cyclic GMP/protein kinase G signaling.

Conclusions

Rifampin increases miR-155 expression induced by cytokines, which is mediated by the increase in NO concentration caused by rifampin. The increased miR-155 expression by rifampin might have significant consequences, especially with prolonged therapy. Physicians should be aware of the non-antimicrobial effects of rifampin and of antimicrobial agents in general.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0497
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

CHARACTERISTICS AND OUTCOMES OF A TERTIARY PAEDIATRIC OUTPATIENT PARENTERAL ANTIBIOTIC THERAPY (P-OPAT) SERVICE AT A CHILDREN'S HOSPITAL IN THE UNITED KINGDOM

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Background

Data in adults suggest that Outpatient Antibiotic Therapy (OPAT) is a feasible option that allows to reduce the length of hospital stay of patients requiring long-term antibiotic treatment. Although the use of OPAT in Paediatrics (p-OPAT) has been increasing over recent years, the currently available data remain limited.

Methods

Retrospective analysis of prospectively collected data from children under the care of the Southampton Children's Hospital tertiary p-OPAT service over a 3-year-period (2012-2015) evaluating patient characteristics, complications and outcomes.

Results

130 patients were managed by p-OPAT during this period, resulting in a total of 1686 bed-days saved. Infections managed by the p-OPAT service comprised a broad spectrum, including osteoarticular (44%), respiratory (11%), CNS (9%), and blood-stream (8%) infections. A causative pathogen was identified in 87 patients (66%). The most frequently used antimicrobial was ceftriaxone (n=103;79.2%); other antimicrobial agents comprised flucloxacillin, piperacillin/tazobactam and teicoplanin (n=6;4.6% each), followed by daptomycin (n=5;3.8%) and ceftazidime + tobramycin (n=4;3.0%). A total of 109 peripherally inserted central cathether (PICC) lines were placed; a total of 11 (11%) catheter-related complications occurred, comprising line migration/dislodgement (n=5;5%), line blockage (n=3;3%), probable line infection (n=2;2%), and line fracture (n=1;1%). Overall, 109 (83.8%) p-OPAT episodes resulted in cure, 16 (12.4%) in improvement; treatment failure occurred in 2 (1.5%) and 3 (2.3%) proved to be non-infectious conditions. The large majority of the cases (n=108;83%) completed p-OPAT therapy with no change in their antibiotic regimen, no adverse events and without the need for readmission.

Conclusions

Our experience demonstrates that p-OPAT provides a safe and effective way of managing children on long-term intravenous antibiotics at home, and that line-related complications and other adverse events are rare.

ESP16-0522
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

REASSURING SEQUENTIAL ANTIBIOTIC THERAPY IN OSTEOMYELITIS: ASSESSMENT OF BONE ANTIBIOTIC BIOAVAILABILITY IN SKELETALLY IMMATURE ANIMAL

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Background

Acute osteomyelitis may lead to functional sequelae if not appropriately treated. Sequential antibiotic therapy with early switch to oral route is currently recommended, but there is a lack of pharmacokinetic data reassuring this approach.

We aimed to develop an animal model of oral and intravenous administration of a single-dose of cloxacillin (100 mg/Kg) and to quantify and compare bone concentration in three different ages of healthy animals.

Methods

Two groups of skeletally immature (8 and 13 weeks of age) and adult (30 weeks) male rabbits were used. A pilot test using a bicompartimental pharmacokinetic model was performed to ensure that sampling points were sufficient to draw the curve accurately enough to determine pharmacokinetic parameters. Subsequently, bone concentrations were quantified by chromatography/tandem mass spectrometry (ACQUITY-Xevo-TQ-S; Waters Corp, Milford, MA, USA).

Results

Plasma and bone tissue samples were collected at 10 minutes after intravenous and 35 minutes after oral administration. Overall, plasma levels were almost 50-fold greater after IV administration (233 vs 4.8 mg/ml) without significant differences between ages as well as bone concentration (73 vs 1,02 mcg/g). Bone antibiotic penetration was greater in younger animals both for IV (40%, 33% and 25% in 8, 13 and 30 weeks rabbits, respectively) and oral route (24%, 25% and 12% respectively).

Conclusions

Bone antibiotic penetration was significantly greater in the skeletally immature animals. In our model, bone concentration with oral route led to low concentrations that may be insufficient to treat -even theoretically susceptible strains of *S. aureus* (<2 mcg/ml). Clinical relevance of

these findings will be assessed by creating an infected model with methicillin sensitive *S. aureus* strains to reproduce full conditions of *in vivo* infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1022
E-POSTER DISCUSSION SESSION 10 - USE OF ANTIMICROBIALS (station 3)

ACHIEVING TARGET TROUGH CONCENTRATIONS OF VANCOMYCIN: AN AUDIT OF INTERMITTENT VANCOMYCIN DOSING IN THE PAEDIATRIC AND NEONATAL INTENSIVE CARE SETTING

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Background

Intermittent intravenous vancomycin is widely used in paediatric and neonatal populations to empirically treat infections in the intensive care setting. Limited national guidance often results in clinicians referring to adult guidelines for therapeutic monitoring and dosage adjustments. The literature suggests that current dosing recommendations are failing to achieve the target range (10-15mg/L).

Objectives
To assess the adherence of clinical practice to local guidance at Evelina London Children's Hospital (ELCH), and to examine the length of time taken to attain target trough levels and the requirement for dose adjustments.

Methods

This retrospective chart review evaluated paediatric and neonatal patients who received intermittent vancomycin infusions in the intensive care setting at ELCH from June 2014 to July 2015. Patient demographics, renal function and trough concentrations with responsive dose alterations were analysed for the first 4 days of the antibiotic course.

Results

31% (10 of 32) of patients, none neonatal, achieved initial target trough concentrations. Of these, two maintained the target range for 48 hours. Overall, those who reached target trough concentrations took on average two days, with 25% of patients requiring dosage increments. 38.2% had trough concentrations of >20mg/L requiring dosage reductions or changes of regimen to BD dosing, most prevalent in renal dysfunction. 21.9% never reached target range.

Conclusions

Recommended dosing of 15mg/kg 8 hourly did not provide steady-state target trough concentrations in a large proportion of paediatric and neonatal patients. Given this data, the authors recommend BD dosing in renal impairment. Further studies into age appropriate dosing regimes and detailed guidelines on dosage adjustments are required.

ESP16-1025
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

EPIDEMIOLOGY OF RESPIRATORY VIRUSES IN A UNIVERSITY TERTIARY HOSPITAL OF MADRID FROM JANUARY 2014 UNTIL JUNE 2015

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Background

The objective is to describe the epidemiological and clinical characteristics of children (< 16 years) with lower respiratory virus infection (LRVI) in the emergency room (ER).

Methods

A retrospective study was performed on the characteristics of all patients (< 16 years) with respiratory distress or oxygen supplementation, attended to the ER from our hospital with LRVI in Madrid from January 2014 until June 2015.
The diagnosis was made by rapid-RSV and influenza antigen test, or nasopharyngeal aspiration Multiplex-PCR that included the most common 15 respiratory viruses causing community acquired respiratory infections in children.

Results

570 patients (54% male) were included, microbiological diagnosis was established in 158 (28%), median age 2 years (IQR 3-1);137 were infected by a single virus, and 14% were co-infected by 2 or more. VRS was the most prevalent (44%), followed by influenza A (18%), influenza B (13%), rhinoviruses (13%), metapneumovirus (5%), parainfluenzae (4%) adenovirus (2%) and influenza C and bocavirus (1%). The proportion of admission was 58% (median 3 days).

Influenza was found in winter, rhinovirus from October 2014 until June 2015, metapneumovirus and parainfluenzae in spring.

80% of co-infections were younger than 24 months. Instead, all the children with influenza B were over two (mean 6.8 years, IQR 9-4).

Children with influenza A, B and co-infections had higher fever (>39°C) and mean duration (4-5 days) than other viruses.

In relation to hospitalization, 100% with metapneumovirus and parainfluenzae and 76% co-infections (4 in PICU) were admitted.

100% of rhinovirus infected had chest X-ray infiltrates; and according to the clinician criteria, 88% metapneumovirus infections were given antibiotics, his findings were less prevalent in the other viruses.

Conclusions

In our selected population the diagnostic yield was 28%. Metapneumovirus and co-infections had a more aggressive course.

ESP16-0570
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

SERUM CRP AND PROCALCITONIN AS MARKERS FOR DISEASE SEVERITY AND PROGNOSIS IN CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA

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Background

Community acquired pneumonia (CAP) is one of the most often diseases requiring hospitalization in children. Assessing the severity of infection and choosing the empiric antibiotic treatment based on clinical signs, radiographic imaging and traditional inflammatory markers as leucocytosis and blood sedimentation rate remains challenging. The aim og the study is to investigate the diagnostic and prognostic value of serum biomarkers high sensitive CRP (hsCRP) and procalcitonin in hospitalized children with CAP.

Methods

Included are 88 children between 2 and 18 years old, hospitalized in the clinic with CAP from September 2014 to December 2015. Serum levels of hsCRP and procalcitonin, taken on the day of hospitalization are analysed using SPSS v.20.

Results

On hospitalization elevated levels of hsCRP (>5mg/l) have 91.8% and of procalcitonin 74.2% from the children. The levels of hsCRP are significantly elevated in children with more severe clinical picture ($p=0.03$ for fever over 38^0C, $p=0.001$ for tachypnea, $p<0.0001$ for dehydration) and infiltrative versus interstitial pneumonia ($p<0.0001$). The levels of procalcitonin are significantly higher in patients witch remain feverish 72 hours after the start of parenteral antibiotic treatment ($p=0.018$) or needed change/adding of a new antibiotic ($p=0.04$). The children treated with antibiotic at home have lower hsCRP and procalcitonin on admission at the hospital ($p<0.05$).

Conclusions

Measurement of CRP levels contributes to the assessment of pneumonia severity and the procalcitonin has also prognostic value. Caution is needed analysing the results in children with started antibiotic at home.

ESP16-0575
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

RECURRENT RESPIRATORY TRACT INFECTIONS, ADENOID HYPERTROPHY AND IMMUNITY IN CHILDREN UNDERGOING ADENOIDECTOMY

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Background

Recurrent respiratory tract infections (RRTIs) represent a common problem in paediatric praxis. One of the most common reasons of RRTIs is adenoid hypertrophy (AH). Adenoids are active lymphoid organs and can have negative influence on the immune system and microbiome of the airways.

Methods

In our prospective study, we aimed to examine the influence of AH and adenoidectomy on immune parameters and microbiome of upper airways. We enrolled 72 children (48 boys, 66.7%; aged 4.5±2.2 ys.) with AH treated with adenoidectomy in general anaesthesia. All the subjects underwent the panel of laboratory and clinical tests (humoral and cellular immunity, complement analysis, cultivation studies, skin prick tests) before and 6 months after adenoidectomy.

Results

In general, we were not able to detect any significant changes in cellular immunity associated with adenoidectomy. However, we found a significant increase of IgG_1, IgG_2, total IgE and complement components (C3, C4). On the other hand, the serum concentration of mannose binding lectin (MBL) declined significantly after surgery. Interestingly, in 14 children (19%) we detected the complete deficiency of MBL. Atopy was detected in 83% of children. There was no correlation between cultivation studies sampled from medial nasal meatus and nasopharynx and adenoidectomy led to the decreased colonisation by pathogenic microorganisms in the upper airways. Exposure to tobacco smoke was associated with *Streptococcus pneumoniae* carriage in nasopharynx and increase of IgG a IgA in serum.

Conclusions

Adenoid hypertrophy negatively influences the upper airways microbiome and immune system defence mechanisms. Atopy and passive smoking could contribute to the AH development. Adenoidectomy leads to the compensatory changes especially in humoral and complement

part of immunity, decreases mucosal inflammation and corrects the upper airways microbiome composition. *Study supported by VEGA 1/0252/14.*

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0380
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

RESPIRATORY SYNCYTIAL AND INFLUENZA VIRUSES IN CHILDREN HOSPITALIZED WITH ACUTE RESPIRATORY TRACT ILLNESS

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Background

Acute respiratory illnesses are major causes of morbidity in early childhood. They are mainly caused by viruses, of which influenza viruses (IV) and respiratory syncytial virus (RSV) are most frequent and important ones. Emergence of resistant bacteria is a growing concern. This, in part, is due to inappropriate antibiotic therapy for children with respiratory diseases.

Objective: To investigate the burden of RSV and IV in children < 5 years of age hospitalized for acute respiratory diseases and to show the impact of RSV/IV rapid testing on antibiotic prescriptions.

Methods

All patients <5 years admitted with acute respiratory infection to pediatric hospital in Armenia-Arabkir medical centre, between November 1, 2013 and April 1, 2014 were included in the study. Nasopharyngeal swabs were tested for RSV, IV types A, B by direct antigen detection.

Results

998 patients were included in the study. 398 (39.9%) were tested positive: 274 (27.5%) for RSV and 124 (12.4%) for IV (IV A 121, IV B 3), respectively. 342/998 (34.3%) were pretreated with antibiotics: the most commons were oral amoxicillin-clavulanate in 53 (15.5%), sulfamethoxazole/trimethoprim in 44 (12.8%) and intramuscular ceftriaxone in 36 (10.5%). 378/998 (37.9%) were treated with antibiotics in the hospital, but the rate was higher in RSV/IV negative children 44.7% (268/600) compared with children tested positive for RSV or IV 27.6% (110/398).

Conclusions

The antigen tests for detection of respiratory viruses thanks to cooperation with Zurich University Children's Hospital allowed to document high burden of RSV and IV in children admitted to our hospital. In settings were PCR method is not easily available implementation of rapid antigen tests for detection of respiratory viruses is important in the management of patients including cohorting and more targeted use of antibiotics.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0918
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

IMPROVED DETECTION OF PNEUMOCOCCAL CARRIAGE BY COMBINING LAWN CULTURE AND PCR

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Background

The recognition that the effectiveness of conjugate pneumococcal vaccines depends upon their impact on upper respiratory colonisation and thus transmission within the population has galvanised interest in the study of carriage of this organism. PCR detection reduces cost and improves quantification but fails to detect low level colonisation in some cases.

Methods

We compared direct quantitative PCR (lytA) detection (<35 cycles) of pneumococcus (Sp) in STGG broth samples containing nasal swabs with detection in DNA extracts of lawn cultures on colistin blood agar (COBA) plates prepared using 50ul of the same samples. We analysed 182 nasal swabs taken during the 2011-2012 winter season from healthy 2-4 years olds attending daycare nurseries in Coimbra, Portugal.

Results

Sp was detected in 129 (71%) swab samples and 141 (78%) of COBA lawn extracts (P<0.02). This change in overall sensitivity was due to 19 (10%) negative swab samples which were positive by lawn PCR and 9(5%) positive swabs, negative by lawn culture. The Cycle threshold values for the 120 samples positive by both techniques were (mean, (SD)) 12.5(3.8) cycles lower in COBA lawn extracts representing approximately 3.8 logs of amplification by culture with modest variation between samples – only a handful of lower density samples failed to do this.

Conclusions

We show that by combining culture and PCR, sensitivity of detection of Sp in nasal swab samples can be significantly increased for low density carriage. This approach also permits samples containing pneumococcal DNA but no viable organisms to be identified. The technique results in a large amplification and rather consistent amplification of bacterial DNA by culture allowing comparisons to be drawn in the density of colonisation between individuals identified by this method.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0930
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

DIAGNOSIS OF TUBERCULOSIS INFECTION IN CHILDREN BEFORE TREATMENT WITH TUMOR NECROSIS FACTOR ALPHA INHIBITORS. A MULTICENTER STUDY COMPARING IGRA AND TUBERCULIN SKIN TESTS IN SPAIN

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Background

Inhibitors of tumor necrosis factor (TNF)-α represent an important treatment advance in inflammatory-mediated diseases but are associated with increased risk of tuberculosis (TB). Diagnosing latent TB infection (LTI) in these children remains challenging; the tuberculin skin test (TST) shows several limitations and scarce data are available on the use of interferon-γ release assays.

Methods

National multicenter retrospective-prospective cross-sectional study including pediatric patients affected with inflammatory diseases in whom LTI screening was performed simultaneously with TST and QuantiFERON®-TB Gold-In-Tube (QFT-G) test before anti-TNFα treatment implementation. Patients with history of TB infection or previous anti-TNFα treatment were excluded. Any positive result was considered diagnostic of TB infection.

Results

Overall, 225 patients (127 girls, 56.4%) from 15 hospitals were included: 126 with rheumatic diseases, 82 with inflammatory bowel disease, 16 with idiopathic uveitis and one with psoriasis. The mean(SD) age at diagnosis and LTI screening were 8.6(7.9) and 10(4.4) years, respectively. Along the 3 months before LTI screening, 84 (37.3%), 151 (67.1%) and 65 (28.9%) patients had received steroids, DMARDs and steroids+DMARDs, respectively.

Ten patients tested positive for TB (n=1) or LTI (n=9) (4.4%, 95%CI 1.8-7.1). Three of them were BCG-vaccinated and none had known risk factors for TB. The level of agreement between TST and QFT-G was moderate (weighted Cohen's kappa coefficient:0.45; 95%CI:

0.04-0.85). QFT-G tested indeterminate in 10 patients. Patients with indeterminate QFT-G results had higher C-reactive protein levels at screening (34.3 vs 13.1 mg/L; p=0.025), but showed no differences in gender, age, previous treatments or erythrocyte sedimentation rate.

		QFT-G			
		+	-	indeterminate	
TST	+ (>5mm)	3	4	-	*7*
	-	3	205	10	*218*
		6	*209*	*10*	*225*

Disease	Age at screening	Gender	TST (mm)	QFT-G	Previous treatment
JIA, oligoarticular	9y3m	f	10	positive	MTX
JIA, oligoarticular	10y9m	f	15	positive	-
JIA, systemic*	9y9m	f	15	positive	MTX, TCZ
JIA, polyarticular RF-negative	10y3m	m	0	positive	MTX
Psoriasis	8y6m	f	0	positive	-
Systemic sclerosis	10y1m	m	0	positive	-
JIA, oligoarticular	10y5m	m	6	negative	CS, MTX
JIA, oligoarticular	9y10m	f	9	negative	MTX
JIA, polyarticular RF-positive*	13y7m	f	10	negative	CS, MTX
Idiopathic uveitis*	10y10m	m	10	negative	-

** BCG-vaccinated patients*

QFT-G indeterminate

Disease	Age at screening	Gender	ESR (mm)	CRP (mg/L)	Previous treatment
Crohn's Disease	11y2m	m	-	0.6	CS, AZA
Idiopathic uveitis	12y1m	m	2	0.3	MTX
Ulcerous colitis	13y2m	m	2	2.1	CS
JIA, polyarticular RF- negative	4y1m	m	16	15	CS, MTX
JIA, oligoarticular	2y6m	f	32	23.7	MTX
Ulcerous colitis	5y3m	f	37	37.8	CS
Crohn's Disease	12y1m	f	30	82.4	-
JIA, polyarticular RF-negative	7y5m	m	49	91	-
JIA, systemic	1y3m	f	113	65.8	CS, CLP
JIA, ERA	8y1m	f	103	24.4	CS, MTX

AZA: azathioprine; BCG: Bacillus Calmette-Guérin; CLP: cyclosporine; CRP: C-reactive protein; CS: corticosteroids; DMARD: disease-modifying antirheumatic drug; ESR: erythrocyte sedimentation rate; f: female; JIA: juvenile idiopathic arthritis; m: male; MTX: methotrexate; QFT-G: QuantiFERON Gold-In tube® test; TB: tuberculosis; TZC: tocilizumab; TST: tuberculin skin test

Conclusions

Agreement between TST and QTF-G was moderate. Our data support current recommendations regarding a dual screening strategy (TST and an IGRA test) before antiTNFα treatment in children without known risk factors for TB.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1006
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

BOTH LATENT AND ACTIVE TUBERCULOSIS ARE COMMON IN ADOLESCENTS FROM HIGH INCIDENCE COUNTRIES SEEKING ASYLUM IN SWEDEN

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Background

A disproportionate number of refugees from Africa and Asia to Europe seek asylum in Sweden. The rates of tuberculosis (TB) among them is not yet fully known. To rationally plan health care and prevention such information is needed. We therefore performed a survey of the referrals to our paediatric TB clinic from new entrant screening during 2015.

Methods

The Migration Agency offers a health screening that includes a TST or an IGRA at designated clinics to asylum seekers <18 years from countries with a high (>100/10^5) incidence of TB or other risk factors. It usually takes place 2 to 3 months after arrival in Sweden. Those with a positive test have a chest X-ray and are referred to the hospital TB clinic. Epidemiological and clinical data are prospectively entered into a database.

Results

We recieved 274 referrals, 76 IGRA positive and 198 TST positive. Most were unaccompanied, teenage males from Afghanistan (n=89), Somalia (87) or Eritrea (40). An IGRA was obtained in 156 of the TST positive children, and was positive in 82. 108 were considered uninfected, 152 had LTBI and 11, active TB. 4 screened children developed symptoms during the referral process and presented at the emergency department. Another 6 migrants presented clinically with TB without yet being sceened. Of the 21 cases of active TB, 11 were confirmed, 6 probable, and 4 possible. They came from either Somalia (10), Afghanistan (8) or Eritrea (3).

Conclusions

TB infection and disease are common in migrants from high incidence countries. Urgent cases need to by-pass our screening system.

ESP16-0344
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

IMPROVING THE DIAGNOSIS OF CHILDHOOD TUBERCULOUS MENINGITIS USING SCORING SYSTEMS

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Background

Early diagnosis of tuberculous meningitis (TBM) is crucial to achieve optimum outcomes. There is no validated scoring system or rapid diagnostic test available for TBM. A research case definition for TBM has been proposed, but its use in predicting microbiologically confirmed TBM in children has not been evaluated.

Methods

Retrospective case control study across 7 hospitals in KwaZulu-Natal, South Africa (2010-2013). The performance of the research case definition was evaluated in children (3 months-15 years) with microbiologically confirmed TBM and matched controls. A novel scoring system was developed from the most predictive variables identified on univariate analysis and performance tested on an independent sample group.

Results

Of 865 children with suspected TBM, 3% (25) had microbiologically confirmed TBM. Clinical information was retrieved for 22 microbiologically confirmed cases of TBM and compared with 66 age, ethnicity, sex and geographical origin matched controls. The research case definition classified 55% (12/22) of microbiologically confirmed cases as “probable TBM”, and the remainder as “possible TBM”. A novel score (CHILD TB LP) was developed using the 9 most predictive variables among the confirmed cases: altered **C**onsciousness; caregiver **H**IV infected; **I**llness length >7 days; **L**ethargy; focal neurological **D**eficit; failure to **T**hrive; **B**lood/serum sodium <132mmol/L; CSF >10 **L**ymphocytes x 10*6/L; CSF **P**rotein >0.65g/L. The novel score successfully classified an independent sample of the confirmed TBM cases with a sensitivity of 100% and specificity of 90%.

Conclusions

The CHILD TB LP score was able to classify microbiologically confirmed TBM more accurately than the research case definition. We propose CHILD TB LP as a simplified novel scoring system for use in the initial evaluation of children with suspected central nervous system infection presenting to hospitals in similar settings.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0916
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

EFFECTIVENESS AND SAFETY OF LINEZOLID CONTAINING-REGIMENS FOR THE TREATMENT OF TUBERCULOSIS

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Background

Studies from adults have shown the effectiveness of linezolid in the treatment of tuberculosis (TB), but data in children are limited. The aim of our study was to evaluate the effectiveness and safety of linezolid as a compound of the treatment against TB in patients under 18 years.

Methods

Retrospective observational multicenter study, including patients within the Spanish Pediatric TB Network (pTBred) who received linezolid.

Results

Fifteen patients (8 males), with a median age of 4.7 years (IQR 2.3-9.5), were included. Five patients (33%) were on immunosuppressive therapy. Extrathoracic TB was common (46.6%). TB was bacteriologically-*confirmed* in 9 children (60%), and 3 cases presented multidrug-resistant TB. The indication for linezolid was the treatment of confirmed/suspected drug resistant TB in 7 cases (46.6%), and hepatotoxicity in 9 (60%). One child with drug resistant TB presented hepatotoxicity as well. The median time of linezolid exposure was 365 days (IQR 28-441). Hematologic toxicity was observed in 7 patients (46.6%). In 3 cases (20%), linezolid was discontinued due to adverse events (gastric intolerance, thrombocytopenia, and suspected drug allergy), and a dose reduction was required in another 2 (diarrhea, neutropenia). None of the patients presented linezolid associated neuropathy. One patient was lost to follow-up, but the rest 14 patients had no TB relapses.

Conclusions

Linezolid should be considered in case of MDR- TB and/or liver toxicity of first-line antitubercular agents. However, hematologic toxicity may limit its use. More safety and efficacy data are required to recommend linezolid in TB-containing-regimens in children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0825
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

TRENDS IN COMPLICATED PARAPNEUMONIC EFFUSION ADMISSIONS AFTER PNEUMOCOCCAL CONJUGATE VACCINE INTRODUCTION IN GREECE: A MULTI-CENTER STUDY IN THE AREA OF ATHENS

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Background

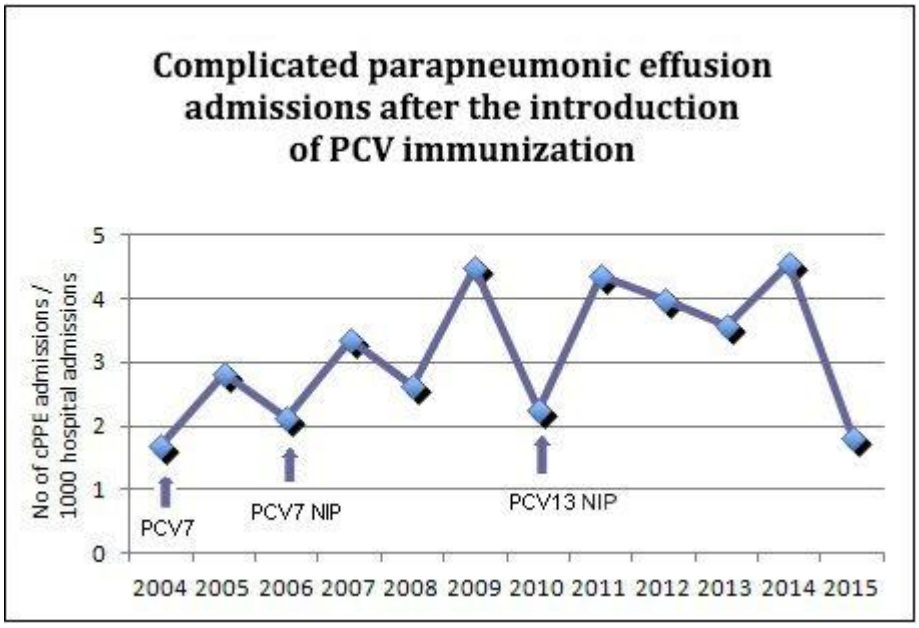
Parapneumonic effusion (PPE) is a common complication of pneumonia and a potentially severe one in case of empyema. The most common cause is bacterial pneumonia usually due to *Streptococcus pneumoniae*. After the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7), an increase in the incidence of pleural empyema was recorded in some countries. We aim to examine the impact of PCV introduction on the number of complicated parapneumonic effusion (c-PPE) admissions among children in our area.

Methods

We analyzed cases of pneumonia with c-PPE requiring chest tube insertion in the 3 public Children's hospitals in Athens between January 1st 2004 and December 31st 2015. Mean annual number of pediatric admissions in these hospitals was 24,082. Data were collected retrospectively before 2013 and prospectively thereafter. The annual rate of c-PPE cases per 1,000 general pediatric hospital admissions was recorded and time trend was examined with the Chi-square test for trend. Complete PCV immunization rate during 2010-2011 was over 70%.

Results

A total of 316 cases of pneumonia with c-PPE were recorded of which 166 (23.5/yr) between 2004 and 2010 (period A) and 150 (30/yr) between 2011 and 2015 (period B). Annual rate of c-PPE admissions is shown in the figure. An increasing trend was noted after PCV7 introduction although not statistically significant (P=0.132). The annual c-PPE admission rate was shown to decrease significantly during period B (P=0.01).



Conclusions

A decreasing time trend in c-PPE cases among children was shown after the introduction of PCV13 in our area. Continuous surveillance is required to confirm these findings over time.

ESP16-0813
E-POSTER DISCUSSION SESSION 11 - RESPIRATORY TRACT INFECTIONS (station 4)

DIFFERENTIAL EXPRESSION OF BASOPHIL ACTIVATION MARKER IN RESPIRATORY SYNCYTIAL VIRUS INFECTED PATIENTS

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Background

INTRODUCTION
Basophils are key cellular participants in allergic mechanism of asthma and might be involved in the immunopathology of respiratory syncytial virus (RSV) infection and its link with later wheezing/asthma development.
OBJECTIVE
To determine the expression of the basophil activation marker CD63 in peripheral blood basophils in children infected with RSV

Methods

Flow cytometry analysis of surface basophils activation marker CD63 in peripheral blood basophils was performed in 44 children: 15 healthy controls and 29 children with respiratory infection attending the emergency department (of which 15 were confirmed to be RSV positive and 14 RSV negative). Median fluorescence intensity (MFI) of surface CD63 expression in peripheral blood basophils were analysed in all patients by a three-colours laser flow cytometry.

Results

Mean (SD) of MFI for CD63 was: 20 (12) MFI in RSV positive, 12.47 (5.39) MFI in RSV negative and 9.91 (2.53)MFI in the control group ($p = 0.0386$); *Figure*. Interestingly, both control and RSV negative patients showed a MFI for CD63 expression < 25, while in the RSV positive group 6 out of 15 had a MFI above 25.

Conclusions

There seems to be a differential expression of basophil activation marker CD63 in RSV infected patients compared to other respiratory infections and healthy children. Further studies

are needed in order to confirm the eventual role of basophils in RSV-elicited recurrent wheezing/asthma.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1069
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

SAFETY OF BIVALENT rLP2086, A MENINGOCOCCAL SEROGROUP B VACCINE, IN ADOLESCENTS: RESULTS FROM A PHASE 3 TRIAL

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Background

Bivalent rLP2086 was the first vaccine approved in the US to prevent meningococcal serogroup B (MnB) disease in 10- to 25-year-olds, through an accelerated approval process involving the review of the safety and immunogenicity results of three trials including 4459 subjects, 2293 of whom received three doses of bivalent rLP2086 at 0, 2, and 6 months. Additional safety data are presented from a pivotal phase 3 trial (ClinicalTrials.gov: NCT01830855) of bivalent rLP2086 in adolescents.

Methods

Healthy subjects aged 10-<19 years were randomized to receive bivalent rLP2086 at 0, 2, and 6 months, or hepatitis A virus vaccine at 0 and 6 months and saline at 2 months. Subjects who received ≥1 dose were included in the safety evaluation (bivalent rLP2086, n=2693; control, n=897). Reactogenicity, antipyretic use, and unsolicited AEs including medically attended AEs (MAEs), SAEs, and newly diagnosed chronic medical conditions (NDCMCs) were assessed.

Results

Local and systemic reactions were reported more commonly with bivalent rLP2086. Reactogenicity events were mostly mild-to-moderate in severity and of short duration (median, 1-2 days). Injection-site pain (92.6%) and headache (67.1%) were the most common local and systemic reactions with bivalent rLP2086, respectively. 9.8% and 5.2% of bivalent rLP2086 and control recipients, respectively, reported fever ≥38°C. No bivalent rLP2086 recipient experienced fever >40.0°C; antipyretics were used by 32.1% and 20.2% of bivalent rLP2086 and control recipients, respectively. AEs were generally similar between the two study groups

(Table).

Table. Summary of Adverse Events

Adverse events[a]	Bivalent rLP2086			HAV/Saline		
	N	n	% (95% CI)	N	n	% (95% CI)
≥1 Adverse event	2693	1097	40.7 (38.9, 42.6)	897	392	43.7 (40.4, 47.0)
≥1 Vaccine-related adverse event	2693	52	1.9 (1.4, 2.5)	897	16	1.8 (1.0, 2.9)
≥1 Serious adverse event	2693	51	1.9 (1.4, 2.5)	897	22	2.5 (1.5, 3.7)
Medically attended adverse events	2693	872	32.4 (30.6, 34.2)	897	319	35.6 (32.4, 38.8)
Newly diagnosed chronic medical condition	2693	15	0.6 (0.3, 0.9)	897	10	1.1 (0.5, 2.0)

[a]Occurring during the vaccination phase (AEs, vaccine-related AEs) and throughout the study (SAEs, MAEs, NDCMCs) and regardless of severity.

Conclusions

These safety findings indicate that bivalent rLP2086 is safe and tolerable for use in adolescents. These findings extend the safety data for bivalent rLP2086 and are consistent with the vaccine's favorable safety and tolerability profile reported in phase 2 studies. Funded by Pfizer.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov: NCT01830855

ESP16-0309
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

TITLE: PASSIVE ENHANCED SAFETY SURVEILLANCE IN CHILDREN RECEIVING FLUENZ® TETRA VACCINATION IN ENGLAND DURING THE EARLY 2015/2016 INFLUENZA SEASON

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Background

Fluenz® Tetra is a quadrivalent, live attenuated, intranasal, influenza vaccine recommended for use in children vaccinated as part of the seasonal influenza immunisation programme in England. We report interim results[1] from a pilot safety surveillance programme consistent with regulatory guidance for all influenza vaccines. The project aimed to measure and assess the frequencies of suspected adverse drug reactions (sADRs) in children receiving Fluenz® Tetra during the early 2015/2016 influenza season in England.

Methods

Passive enhanced safety surveillance was conducted through stimulated spontaneous reporting of sADRs. Vaccinees or parents/guardians received a Safety Report Card (SRC) to return if children experienced sADRs after vaccination with Fluenz® Tetra. At participating sites, 42 general practices and 25 primary schools in England, immunisation teams provided numbers of SRCs distributed.

Results

Between 8th October and 18th November 2015, 6,366 SRCs were issued for 2,507 children (39.4%) aged 2 to 4 years, 3,492 (54.8%) aged 5 to 10 years and 367 (5.8%) aged 11 to 17 years. Of 242 SRCs returned during this period, 162 were fully processed by 18th November 2015, including 40 SRCs with at least one sADR. Among these 40 SRCs, the most frequent sADRs were pyrexia (n=13), rhinorrhoea (12) and cough (10). One serious and unexpected sADR involved a child with flu-like symptoms requiring a hospital visit 2 days after vaccination.

Conclusions

These interim data[1] are broadly comparable with the frequency of adverse events reported for Fluenz® Tetra in clinical trial and post-marketing data, despite differences in methods. No evidence from the limited data available thus far suggests an increased frequency of minor expected events or other safety signals.

Study co-sponsored by DSRU and AstraZeneca. *[1]Final data presented at conference.*

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0984
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

SAFETY OF BIVALENT RLP2086, A MENINGOCOCCAL SEROGROUP B VACCINE, IN YOUNG ADULTS: RESULTS FROM A PHASE 3 TRIAL

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[7]Pfizer Ltd, Pfizer Vaccine Research, Brussels, Belgium

Background

Bivalent rLP2086 was the first vaccine approved in the US to prevent meningococcal serogroup B (MnB) disease in 10- to 25-year-olds, through an accelerated approval process involving the review of the safety and immunogenicity results of three trials including 4459 subjects, 2293 of whom received three doses of bivalent rLP2086 at 0, 2, and 6 months. Additional safety data are presented from a pivotal phase 3 trial (ClinicalTrials.gov: NCT01352845) of bivalent rLP2086 in young adults.

Methods

Healthy subjects aged 18-<26 years were randomized to receive bivalent rLP2086 or saline at 0, 2, and 6 months. Subjects who received ≥1 dose were included in the safety evaluation (bivalent rLP2086, n=2471; control vaccine, n=822). Reactogenicity, antipyretic use, and unsolicited AEs including medically attended AEs (MAEs), SAEs, and newly diagnosed chronic medical conditions (NDCMCs) were assessed.

Results

Local and systemic reactions were reported more commonly with bivalent rLP2086. Reactogenicity events were mostly mild-to-moderate in severity and of short duration (median, ≤3 days). Injection-site pain (89.6%) and fatigue (64.6%) were the most common local and systemic reactions with bivalent rLP2086, respectively. 4.4% and 1.7% of bivalent rLP2086 and control recipients, respectively, reported fever ≥38°C. One bivalent rLP2086 recipient experienced fever >40.0°C one day after dose three, which resolved within one day. Antipyretics were used by 24.9% and 15.0% of bivalent rLP2086 and control recipients, respectively. AEs were generally similar for the 2 study groups (Table).

Table. Summary of Adverse Events						
	Bivalent rLP2086			Saline		
Adverse events[a]	N	n	% (95% CI)	N	n	% (95% CI)
≥1 Adverse event	2471	771	31.2 (29.4, 33.1)	822	256	31.1 (28.0, 34.4)
≥1 Vaccine-related adverse event[b]	2471	114	4.6 (3.8, 5.5)	822	20	2.4 (1.5, 3.7)
≥1 Serious adverse event	2471	33	1.3 (0.9, 1.9)	822	11	1.3 (0.7, 2.4)
Medically attended adverse events	2471	541	21.9 (20.3, 23.6)	822	174	21.2 (18.4, 24.1)
Newly diagnosed chronic medical condition	2471	10	0.4 (0.2, 0.7)	822	2	0.2 (0.0, 0.9)

[a]Occurring during the vaccination phase (AEs, vaccine-related AEs) and throughout the study (SAEs, MAEs, NDCMCs) and regardless of severity.
[b]The difference between groups in vaccine-related AEs is driven by reactogenicity events in addition to those captured by the subject-reported electronic diary and mainly includes injection-site pain and headache.

Conclusions

These safety findings indicate that bivalent rLP2086 is safe and tolerable for use in young adults. These findings extend the safety data for bivalent rLP2086 and are consistent with the vaccine's favorable safety and tolerability profile reported in phase 2 studies. Funded by Pfizer.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov: NCT01352845

ESP16-0549
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

THE CONTRIBUTION OF NON-VACCINE TYPE SEROTYPES TO CHILDHOOD INVASIVE PNEUMOCOCCAL DISEASE

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Background

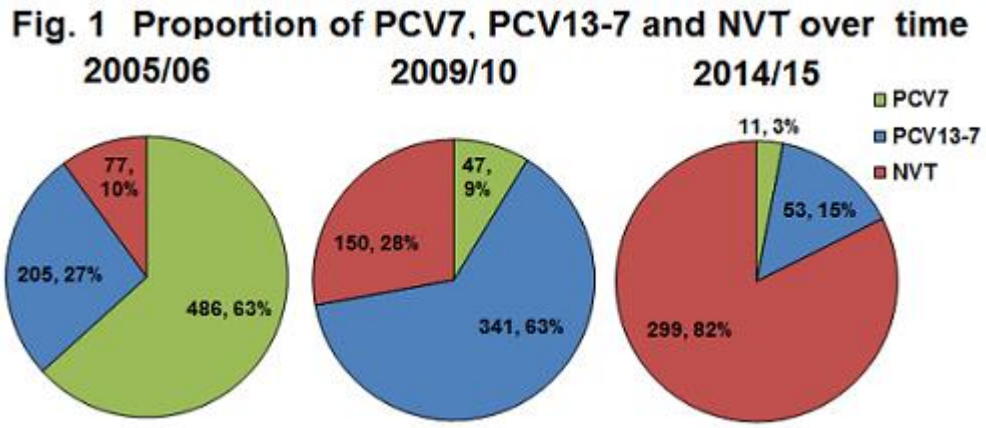
The PCV7 vaccine was introduced in England and Wales in 2006 and replaced by PCV13 in 2010. Both vaccines were associated with rapid declines in vaccine type (VT) invasive pneumococcal disease (IPD) and a subsequent increase in non-vaccine type (NVT) IPD. We describe the serotype distribution of NVT-IPD in children during the 2014/15 epidemiological year and compare to pre-PVC7 (2005/06) and PCV7 (2009/10) years

Methods

Public Health England routinely serotypes invasive pneumococcal isolates from patients across England and Wales. A data extract of all isolates from children aged <15 years during the 2005/06 2009/10 and 2014/15 epidemiological years was created. Cases were grouped by serotype into NVT, PCV7, or PCV13-7 IPD.

Results

In 2014/15, 82% (299/363) of IPD isolates from children were NVT, 15% PCV13-7 and 3% PCV7 (Fig. 1). NVT serotypes contributed to only 10% of cases in the pre-PCV7 and 28% in the PCV7 years (Fig. 1). NVT-IPD contributed to 86% of cases in <1 year olds, 87% in 1-4 year olds, 72% in 5-9 year olds, and 65% in 10-14 year olds. In 2014/15, 16% of NVT IPD cases were 12F, 10% were 8 and 9% were 24F; the most prevalent VT IPD was 19A (27%; 17/64).



Conclusions

A successful immunisation programme has resulted in a marked decline in IPD due to PCV13 serotypes. Now, NVT accounts for 83% of childhood IPD. To combat the rise in NVT-IPD, higher valency vaccines are being developed; however, as no single serotype predominated the additional benefit may be limited. A serotype-independent vaccine could make a significant impact on the burden on IPD.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0209
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

CROSS-PROTECTION OF LIVE ATTENUATED INFLUENZA VACCINE AGAINST ANTIGENICALLY DRIFTED INFLUENZA A(H3N2) STRAINS

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Background

In randomised controlled trials (RCTs) in children, live attenuated influenza vaccine (LAIV) has demonstrated cross-protection against antigenically drifted influenza strains. However, low vaccine effectiveness (VE) was observed for LAIV in children in the 2014/2015 influenza season against drifted A(H3N2) strains.

Methods

This study evaluated the extent of drift for A(H3N2) strains during the 2014/2015 season. Antigenic characterisation of the 2014/2015 A/Texas/50/2012 H3N2 vaccine strain was evaluated using ECDC haemagglutination inhibition (HAI) tests. Ferret antisera raised against the A/Texas/50/2012 LAIV virus was reacted with 2014/15 H3N2 virus isolates. Egg-grown and cell-grown isolates were evaluated. The homologous virus HAI titre was divided by circulating virus HAI titre to give the HAI fold difference. For context, historical data on LAIV efficacy against drifted A/H3N2 viruses from RCTs in children were analysed by degree of antigenic match.

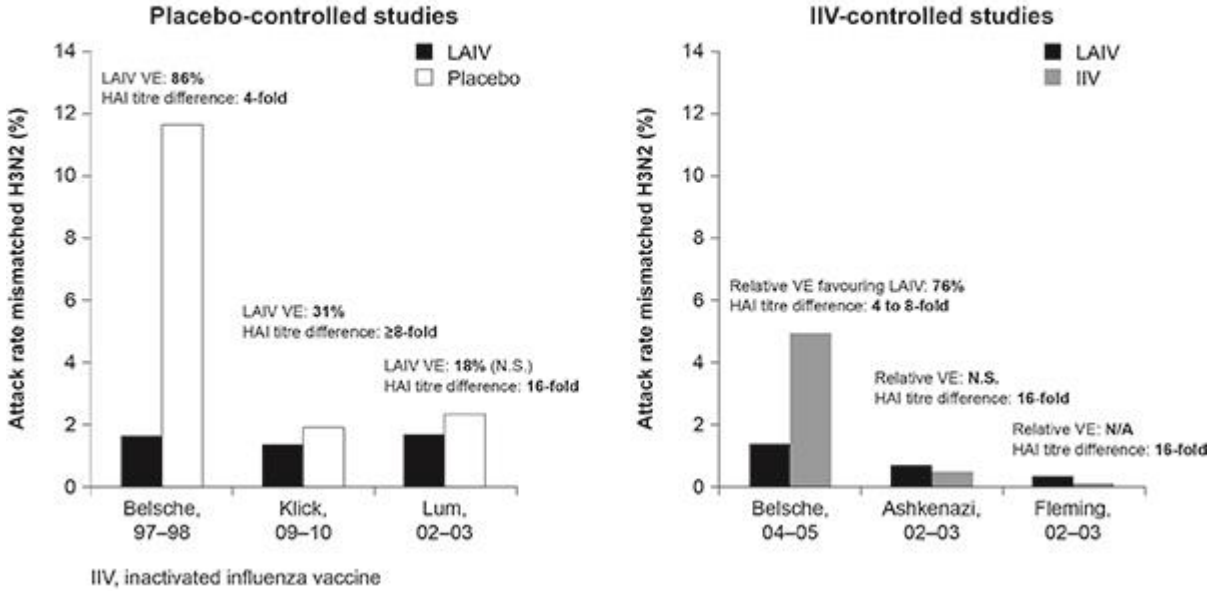
Results

HAI fold differences for egg-grown and cell-grown 2014/2015 circulating A/H3N2 viruses relative to A/Texas/50/2012 were 8-fold and ≥32-fold different, respectively (Table).

2014/2015 A/H3N2 virus antigenic characterisation			
Test virus	**Clade**	**A/Texas/50/2012 post-infection ferret antisera**	
HAI titre	**HAI fold change**		
A/Texas/50/2012 (homologous virus)	3C.1	1280	–
A/Switzerland/9715293/2013, cell	3C.3a	40	32
A/Switzerland/9715293/2013, egg	3C.3a	160	8
A/Stockholm/6/2014, cell	3C.3a	40	32
A/Stockholm/6/2014, egg	3C.3a	160	8
A/England/528/2014	3C.2a	<40	>32
A/England/530/2014	3C.2a	<40	>32

Upon review of historical LAIV efficacy data, LAIV demonstrated high efficacy in seasons with antigenic drift of 4–8-fold, but low efficacy with antigenic drift ≥8-fold (Figure 1).

Figure 1. Historical LAIV VE against drifted A(H3N2) strains and antigenic distance



IIV, inactivated influenza vaccine

Conclusions

The cumulative data demonstrate that LAIV cross-protection against drifted A(H3N2) strains has been high with a 4–8-fold HAI titre difference, but low with ≥8-fold difference, as occurred during the 2014/2015 season.

This study was sponsored by MedImmune, the biological division of AstraZeneca.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0730
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

FREQUENCY OF THE DIAGNOSIS "PNEUMONIA" IN CHILDREN IN GERMANY FOLLOWING THE INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINATION

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Background

Aim of this analysis was to investigate any potential impact of pneumococcal conjugate vaccines (PCVs: PCV7, and the higher-valent PCVs, PCV10 and PCV13) on the frequency of diagnosis "pneumonia" in children in Germany.

Methods

TheIMS Health VIP® panel was used to analyse the data continuously and retrospectively. The alterations of frequency of ICD 10 (10th revision of International Statistical Classification of Diseases and Related Health Problems) Pneumonia diagnosis (J18) were primary endpoints. Additionally, the sub-diagnosis lobar pneumonia (J18.1), frequently caused by pneumococci, was analysed. The period before launch of vaccines (2003-2006) was used as baseline and compared with diagnoses collected from 2007 to 2014. According to age cohorts the respective reduction was evaluated. The Poisson model was applied for statistical analysis.

Results

Two years after introduction of PCV7, a reduction of 17% was detectable with regard to the diagnosis "pneumonia" in children between 0 to 4 years. Until 2011, a slight increase in pneumonia diagnoses (J18) was visible for children in this age group, and even a considerable rise for children between 5 and 10 years. After introduction of higher-valent PCVs a significant ($p<0.0001$) decrease was evident for both age groups (31.1%/30.5% in 2013 vs. baseline). For lobar pneumonia (J18.1) the reduction of diagnoses was dramatic (87.6%) in children 0 to 4 years esp. in 2008. After a transient incline, a steady decrease since introduction of PCV10/13 was monitored (74.1% vs. baseline, $p<0.0001$). Altogether 804,023 less children aged 0 to 10 years suffered from pneumonia comparing the period 2007 to 2014 to the mean of baseline years.

Conclusions

This analysis revealed a significant decrease in pneumonia diagnoses in children after PCV7 vaccination and introduction of higher-valent PCVs.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0968
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINATION OF INFANTS ON PNEUMONIA HOSPITALIZATION IN ALL AGE GROUPS IN GALICIA (SPAIN)

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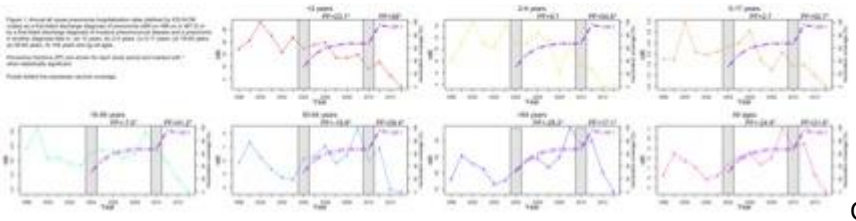
Background

7-valent pneumococcal conjugate vaccine (PCV7) was introduced in the private market in Galicia (Spain) in 2001 with 31 to 67% coverages. In 2010, 13-valent pneumococcal conjugate vaccine (PCV13) replaced PCV7, and it was included in the national immunization program in January 2011 with virtually 100% coverage. The objective was to assess direct and indirect benefits of PCV vaccination in Galicia over all-cause pneumonia hospitalizations (ACPH).

Methods

Annual hospitalization rates and preventive fractions (PF) (1–odds-ratio) were calculated using the official surveillance system for hospitalization data (CMBD) and compared between three study periods: pre-vaccination (1998-2003), PCV7-vaccination (2005-2009) and PCV13-vaccination (2011-2013). Changes in hospitalization rates for bone fractures and acute pyelonephritis were used as controls.

Results



Our study cohort included 34.394 patients with ACPH. A global reduction in ACPH of 21.6% (CI95%=19.4, 24.0) was observed with PCV13 vaccination but not with PCV7 (Figure). With PCV7 a significant decrease was only observed in children <2 years with a reduction of 23.1%(CI95%=10.9,33.6). With PCV13 this reduction was 58.0%(CI95%=47.6, 67.3) in <2 years, 54.8%(CI95%=43.1, 64.4) in 2-4 years, 52.7%(CI95%=39.6, 63.3) in 5-17 years, 41.2%(CI95%=35.0,46.9) in 18-49 years, 29.4%(CI95%=23.1, 35.2) in 50-64 years and 17.1%(CI95%=13.9, 20.2) in >64 years, respectively. These findings were not replicated in the control categories.

Conclusions

1 of each 5 pneumonia hospitalizations has been avoided since PCV13 introduction into the NIP of Galicia. These findings suggest that in the pre-PCV era, a large proportion of all-ages pneumonia hospitalizations were caused by the pneumococcal serotypes included in PCV7/PCV13. PCVs, and particularly PCV13, have shown an outstanding direct and indirect benefit against all-cause pneumonia hospitalization in our country

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0055
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

PERSISTENT ROTAVIRUS ACTIVITY IN OLDER CHILDREN AND ADULTS 5–6 YEARS AFTER UNIVERSAL ROTAVIRUS VACCINATION

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Background

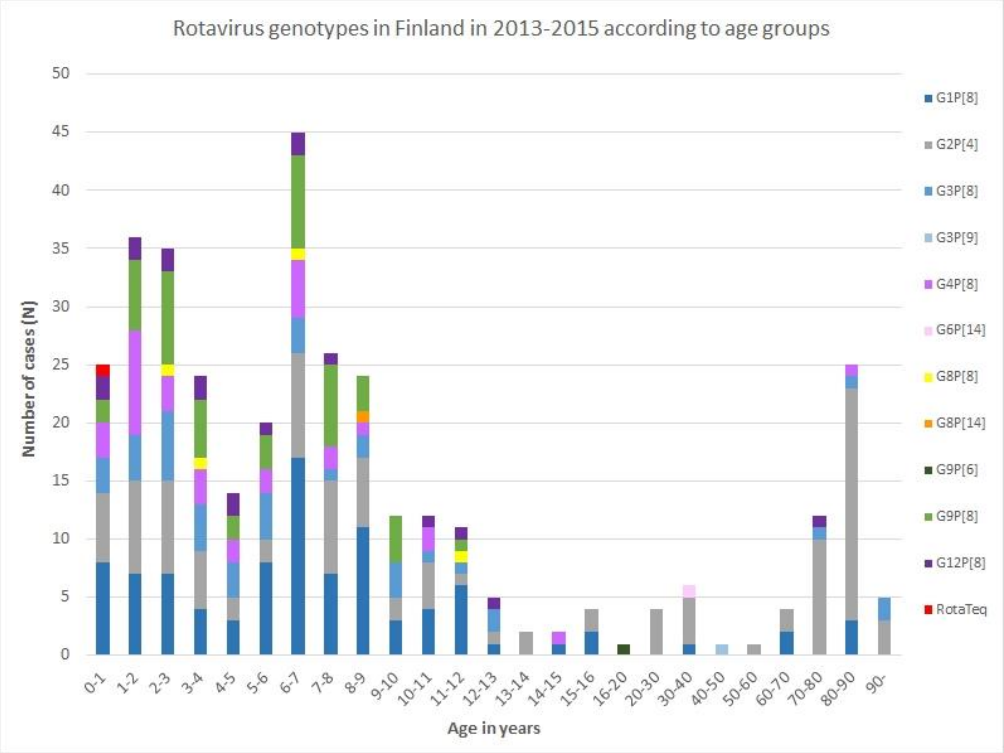
Rotavirus (RV) vaccination using RotaTeq® vaccine exclusively was introduced into the National Immunization Program (NIP) in Finland in 2009 and has reached a high (>95%) coverage. In the years 2009–2013 there was an 88% reduction in RV hospitalizations in Finland. Since mid 2013 all stool samples from laboratory diagnosed cases of RV gastroenteritis from the entire country have been referred to THL and onwards to the University of Tampere for genotyping.

Methods

RVs were G- and P-typed using RT-PCR, and the results were confirmed by sequencing. In addition, the genome encoding for VP6 was sequenced to distinguish between wild-type and vaccine origin (bovine) RVs.

Results

Two distinct RV epidemic seasons were observed in 2013–2014 and 2014–2015. Both seasons were late, each lasting until July. The age distribution (Fig.) showed two unusual clusters: one in older children 5–12 years of age and the other in people 70–90 years of age. In children, diverse genotypes of RV including G1P[8], G2P[4], G3P[8], G4P[8], G8P[14], G9P[8] and G12P[8] were observed without any obvious predominance. In contrast, most cases in the elderly were associated with G2P[4]. A vaccine derived RV was detected in only one infant aged 3 months.



Conclusions

It is concluded that RV disease can be controlled but not eliminated by vaccinations. Even at high vaccine coverage and high effectiveness of RV vaccine, RV activity continues to persist in unvaccinated older children and in the elderly. RV genotypes show greater diversity than before RV vaccinations.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0151
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

PNEUMOCOCCAL CARRIAGE BY CHILDREN AND THEIR PARENTS POST-PCV13 INTRODUCTION IN THE UNITED KINGDOM

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Background

In 2010 PCV13 was introduced into the UK routine infant vaccine schedule, replacing PCV7. This study measured the serotype distribution of pneumococcal carriage in children and their parents from the Thames Valley region in the post-PCV13 era.

Methods

Children aged between 13 and 48 months who had received three doses of PCV13 and their parents were recruited. Nasopharyngeal swabs were collected and processed according to WHO guidelines. Presumptive pneumococcal isolates underwent DNA extraction followed by molecular serotyping using the BµG@S SP-CPS microarray.

Results

Between February 2014 and August 2015, 985 children and 200 parents had swabs analysed. 483/985 (49.04%) swabs from children had pneumococcus isolated. NVTs represented the vast majority of isolates (96.07%), followed by the additional serotypes that are in PCV13 but not PCV7 (3.73%), and PCV7 serotypes (0.21%). Comparing these data with pre-PCV13 data showed significant reductions for the PCV13 serotypes 7F ($p=0.0177$), 19A ($p<0.0001$), and 3 ($p=0.0024$). NVTs 6C ($p<0.0001$) and 29 ($p=0.0305$) also had a significant decrease in prevalence. There was a significant increase in the NVTs 15A ($p=0.0097$) and 15B ($p<0.0001$). 21/200 (10.5%) parents had pneumococcus detected on their swabs. No PCV13 covered serotypes were detected from parent's swabs.

Conclusions

There was a significant decrease in the childhood carriage prevalence of PCV13 covered serotypes 7F, 19A, and 3, post-PCV13 compared with the pre-PCV13 era. Additionally, there is a significant reduction in carriage of serotypes 6C and 29, an observation that may reflect cross-reactivity of antibody. The continued expansion of NVTs in the carriage reservoir which coincides with increasing NVT invasive disease prevalence in the English population highlights the importance of continued surveillance of vaccine efficacy.

Clinical Trial Registration (Please input N/A if not registered)

NCT01996007

ESP16-0884
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

THE IMPACT OF HYPORESPONSIVENESS ON OPTIMISING PNEUMOCOCCAL VACCINATION FOR HIGH-RISK INDIVIDUALS

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Background and Objective

Controversy exists regarding the optimal use of the 23-valent pneumococcal polysaccharide vaccine(PPV23) for the protection of high-risk individuals, such as children and adults with immunocompromising conditions and the elderly. Such controversy derives from the limited vaccine effectiveness in such groups and the state of immune hyporesponsiveness to subsequent vaccination that is induced by PPV23.
In this review, we aim to collect all available data regarding PPV23-induced hyporesponsiveness and evaluate the impact of hyporesponsiveness in designing effective vaccination schedules for high-risk individuals.

Methods

A search in PubMed was conducted using the terms ‘hyporesponsiveness’ and ‘PPV23’. Peer-reviewed articles in English that reported immunogenicity data following pneumococcal vaccination in subjects previously vaccinated with ≥1PPV23 were included.
In total, 10peer-reviewed articles were identified that reported PPV23-induced hyporesponsiveness in healthy infants and children(2), high-risk adults(4) and the elderly(4).

Learning Points Discussion

Data from these studies show that previous PPV23 vaccinations impair the immune response to subsequent pneumococcal vaccination in a dose- and time-dependent manner;e.g. more PPV23 doses and shorter intervals between vaccinations lead to more prominent hyporesponsiveness. We propose that the main mechanism for this phenomenon is the depletion of serotype-specific B-memory cells by the free PPV23 polysaccharides, while circulating plasmacells could also block the stratification of naïve B-cells to germinal centers in response to subsequent vaccination by a negative feedback mechanism when the interval between vaccinations is short.
The clinical significance of hyporesponsiveness is yet unknown, but attenuated immune response could lead to increased susceptibility to pneumococcal disease. Consideration of all findings related to PPV23-induced hyporesponsiveness could optimize the use of PPV23 in high risk individuals. The importance of intervals between immunizations has not been taken into account in current recommendations.

ESP16-0278
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

BCG (BACILLUS CALMETTE-GUÉRIN) VACCINE IN CHILDREN WITH DIGEORGE / CHROMOSOME 22Q11.2 DELETION SYNDROME – IS IT SAFE?

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Background

Children withDiGeorge/Chromosome 22q11.2 deletion syndrome (DGS/22q11.2DS) may have a variable degree of immunodeficiency, which may contraindicate the use of live vaccines. *Bacillus* Calmette-Guérinvaccine (BCG) is administered at birth in Portugal, as part of national vaccination program. This study examined documented adverse reactions to BCG in DGS/22q11.2DS patients.

Methods

Retrospective audit of the clinical files of children with 22q11.2DS and DGS phenotype, considering: BCG vaccination; lymphocyte phenotype (flow cytometry) and proliferative responses (PR) to antigens and mitogens; BCG local adverse reactions in a 12 month window (abscesses, lymphadenitis, ostiitis/osteomyelitis, disseminated disease, hospitalization and mortality).

Results

Twenty-three children with DGS/22q11DS were identified, 65.2% were male and the average age at diagnosis was 11.3 months.

A total of 18 (78%) children received BCG vaccine. All had evidence of thymic activity attested by the presence of naïve T cells and recent thymic emigrants (CD31+). Three had moderate CD4 lymphopenia (15%-24%) and those featured abnormal PR: one to mitogens, purified protein derivative (PPD) and tetanus toxoid (TT); one to PPD and TT; and one just to PPD. Additionally, from the 15 with normal CD4 counts, one had abnormal PR to mitogens, four to PPD and two to TT.

No adverse reactions were reported.

Conclusions

In our small cohort BCG vaccine given at birth was well-tolerated even in children with moderate CD4 lymphopenia and those with abnormal PR to antigens/mitogens. In the absence of severe immunodeficiency BCG may be safe in DGS/22q11.2DS children and no specific management may be required in those vaccinated.

ESP16-0792
E-POSTER DISCUSSION SESSION 12 - VACCINES 3 (station 5)

MENINGOCOCCAL B VACCINATION AND FEVER: AUDIT OF MANAGEMENT IN THE REGIONAL CHILDREN'S HOSPITAL IN NORTHERN IRELAND.

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Background

Invasive Meningococcal Disease (IMD) is an important cause of morbidity and mortality. *Neisseria meningitidis* serotype B is the most common cause of IMD in the UK. In September 2015, the JCVI recommendation for a 4CMenB vaccination programme was implemented. Immunisation with 4CMenB causes pyrexia. Pyrexia is present in up to 70% of infants and up to 40% infants with administration of paracetamol.

We audited management of vaccine reactions in this group of infants with reference to the NICE guidelines.

Methods

We performed a prospective audit of all infants under 6 months attending to a Paediatric Emergency department after receiving the 4CMenB vaccination.

Results

26 infants have been identified to date, 21 of which presented with pyrexia. 25 were given paracetamol.

16 infants had blood tests taken, 12 were admitted to hospital and 8 received broad spectrum antimicrobials. Leucocytosis was common in those who had bloods taken and most patients were admitted to hospital. Length of stay was 11-64 hours. All cultures taken were negative.

Table showing investigations performed on infants presenting after 4CMenB vaccination

	Bloods	CSF	Antibiotics	Urine	Admitted
Fever n=21	12	4	7	15	10
Fever +irritable or poor colourN=13	9	4	6	8	7
Fever + WCC >15N=8	8	3	4	8	7

Conclusions

Infants under 6 months of age are a vulnerable group for serious bacterial infection, with pyrexia an important indicator. NICE guidelines exist on management of fever in infants, but do not take into consideration the subgroup of infants post 4CMenB vaccination. Leucocytosis with fever is common in this group, and drives further investigation and antimicrobial administration. We suggest a guideline to reduce unnecessary investigation, broad spectrum antibiotic use and admission to hospital.

ESP16-1038
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

COMPARISON OF THE EPIDEMIOLOGY OF NEONATAL INFECTIONS BETWEEN TWO EUROPEAN COUNTRIES FROM THE NEONIN INFECTION SURVEILLANCE NETWORK

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[3]University of Athens- School of Medicine, The Stavros Niarchos Foundation- CLEO, Athens, Greece
[4]Evelina London Children`s Hospital, Neonatal Services, London, United Kingdom
[5]University of Tartu, Medical Microbiology, Tartu, Estonia
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Background

Neonatal sepsis is a major cause of morbidity and mortality. The epidemiology of neonatal infections differs across Europe.This study aims to compares the epidemiology of neonatal sepsis between the UK and Greece using data from the neonIN infection surveillance network

Methods

neonIN is an international web-based surveillance database for culture proven neonatal infections. Data from January 2012 to August 2015 were extracted. Early-onset sepsis (EOS) was defined as occurring within 48 hours of birth

Results

A total of 2363 episodes of infection (involving 2151 infants) were recorded. There was no significant difference in the overall infection incidence between Greece and the UK (50 vs 39 /1000 NNU-admissions (p=0.28). However, when CoNS cases were excluded infection incidence was higher in Greece (35 vs. 19/1000 NNU-admissions (p<0.001). Details of incidence, prevalence and pathogens distribution by country are shown in the table. Babies in the UK were of lower gestational-age and birth-weight compared to Greece (p<0.001 for both). In Greek units, higher rates of resistance of *Klebsiella spp* to aminoglycosides (p<0.001) and 3rd generation cephalosporins (p=0.001) and of *Enterobacter spp* to

carbapenems (p=0.002) were recorded

		Greece (16 NNUs, n=459)	UK 30 NNUs, n=1904	p value
Incidence rates by country	EOS Incidence (/1000 NNU admissions)	4.6	6.9	0.006
	LOS Incidence (/1000 NNU admissions)	45.4	32.2	0.001
	Overall GP (n (%))	188 (41%)	1447 (76%)	<0.001
	Overall GN (n (%))	225 (49%)	400 (21%)	<0.001
	Overall fungi (n (%))	46 (10%)	57 (3%)	<0.001
Most common pathogens by country	Most common pathogen in EOS-GPS (CoNs excluded)	GBS (30%)	GBS (62.2%)	0.008
	Most common pathogen in EOS-GNS	*E. coli* (47.1%)	E. coli (73.9%)	0.044
	Most common pathogen in LOS-GPS (CoNs excluded)	*E.faecium* (37.5%)	*E.faecalis* (26.3%)	-
	Most common pathogen in LOS-GNS	*Klebsiella* spp. (38.7%)	*E. coli* (35.5%)	-
	Most common fungi in LOS	*Candida parapsilosis* (52.3%)	*Candida albicans* (65.1%)	-

Median (IQR)

GP: Gram-positive bacteria, GN: Gram-negative bacteria, GPS: GP sepsis, GNS: GN sepsis, LOS: Late-onset sepsis, CoNS: Coagulase-negative staphylococci

Conclusions

Variations in disease burden, pathogen distribution and antibiotic resistant patterns exist between the two countries, particularly amongst Gram-negative organisms. Understanding the basis for these differences may lead to new strategies for prevention.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0184
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

EVALUATION OF THE G145R MUTANT AS A MINOR FORM IN MOTHER-TO-CHILD TRANSMISSION OF HEPATITIS B VIRUS

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Background

A single mutation of the amino acid 145 of the surface protein (G145R) of HBV is well known as one of the causes which induce breakthrough infection.

Methods

The major form and minor form of the G145R mutant was detected in the three groups using LNA probe-based real-time PCR assay. Failure group (retrospective study): HBV children, who were born to HBV carrier mothers, became HBV carriers despite immnoprolylaxis (n=25). Control group (retrospective study): HBV carriers who had no history of receiving HB vaccine or HBIG (n=126).Pregnant group (prospective study): pregnant women with chronic HBV infection (n=31).

Results

In the failure group, 6 (24%) were positive for the PCR (major from;2, minor form 4). In the control group, 13 (10.1%) were positive for the PCR (major from;0, minor form 13). The detection rate of the G145R mutant was associated with the positivity of HBeAg. Deep sequencing was performed in the total of 11 children who were positive for the PCR. In the failure group, the frequency of the G145R ranged from 0.54% to 6.58%. In the control group, the frequency of the G145R ranged from 0.25% to 4.10%. Of the 31 pregnant women, 4 (12.9%) were positive for the PCR (major from;0, minor form 4). Four babies were born from pregnant women with G145R mutant but one baby dropped out of the study. After the completion of immunoprophylaxis, 2 infants became negative for HBsAg. One became negative for HBsAg after the first dose HB vaccine.

Conclusions

Immunological pressure induced by immunoprophylaxis and HBeAg positivity could increase the frequency of the G145R mutant. Immunoprophylaxis could prevent breakthrough infection in children born to HBV carrier mother infected with a minor form of the G145R mutant.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0728
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

RISK FACTORS ASSOCIATED WITH HEARING LOSS AND NEUROLOGIC IMPAIRMENT IN THE SPANISH NETWORK OF INFANTS WITH CONGENITAL CYTOMEGALOVIRUS INFECTION (REDICCMV)

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Background

We aimed to study risk factors associated with hearing loss and neurologic abnormalities at 12 months of age in the Spanish cohort of children with congenital cytomegalovirus infection (cCMV; REDICCMV).

Methods

A prospective multicentric study was performed from January-2011 to May-2015 in Spain. All children with confirmed cCMV were included. Hearing loss (>25dB in ABR) and neurologic abnormalities (motor impairment, microcephaly, epilepsy and neurodevelopmental delay evaluated by a pediatric neurologist) were studied at birth and at 12 months of age.

Results

297 children with cCMV from 34 hospitals were included. 229 (82.7%) children were diagnosed during the fetal or newborn period, and 111/225 (49.3%) were symptomatic at birth. Among asymptomatic infants at birth (n=61), 23.0% and 7.8% presented hearing loss and neurologic abnormalities at 12 months, respectively. Symptomatic children at birth presented higher risk of hearing loss and neurologic sequelae at 12 months of age (OR:3.2[CI95%:1.5-7.2] and OR:9.0[CI95%:2.9-27.9]respectively). Blood viral load at birth was not associated with sequelae. Children with severe disease were given a longer course of antiviral treatment. In a multivariate logistic regression analysis, only hearing loss at birth was associated with hearing loss at 12 months (OR:33.2 [IC95%9.8-112.4]; p=0.0001). GPT>80 IU/L and hearing loss at birth were associated with neurologic abnormalities at 12 months (OR:7.5[IC95%:1.0-57.0]; p=0.05 and OR:6.9[IC95%:2.1-22.2], p=0.001 in both).

Conclusions

In our cohort, symptomatic cCMV newborns were at high risk of sequelae at 1 year of age, which also affected one fourth of asymptomatic patients at birth. Hearing loss at birth was associated with both hearing loss and neurologic impairment at 1 year of age; neonatal hepatitis was also a risk factor for neurologic sequelae at 12 months of age.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0523
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

PRESENCE OF CLOSTRIDIUM PERFRINGENS FROM PREMATURE NEONATES WITH A DIVERSE TOXIN ARSENAL: ASSOCIATIONS WITH NECROTISING ENTEROCOLITIS ?

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Background

Clostridium perfringens is well-established as part of the commensal microbiota in adults and neonates but has been repeatedly associated with Necrotising Enterocolitis (NEC) – an inflammatory bowel disease affecting premature neonates. We sought to examine the toxin profiles of *C. perfringens* isolates from premature neonates and determine associations with the development of NEC.

Methods

C. perfringens was cultured from frozen faecal samples taken weekly from 348 premature infants (under 32 weeks gestation) enrolled into the Neonatal Microbiota study. Isolates were toxin-typed using PCR to screen for ten toxin genes.

Results

99 infants (28.45% of the cohort) carried *C. perfringens* at some time during their stay. In general, strains harboured multiple toxin genes; 20% of infants carried isolates harbouring ≥ four toxin genes. The toxin arsenal generally diversified over time. Half of isolates carried the beta2 toxin gene (48.64%) – putatively involved in enteric disease –, and the pore-forming toxin perfringolysin O (51.02%). The necrotising beta toxin gene was present in 10.20% of isolates. The NetB toxin gene, until now considered to be exclusive to cases of necrotic enteritis in poultry, was found in 3.40% of isolates.

A NEC-toxin signal is yet to be established; there was no significant difference between the prevalence of each toxin gene in *C. perfringens* isolates from NEC cases versus healthy infants.

Conclusions

We demonstrate a high and diverse toxin gene burden in *C. perfringens* carried by premature neonates. We are currently culturing strains from 2-year faecal samples from the same cohort to assess longevity of carriage and toxin gene succession.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0879
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

PREVENTION AND TREATMENT OF FETAL CYTOMEGALOVIRUS INFECTION WITH CMV-HYPERIMMUNE GLOBULIN: A MULTICENTER STUDY IN MADRID

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Background

Aims: To investigate the use of cytomegalovirus (CMV) hyperimmune globulin (HIG) in prevention and treatment of CMV fetal infection.

Methods

A retrospective observational study comprising all pregnancies treated with CMV-HIG(2009-2015) in three hospitals in Madrid was conducted. Investigators offered HIG treatment in pregnancies with a CMV primary infection (prevention group) or with fetal infection (treatment group: positive PCR in amniocentesis/cordocentesis).

Results

36 mothers received at least one dose of HIG. No severe adverse events were observed. Prevention group included17 pregnancies and one of them was interrupted due to abnormal cordocentesis. Fetal infection was confirmed in 7/17(38.5%) patients, and 1/16(5.9%) was symptomatic at birth (mild hearing loss, and good neurodevelopmental outcome at 12 months of age). No other children presented long term sequelae at 12 months in the prevention group. Treatment group included 19 pregnancies with positive PCR (amniotic fluid/fetal blood). One child was born uninfected. Hearing loss at birth was present in 4/19(21%), motor impairment in 3/19(16%) and 9/19(47%) were symptomatic at birth. Three children from treatment group were lost to follow up. At 12 months, three children (3/16;18.8%) in the treatment group presented motor impairment and 4 (4/16;25%) presented hearing loss. Fetuses with abnormalities in CNS in fetal US before HIG treatment, presented a high risk of long term sequelae (p=0.009; OR=77; 95%CI:3-1954).

Conclusions

In our population CMV-HIG treatment was not associated to relevant adverse events. A high rate of infected fetuses were found in the prevention group. Almost half of children in the treatment group had symptoms at birth. Fetuses without CNS abnormalities in US before HIG treatment presented low risk of long term sequelae. HIG seems not to be useful in fetuses with previous brain abnormalities in US.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1060
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

ENTEROBACTERIACEAE INFECTION IN HOSPITALISED NEONATES IN THE NEONIN INFECTION SURVEILLANCE NETWORK

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Background

Enterobacteriaceae are a common cause of hospital-acquired (HAI) infections and outbreaks in neonatal units (NNUs). The emergence and spread of resistance in *Enterobacteriaceae* infections is complicating the treatment of serious nosocomial infections. We aimed to describe the epidemiology and characteristics of *Enterobacteriaceae* infections across European countries participating in a neonatal infection surveillance network.

Methods

neonIN is an international surveillance database for culture proven neonatal infections. *Enterobacteriaceae* cases between 2012 and 2014 were extracted. Late-onset sepsis (LOS) was defined as occurring after 48 hours from birth. Repeated growth of the same organism was considered the same episode if occurring within 7 days.

Results

There were 464 episodes from 49 NNUs. The incidence by country and details of pathogen distribution is shown in the table. Overall, *E.coli* was the commonest species (197, 42%) followed by *Klebsiella sp.* (128, 28%). EOS was mainly due to *E.coli* infections (53, 91%). *Enterobacteriaceae* infection was associated with a lower gestational-age than other species (median 27,p<0.001). Babies with *Enterobacteriaceae* infection in the UK are of younger gestational-age and smaller birth-weight (p<0.001) than those in Greece and Estonia. Overall there was moderate resistance to 3rd generation cephalosporins (78/391, 20%) and aminoglycosides (102/532, 19%) while almost all tested isolates were susceptible to

		UK (29 NNUs, n=298)	Greece (14 NNUs, n=298)	Estonia (6 NNUs, n=298)
Incidence by country	Incidence of IE (/1000 NNU admissions)	40.74	47.82	30.45
	Incidence of GNI episodes (/1000 NNU admissions)	8.25	19.92	8.46
	Incidence of *Enterobacteriaceae* (/1000 NNU admissions)	6.91	18.24	7.95
Most common pathogens by country	*E.coli* n (%)	148 (50%)	40 (34%)	9 (19%)
	Klebsiella sp n (%)	65 (22%)	47 (40%)	16 (34%)
	Enterobacter sp n (%)	50 (17%)	21 (18%)	19 (40%)
	Serratia sp n (%)	18 (6%)	8 (7%)	2 (4%)
	Citrobacter n (%)	9 (3%)	1 (1%)	0 (0%)
	Proteus n (%)	2 (1%)	0 (0%)	1 (2%)
	Other	6 (2%)	2 (2%)	0 (0%)

Table: Incidence and pathogen distribution by country (IE: infection episodes, GNI: Gram-negative infection).

Conclusions

Enterobacteriaceae infections are an important cause of LOS in preterm infants. The disease burden and epidemiology varies by country; knowledge of local antibiotic susceptibility is required to direct appropriate empiric antibiotic therapy in LOS and to guide effective infection-control measures.

On behalf of the Neonatal Infection Surveillance Network (neonIN)

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1084
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

COAGULASE-NEGATIVE STAPHYLOCOCCAL (CoNS) INFECTIONS IN UK NEONATAL UNITS (NNUs)

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Background

Advances in neonatal care have resulted in improved survival of preterm neonates. However, invasive interventions contribute to higher rates of infections in this population. This study describes the epidemiology of CoNS infections in UK NNUs participating in a neonatal infection surveillance network (neonIN).

Methods

neonIN is a web-based surveillance system (www.neonin.org.uk). Details of CoNS cases from participating UK NNUs (2004-2014) were extracted. CoNS infection was considered significant if the infant was treated with at least 5 days of appropriate antibiotics. Late-onset sepsis (LOS) was defined as occurring after 48hrs of birth. Repeated growth within 10 days was considered the same episode.

Results

2541 CoNS episodes were reported; incidence 27.0/1000 NNU-admissions. The majority were LOS (93%), representing 59% of all LOS episodes. Baseline characteristics are displayed in table-1. CoNS primarily occurred in extremely premature (83%) and ELBW (62%) infants ($p<0.001$), and were isolated almost exclusively from blood (96%). Since 2011, CRP has also been reported; and 683/1,158 (59%) episodes had a CRP≥10 mg/L. 253 CoNS-episodes were subspeciated: *S. epidermidis* (155/253), *S. capitis* (76/253) and *S. haemolyticus (11/253).* Compared to *S. epidermidis*, infants with *S. capitis* were more likely to be ELBW (p=0.019), <32 weeks (p=0.004) and have a later PNA (p=0.094).

Resistance data were available for 1390/2541 (55%) episodes with high rates of resistance to flucloxacillin (87%), moderate to teicoplanin (17%) and low to vancomycin (2%).

	Infection Episodes (N=2541)
Sex (male), n (%)	1,424 (56%)
Gestation (weeks)	26 (25-30)
Birth weight (g)	860 (688-1280)
PNA (days)	13 (7-30)
C-reactive protein (mg/L)	16 (2-54)
CVC in-situ, n (%)	1,434 (61%)
CVC removal, n (%)	601 (35%)

Table-1 median (IQR). LOS: late-onset sepsis, occurring after 48-hours of age. PNA: post-natal age. CRP: maximum CRP within 48 hours of the positive culture. CVC: central-venous catheter. CVC removal: removal of the CVC due to the infection episode

Conclusions

This is the largest reported cohort of neonatal CoNS infections. CoNS are an important cause of infection in hospitalized neonates but features may differ among subspecies. Antimicrobial susceptibility data support the use of vancomycin in clinically significant LOS CoNS episodes.

On behalf of the Neonatal Infection Surveillance Network (neonIN)

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0243
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

ETIOLOGY OF FEVER OCCURRING WITHIN 30 DAYS OF PEDIATRIC LIVER TRANSPLANTATION

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Background

Fever in liver transplant recipients suggests presence of infection and/or rejection, which requires immediate and appropriate intervention. However, the etiology of fever is unclear at the time of onset.

Methods

We evaluated children under 15 years of age who underwent their first liver transplantation at our institution over one year. All febrile episodes that occurred within 30 days of liver transplantation were identified from the medical records. Recipient's characteristics, surgical data, vital signs, medical device, laboratory data at the onset of fever, that differentiated bacterial infection from acute rejection was analyzed. Long term outcome (mortality and re-transplantation beyond 30 days) was also evaluated.

Results

Eighty-eight liver transplantations (86 living and 2 deceased donor) were performed during the study period. One hundred and thirty three febrile episodes were observed in 77 recipients. Of these 133 febrile episodes, 27 (20%) had definitive evidence of infection (8 blood stream infections including 5 catheter related infections, 6 urinary tract infections, 5 peritonitis, 5 pneumonia, and 3 enterocolitis), and 7 (5%) had biopsy proven acute rejection. There were no patients with cytomegalovirus or Epstein Barr virus infection. Of the 99 febrile episodes that were managed based on clinical judgment, 9 episodes were treated as infection, and 23 were treated as rejection. Overall, fifty three episodes improved without any antibiotics. Increasing bile acid level was statistically associated with acute rejection compared with bacterial infection (P=0.01). Bacterial infection was associated with increased mortality (bacterial infection n=3, rejection n=1, P=0.02), whereas acute rejection was associated with increased risk of re-transplantation (bacterial infection n=1, rejection n=2, P=0.005).

Conclusions

Increasing bile acid levels in children who developed fever within 30 days of liver transplantation suggests acute rejection rather than infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0857
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

BURDEN OF VARICELLA IN PAEDIATRIC ONCOLOGY PATIENTS AFTER INTRODUCTION OF GENERAL VARICELLA VACCINATION IN BAVARIA (GERMANY)

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Background

Varicella may cause severe complications in immunocompromised patients. We investigated changes in the burden of varicella in paediatric oncology patients during the first seven years following introduction of routine varicella childhood vaccination in Germany.

Methods

An annual data query on hospital databases of 22-29 paediatric hospitals in Bavaria (Germany) was performed from 2005 to 2011. All children <17 years of age with an ICD-10 discharge diagnosis of varicella were reported with basic demographic data, diagnostic and procedural codes, duration of hospital stay and outcome. Oncology and non-oncology varicella patients were compared, and annual incidences were estimated.

Results

42 children (3.3%; 57% males; median age 4 years) of a total of 1,263 paediatric varicella-associated hospitalizations (VAH) were reported with an underlying malignancy (67% acute lymphoblastic leukaemia, 21% solid tumors, 12% other leukaemia or lymphoma). Oncology varicella patients showed most frequently haematological (29%) and gastrointestinal complications (19%), and non-systemic (19%) and systemic co-infections (12%). There were no fatalities. Compared to non-oncology varicella patients, complications occurred significantly less often in oncology varicella patients (62% vs. 77%, p=0.041), especially neurological (5% vs. 19%) or respiratory tract complications (7% vs. 29%). However, oncology varicella patients stayed longer in the hospital (median 5 vs. 3 days; p<0.001). Incidence of VAH in paediatric oncology patients decreased from an annual average of 4.9 per 10^6 children for the period 2005-2007 to 1.5 per 10^6 children for the period 2009-2011.

Conclusions

The lower proportion of complications in oncology varicella patients may suggest more frequent or rapid admittance for early therapy compared to non-oncology varicella patients. The decrease of VAH in paediatric oncology patients may result from either herd protection effects or pre-existing vaccine-induced immunity in the patients themselves.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0588
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

EPIDEMIOLOGY OF VIRAL INFECTIONS AND ASSOCIATED RISK FACTORS IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANT

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Background

Viral infections are a significant cause of morbidity and mortality in paediatric transplantation populations. We determined the epidemiology, the characteristics and the associated risk factors of these infections in paediatric patients undergoing hematopoietic stem cell transplant (HSCT).

Methods

All children undergoing HSCT from 2011-2015 were prospectively followed at the Stem Cell Transplant Unit of our Institution. Initiation of preemptive therapy followed serial weekly monitoring for herpesviruses, BK and adenovirus (AdV) by use of quantitative PCR.

Results

A total of 192 HSCTs (autologous/allogeneic: 53/139) were performed in 165 subjects (median age: 5.6 yrs), and the median follow-up was 27 months. Cumulative incidence of viral infections was 59.5% (95% CI: 51.5-67.5) with a median onset of 105 days (0-946) post-transplant. Viruses most commonly isolated were CMV (36.7%), BK (20.6%) and EBV (17.4%)and CMV, EBV, BK, and AdV infections were more frequent in allogeneic versus autologous transplants ($p<0.05$). Haploidentical, compared to HLA fully matched HCSTs, presented the highest incidence rates for herpes viruses (Log-Rank: $p<0.001$, Figure 1). Incidence rates for AdV were increased in recipients from mismatched ($p=0.021$), as opposed for BK, where rates were significantly higher in recipients from matched donors ($p<0.001$). BK infections were more common in patients with hematological malignancies compared to those with non-haematological disorders ($p=0.002$), while CMV in transplants with immunodeficiencies ($p=0.037$). Following multivariate analysis, foreign ethnicity, umbilical cord blood graft, and increased age were statistically significantly associated with increased hazard of CMV (HR=0.357, $p=0.001$), HHV-6 (HR=111.74, $p=0.010$), and BK (HR=2.959,$p=0.031$) infections, respectively. The overall 5-year survival was 68 % (95% CI, 59.8-76.2), and viral

disease attributed mortality was 10.2%.

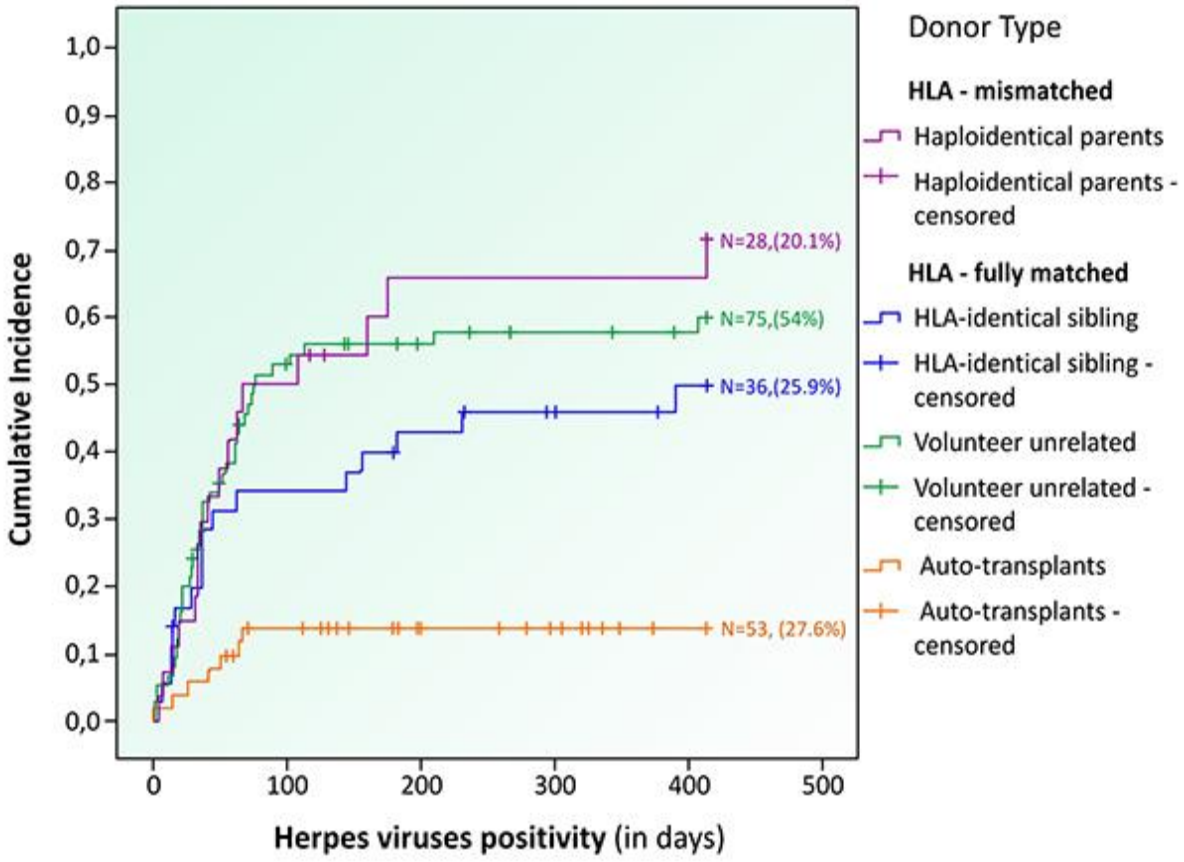

Figure 1. Cumulative probability of herpes viruses post HSCT based on donor type and HLA match

Conclusions

Viral infections were common among paediatric HCST, and were significantly associated with certain demographic and transplantation characteristics.

ESP16-0949
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

CLINICAL RELEVANCE OF A POSITIVE POLYMERASE CHAIN REACTION FOR RESPIRATORY VIRUSES IN CHILDREN WITH CANCER, FEVER AND NEUTROPENIA

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Background

Infection is a main cause of morbidity and mortality in children with cancer and febrile neutropenia(FN). Significance of molecular detection of respiratory viruses(RV) and their relation with disease is not clear. The aim of this study was to determine the clinical relevance of a positive polymerase chain reaction(PCR) for RV in children with cancer and FN.

Methods

Children with cancer,presenting with FN at five hospitals in Santiago,Chile, were prospectively evaluated(May,2012-July,2015) by clinical examination,blood cultures and nasopharyngeal sample for 17 respiratory viruses multiplex-PCR. Clinical outcome variables were determined.

Results

770 episodes of FN were enrolled. 211 episodes with detection of ≥1RV were analyzed. The median age was 60 months and patients consulted with a median of 2 hours from the onset of fever. On admission, 38%(n=82) presented upper respiratory tract infections(URTI), 21%(n=45) lower respiratory tract infection(LRTI) and 40%(n=84) did not present any respiratory symptom. Most frequents RV detected were rhinovirus(48%),RSV(17%),parainfluenza(14%) and influenza(8%). On admission,60% of patients with positive-PCR presented respiratory symptoms/signs,increasing to 80% at discharge(p=0.0001).URTI episodes increased from 39%(n=82) to 41%(n=86) at discharge,while LRTI significantly increased from 21%(n=45) to 33%(n=69;p=0.01) at discharge. 50% of asymptomatic episodes at admission presented URTI/LRTI at discharge.In the control group(no pathogen detected) we observed only 26%(n=79) of episodes with respiratory symptoms/signs($p<0.05$) at admission without significant progression to LRTI.

Conclusions

In children with cancer and FN,positive-PCR for RV in a sample obtained few hours after the onset of fever was associated with respiratory symptoms in 60% of episodes and increased significantly to 80% at discharge. 8 out of 10 children with a positive-PCR at admission developed respiratory disease. A significant progression from URTI to LRTI was observed in the positive-PCR group compared to a control group (FONDECYT-Grants#1130911-1120800).

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0605
E-POSTER DISCUSSION SESSION 13 - CONGENITAL AND PERINATAL INFECTIONS 1/ INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS (station 7)

REDUCED INCIDENCE OF NEONATAL EARLY ONSET GROUP B STREPTOCOCCAL INFECTION WITH RISK BASED INTRAPARTUM ANTIBIOTIC PROPHYLAXIS - A POPULATION BASED STUDY

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Background

National guidelines advocating risk based intrapartum antibiotic prophylaxis (IAP) for prevention of neonatal early onset group B streptococcal (EOGBS) disease were issued in Sweden 2008. The present aims were to investigate the incidence of EOGBS disease before/after promulgation of IAP guidelines, and the occurrence of risk factors and obstetric management in case mothers.

Methods

National registers were searched for a diagnosis of EOGBS disease in infants born 2006-11. Medical records of infants and mothers were retrieved and scrutinized. Chi2 was used for statistical analysis.

Results

550 cases with diagnosis of EOGBS disease were identified. In 528 (96%) the medical records were obtained. 228 cases were verified with positive blood culture, yielding an incidence of 0.34 per 1000 live births. Comparing the time periods 2006-08 and 2009-11 there was a significant decrease from 0.39 to 0.30‰ (p=0.036). There were 168 additional cases with clinical GBS sepsis and/or pneumonia. Including all EOGBS morbidity, the incidences during the two time periods were 0.72 and 0.49‰ (p=0.006).

In 192 out of 228 (84%) verified cases maternal records were available. In 100 (52%) of these parturients ≥1 risk factor was present and in 84 IAP was not administered. In most of these women (85%) the time in the delivery unit would have allowed IAP administration ≥4 h before birth as recommended. There were 5 case mothers given adequate IAP. All had prolonged rupture of membranes (ROM) and fever intrapartum.

Conclusions

The release of national guidelines for risk based IAP coincided with a reduced incidence of neonatal EOGBS infection. A stricter adherence to these recommendations could decrease the incidence even further. EOGBS sepsis may develop despite adequate IAP, particularly in infants of parturients with prolonged ROM and fever.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0326
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

INFECTION WITH CANDIDA ALBICANS CAUSES REDUCED PICD IN CORD-BLOOD MONOCYTES DUE TO IMPAIRED TLR2-SIGNALLING

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Background

Bacterial phagocytosis initializes apoptosis in monocytes (phagocytosis induced cell death, PICD). PICD in neonatal monocytes (CBMO) is reduced in bacterial infections. Invasive fungal infections with *Candida albicans* (*C. albicans*) cause poor outcome and occur frequently in extremely low birthweight (ELBW) infant.

Methods

FACS-based phenotyping (TLR2, TLR4, CD14) and intracellular characterization (P38-phosphorylation, TNF-a-secretion, cleaved caspase-8, -3) of monocytes, isolated from cord blood (CBMO) and blood from adults (PBMO). Infection with GFP-expressing *C. albicans* strains. Kinetics of phagocytosis indices, apoptosis by hypodiploid nuclei (Nicoletti), nick-strand breaks (TUNEL) were analyzed (FACS). In order to show TLR2-involvement, an aTLR2-blocking antibody (aTLR2 Ab) was used. To provide evidence for specificity, TLR-agonists (LPS, Pam3Cys, FSL-1, Zymosan) were used.

Results

Post infection (p.i) phagocytosis indices of PBMO and CBMO were similar. With low basal TLR2- and higher TLR4-expression, specifically TLR2 up-regulation with consecutive MAP kinase P38-phosphorylation and downstream expression of TNF-a were stronger on PBMO after *C. albicans* infection ($p < 0.005$ vs. CBMO). P.i., intracellular caspase-8 and -3 concentrations were higher in PBMO ($p < 0.05$ vs. CBMO), and PICD as well was found more prominent in PBMO ($p < 0.05$ vs CBMO). Utilizing aTLR2 Ab resulted in a significant reduction of P38-phosphorylation, TNF-a-secretion, caspase-8 and caspase-3 concentrations, and, consecutively in an inhibition of PICD of PBMO.

Conclusions

TLR2 expression is regulated by *C. albicans* infection. Regulation of TLR2 on monocytes of adults (PBMO) and neonates (CBMO). *C. albicans* infection induces PICD in monocytes via TLR2-signalling. Pro-apoptotic signaling in *C. albicans* infected CBMO is reduced.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0657
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

CHANGING TOXOPLASMA SEROPREVALENCE IN NORTHERN IRELAND

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Background

Toxoplasma gondii is the causal agent of toxoplasmosis, a common parasitic infection of humans acquired either by ingestion of oocysts voided in cat faeces or tissue cysts in undercooked meat. In humans, infection is mainly asymptomatic or accompanied by mild self-limiting symptoms. Infection or reactivation in immunocompromised patients can have serious clinical consequences. Primary infection in pregnancy can lead to miscarriage, stillbirth or severe congenital toxoplasmosis. The majority of infected neonates do not have detectable disease at birth but carry a significant risk of developing ocular disease in later life. Historically, Northern Ireland was considered an area with a particularly high human toxoplasma seroprevalence of 40% but this relates to samples from several decades ago.

Methods

A convenience set of 5787 samples received from January 2012 until September 2015 were tested for toxoplasma IgG using either Vidas Toxoplasma IgG II assay (bioMérieux UK Ltd, Basingstoke, England) or Elecsys Toxo IgG (Roche Diagnostics, Rotkreuz, Switzerland). Equivocal results were regarded as seronegative for analysis.

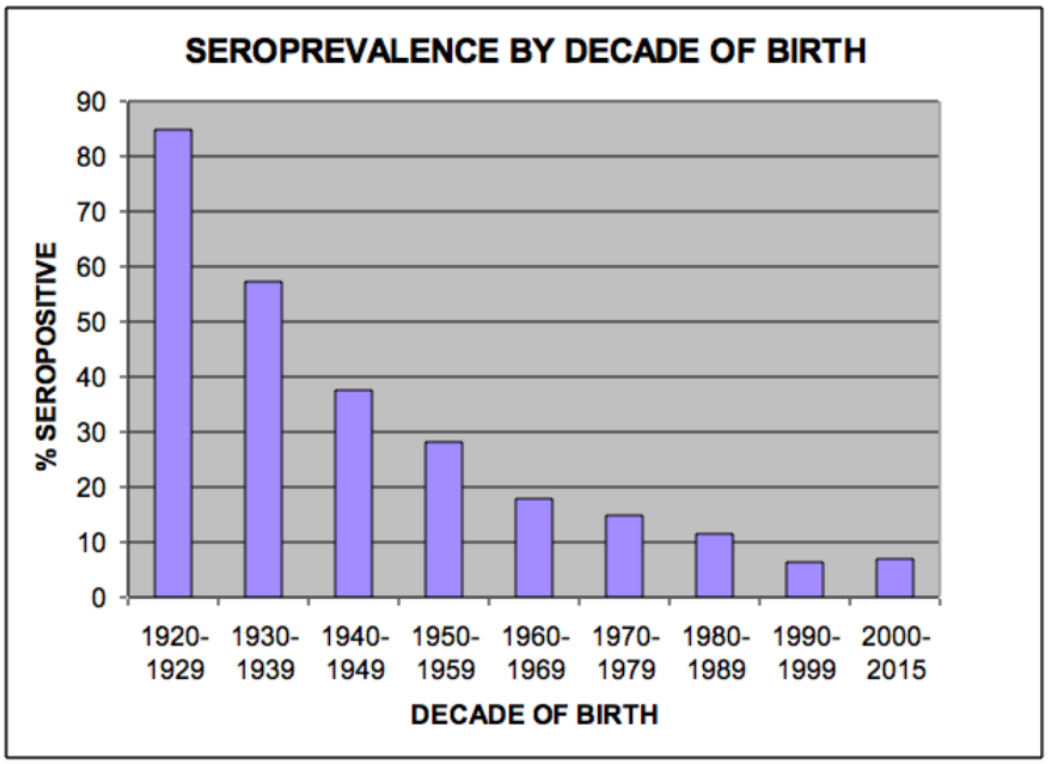
Results

Of 5787 sera tested, 16.07% were seropositive but there was a marked reduction in seroprevalence with younger age (table 1). A total of 85% of samples from patients born between 1920 and 1929 were seropositive contrasting with 6% for patients born between 1990 and 1999.

Table 1 Toxoplasma seroprevalence (IgG) data by age bands

Year of birth	Positive	Positive %	Equivocal	Negative	Total
1920-1929	17	85.00	0	3	20
1930-1939	48	57.14	3	33	84
1940-1949	135	37.70	19	204	358
1950-1959	165	28.30	16	402	583
1960-1969	130	17.96	20	574	724
1970-1979	169	14.83	10	960	1139
1980-1989	179	11.51	9	1367	1555
1990-1999	50	6.29	10	735	795
2000-2015	37	6.99	11	481	529
TOTAL	930	16.07	98	4759	5787

Figure 1 Toxoplasma seroprevalence by age band



Conclusions

The likely interpretation of this data is an age cohort effect suggesting that acquisition in childhood has decreased over the past 50 years. Most samples from patients born between 2010 and 2015 were from babies and reflect maternal seroprevalence (similar to age cohorts 2 decades previously), hence the slight upward trend in this group. Knowledge of current seroprevalence is important for understanding the epidemiology of congenital toxoplasmosis in Northern Ireland and internationally.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0341
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

SECONDARY PROPHYLAXIS IN OCULAR TOXOPLASMOSIS AMONG IMMUNOCOMPETENT PATIENTS

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Background

Chorioretinitis is one of the clinical manifestations of congenital and acquired toxoplasmosis, whose recurrences may lead to significant deterioration of visual acuity. Recently, the usefulness of secondary prophylaxis has been considered with limited data in immunocompetent patients. The aim of this study is to review the follow-up and the efficacy of secondary prophylaxis (SP) in the prevention of recurrences of ocular toxoplasmosis in this population.

Methods

A retrospective observational study was conducted on immunocompetent pediatric patients with toxoplasmosis and ocular involvement (January 1993 - December 2014). Secondary prophylaxis was prescribed until the age of 21 in cases in which macular involvement was higher than 0.1 of visual acuity, or in uncooperative patients where the fovea centrallis was preserved. The incidence rate ratio of patients with secondary prophylaxis to patients without it was calculated.

Results

18 patients were included with a median age at diagnosis of 9.6 years and median follow-up of 142 months (range: 49 - 202). Nine patients were diagnosed with congenital toxoplasmosis. Seven patients received secondary prophylaxis (3 congenital toxoplasmosis): three patients received secondary prophylaxis with cotrimoxazole and four with clindamycin. The incidence rate of recurrence of ocular toxolasmosis was reduced from 36.2 relapses per 1000 person-months to 2.28 relapses per 1000 person-months after starting SP in the subgroup of patients who met the criteria for SP.

Conclusions

In our sample, the group of patients who received SP had a 93,53% reduction of the incidence rate of TO during the period of prophylaxis. According to other published studies, we recommend to perform secondary cotrimoxazole prophylaxis in selected patients with ocular toxoplasmosis.

ESP16-0677
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

CANDIDEMIA IN A JAPANESE CHILDREN'S HOSPITAL

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Background

Candidemia is the leading cause of invasive fungal infection in hospitalized patients. To date, few studies of pediatric candidemia have been conducted in Japan. Our aim was to investigate the clinical and microbiological characteristics of candidemia in children.

Methods

Patients showing a positive blood culture for *Candida* spp. between March 2010 and December 2015 at Tokyo Metropolitan Children's Medical Center in Japan were enrolled in the study. Patient characteristics and microbiological data were collected from electronic patient records.

Results

A total of 23 cases from 17 patients were identified. The median age was 3 years (IQR 0.5 - 20.5 year old) and the number of females was 9 (53%). All patients had an underlying disease, the most common of which was gastrointestinal disease (11/17, 64.7%). Among these, 7 (7/11, 63.6%) had a disease of the small intestine. A central venous catheter was placed in 22 patients (22/23, 95.7%). None of the 19 patients who had undergone an eye examination by ophthalmologist presented any ophthalmologic complications. 6 *Candida* species were isolated: *C. parapsilosis (8), C glabrata* (6), *C albicans* (6), *C tropicalis* (1), *C krusei* (1) and *C colliculosa (1)*. Micafungin was administered to 60.9% of patients. All strains were sensitive to micafungin with the exception of one isolate of *C glabrata,* which was resistant due to a *FKS* mutation. All strains were sensitive to fluconazole except *C glabrata*, and had an MIC ≦1 for Amphotericin B.

Conclusions

In our cohort, Candidemia was mostly observed in patients with a central catheter. Infections due to non *C albicans* were common (73.9%). Micafungin was active against most species except one resistant isolate with a known mutation. Close monitoring against the emergence of resistance is warranted.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0799
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

POSACONAZOLE SALVAGE TREATMENT IN PEDIATRIC IMMUNOCOMPROMISED PATIENTS

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Background

Posaconazole is a recently developed broad spectrum triazole antifungal agent. There are limited data about its use in salvage treatment of pediatric invasive fungal infections (IFI). Here, we present the experience of two university hospitals in posaconazol use for salvage treatment of IFIs developed in immunocompromised children.

Methods

The study population included pediatric patients (0-18 years) in whom posaconazole was used as salvage treatment of IFI between 2010 and 2015. Demographic and clinical features were retrieved from patients' medical records retrospectively. All patients received *Noxafil*® 40 mg/ml oral solution at a dosage of 800 mg/day in two divided doses.

Results

We identified 9 cases (median age of 14 years; range:2.1-16 years), who received posaconazole as salvage treatment for proven (n=2), probable (n=6) and possible (n=1) IFI. Predisposing conditions was primary immune deficiency in 5 cases and hematological malignancy in 4 cases. Posaconazol was utilized as single agent in one case and as combination with other antifungals in others, with a median dose of 5 mg/kg (range: 4-20 mg/kg). Therapeutic drug monitoring could not be performed. Complete response was obtained in 4 cases. Posaconazole had to be changed in two cases due to an adverse event and progression of the infection, respectively. Three cases with uncontrolled primary diseases died while they were on posaconazole treatment.

Conclusions

Posaconazol oral suspension were used in salvage treatment of a complicated patient group with a treatment success of 44.4%. Target serum concentrations may not be achieved due to relatively low weight-based doses in the absence of therapeutic drug monitoring, which is essential for the effective use of posaconazol due to its variable and unpredictable bioavailability.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0573
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

TIMING OF IMAGING FOR CANDIDA CENTRAL NERVOUS SYSTEM INFECTION IN PRETERM NEONATES

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Title of Case(s)

TIMING OF IMAGING FOR CANDIDA CENTRAL NERVOUS SYSTEM INFECTION IN PRETERM NEONATES

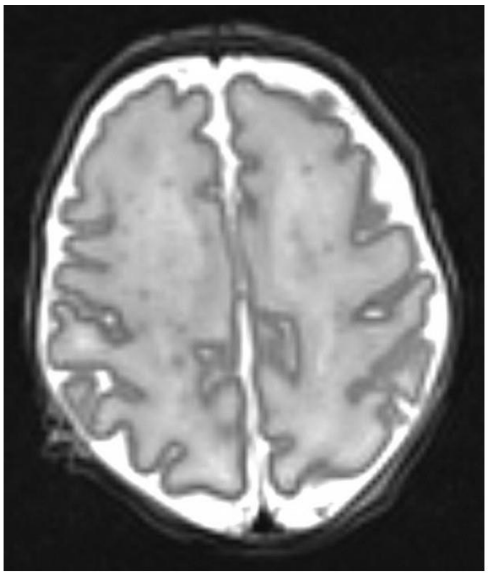
Background

Candida CNS infection in preterm infants is associated with neurodevelopmental impairment and death. Ultrasound and MRI are used as imaging tools with equal sensitivity.

Case Presentation Summary

A 30 weeks female preterm admitted to NICU was investigated for late-onset sepsis at 16 days of life. Blood culture grew coagulase-negative Staphylococcus and Candida albicans. The baby was started on vancomycin and fluconazole in line with local antibiotic sensitivities. An indwelling PICC line was removed. Investigations for disseminated Candida infection, including renal ultrasound, echo-cardiogram, urine and CSF culture, and fundal examination were negative. Cranial ultrasound performed 2 days after positive blood culture with Candida was negative. Repeat blood culture was negative. A 2 weeks course of antifungals was completed and baby was clinically well at the end of the treatment. On day 29 of life, a MRI was performed for research purposes unrelated to the candidal infection, which showed numerous miliary nodular foci through the white matter of both cerebral hemispheres, with a frontoparietal predominance. Due to the likely aetiology of CNS candidiasis, a prolonged course of fluconazole was recommended. 8 weeks after commencement of fluconazole, repeat MRI showed reduction in size and number of the miliary pattern lesions. Treatment was continued for another 5 weeks with complete resolution. At 6 months of age the baby is

developmentally normal.



Learning Points/Discussion

Candidaemia in neonates warrants imaging to detect CNS disease because of its poor neurodevelopmental outcome that can improve with long duration therapy. CNS lesions develop late and LP may be negative; Head imaging should be considered prior to stopping therapy as it may detect otherwise undiagnosed lesions and therefore changes management.

ESP16-0177
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

PREVALENCE OF SEVERE VIVAX MALARIA: A SYSTEMATIC REVIEW AND META-ANALYSIS SINCE 1900

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Background and Objective

Malaria caused by *Plasmodium vivax* (*P. vivax*) was long considered a benign disease, but recent reports from a limited number of geographical areas report severe and complicated vivax malaria cases. . The primary objective of this systematic review and meta-analysis from English-language articles published since 1900 was to describe the reported clinical characteristics and geographical variation in prevalence of severe vivax malaria and its change over time.

Methods

Medline and Scopus databases were searched for original papers on severe vivax malaria, using modified WHO criteria (2010) for the diagnosis of severe falciparum malaria for inclusion. Pre-1949 articles were identified through reference lists in journals, textbooks, and personal collections of colleagues.

Learning Points Discussion

A total of 60 studies (totaling 23,465 vivax-malaria patients) were included, the majority from India (n=25), USA (n=8), and Indonesia (n=5). Only 17/60 reports are from before 2000. Vivax mono-infection was confirmed by PCR in 11 studies; co-morbidities were ruled out in 19 studies; 9 studies used both PCR confirmation and ruled out co-morbidities. In 50 studies in which all vivax malaria cases were included, severe thrombocytopenia (<50,000/mm^3) was the most common complication (425/2945 or 20.3%), whereas death was rare (126/11008 or 0.9%). Another 10 studies reported on severe vivax patients only, with severe thrombocytopenia as the most common presentation (56/203 or 39.6%) and hypoglycemia the least common (11/283 or 2.8%). Case fatality was 57/732 or 6.3%. Severity syndromes varied widely according to geographical area, with severe anemia most prominent in areas of chloroquine resistance. In conclusion, this analysis shows that *P. vivax* mono-infection can cause severe and even fatal disease, with a clear increase in reporting since the new millennium.

ESP16-0773
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

UNUSUAL CAUSE OF SKIN ERUPTION IN INFANTS: SCABIES

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Title of Case(s)

UNUSUAL CAUSE OF SKIN ERUPTION IN INFANTS: SCABIES; REPORT OF 3 CASES

Background

Clinical presentation, diagnosis and management of scabies in infants is quite different than the scabies in adults. Misdiagnosis is more frequent in infants and children compared with adults. Furthermore, permethrin cannot be used in infants younger than 3-months because of their safety profile.

Case Presentation Summary

Case 1: A 42 days-old boy presented with diffuse vesicular eruption on trunk, extremities and scalp. He was consulted to pediatric infectious diseases clinic with the presumed diagnosis of varicella zoster. In history, the mother mentioned itchy lesions on her hands and interdigital area. After the exploration of burrow lesion on dorsum of her hands the mother and the baby were diagnosed as scabies and treated with permethrin and pomad Wilkinson, respectively.
Case 2: A 33-days-old girl presented with vesiculopustuler and crusted eruptions on all over her body and focal exfoliation on her back. She was admitted to pediatrics ward with presumed diagnosis of staphylococcal-scalded-skin-syndrome and treated with parenteral ampicillin-sulbactam. After the exploration of burrow lesion on her mother's hand and the history of the father's itchy, papular skin lesions she was diagnosed as scabies and treated with pomad Wilkinson.
Case 3: A 3-months-old boy presented with diffuse erytematous eruptions which were noticed since postnatal 5th day. He was admitted to another hospital with presumed diagnosis of severe milk-protein allergy and immundeficiency. He was diagnosed as scabies after the history of scabies in his parents. He had succesfully treated with pomad Wilkinson.

Learning Points/Discussion

Failure to diagnosis of scabies in infants is very common. Scabies must be suspected in infants with polymorphic skin eruptions esspecially if the family members had itchy skin lesions.

ESP16-0963
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

VERTICAL TRANSMISSION OF CHAGAS DISEASE IN A COHORT OF NEWBORNS IN A TERTIARY UNIVERSITY HOSPITAL FROM MADRID

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Background

Chagas disease (CD), caused by *Trypanosoma cruzi* ,is endemic in Central and South America. The vertical transmission (VT) is around 5%.
In Spain,where immigrant population from Latin America is high,CD became an important health problem and some hospitals like ours,implemented a routine prenatal screening with serology among all pregnant women from South America.
The aim of this study was to estimate the VT of CD in a cohort of pregnant women with Chagas positive serology in a non-endemic area.

Methods

We performed a retrospective review of pregnant women with positive serology to *T.Cruzi* in our hospital between January 2013 and April 2015 and their newborns. Congenital Chagas was ruled out by PCR at birth and at 1 month and serology from 9 months old.

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Results

45 women with positive serology were included.85% were from Bolivia,10% from Paraguay, 2.5% from Argentina and 2.5% from Ecuador.
We had a prevalence of CD positive serology in our pregnant women around 1%(95%CI 0.8-1.4) and a rate of vertical transmission of 2,5% (95% CI: 0-6).
There was a single case of VT, who presented positive PCR at birth and symptomatic disease treated with benznidazole with good outcome(PCR and late serology were negative).
We lost the follow up in 5 newborns.The rest had 2 negative PCR or a negative PCR and negative serology after 9 months.
The study of the relatives let us to diagnose and treat a sister and to insist affected mothers by the need of treatment.

Conclusions

Screening during pregnancy, in mothers coming from endemic areas is essential because it allows an early diagnosis and treatment of the affected newborns; with best results and less pharmacological toxicity.
Following these children seems a good tool to make a relative´s study.

ESP16-0555
E-POSTER DISCUSSION SESSION 14 - INFESTATIONS, FUNGI AND PARASITES (station 8)

USE OF ANTIGIARDIASIC DRUGS IN PEDIATRIC PATIENTS. STARTING A NATIONAL NETWORK.RED.GIp

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[5]RED.GIp (Spanish Network for the Study of Diagnosis, Genetic Typification and Therapeutical Management in Pediatric Intestinal Giardiasis)

Background

Long-term effects of non-treated intestinal giardiasis (IG) in children, and the evidence of pharmacological resistance, calls for a better knowledge of the available tools. In this context, the Spanish Network for the Study of Diagnosis, Genetic Typification and Therapeutical Management in Pediatric Intestinal Giardiasis (RED.GIp) is constituted.

Methods

The network was created in 2015, and is structured by a Scientific Committee, an Executive Committee and several work groups; integrating professionals from all of the healthcare levels involved in IG treatment throughout the national territory, from assistance and investigation areas.

The first step was an anonymous, nation-wide survey in order to assess the diagnosis-therapeutic guidelines, followed by the professionals.

Results

344 paediatricians from all 17 regions in Spain fulfilled the survey.

44% of them analysed stool samples and treated only confirmed cases; the rest treated empirically. The empirical treatment consisted on: 78% metronidazole, 3% tinidazole and 3% mebendazole.

95% treated symptomatic patients, but only 50% treated asymptomatic patients with risk factors; 44% checked for normalization stool samples, and 75.6% did observance.

96.6% of them used metronidazole anytime, and 31.4% used tinidazol; less than 5% had used anytime nitazoxanide, quinacrine or azoles.

Conclusions

Half of the asymptomatic patients are under-treated, and the follow-up is not standardized. Knowledge of anti-giardiasic drugs as alternative to metronidazole is scarce among professionals.

It´s relevant to reinforce the concept of resistant IG, suggest new researches with second line drugs, and check management guidelines, in order to decrease the number of unnoticed therapeutic failures, and their long-term damages.

A multidisciplinary network will allow obtaining valuable evidence about the disease and compile experiences with alternative drugs, helping to design agreed diagnostic-therapeutic algorithms that will optimize the management of this pathology in paediatric patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1020
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

STAPHYLOCOCCUS CAPRAE CAUSING RECURRENT ENDOCARDITIS

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Title of Case(s)

***"Staphylococcus caprae* causing recurrent endocarditis"**

Background

Staphylococcus caprae is a coagulase-negative staphylococci (CONS), a regular commensal and a very rare cause of otitis externa, bacteremia or bone and joint infections related to prosthetic material. The prevalence of *S. caprae* is likely underestimated and its identification is increasing due to the routine use of molecular or proteomic techniques. We present an adolescent with recurrent endocarditis initially attributed to *S. hominis* infection, subsequently reclassified as *S. caprae.*

Case Presentation Summary

A 11-year-old boy with perimembranous ventricular septal defect and recurrent tonsillitis underwent uneventful tonsillectomy; however he developed fever 15 days post-surgery. Blood cultures were positive for oxacillin-sensitive *S. hominis,* an echocardiography detected a tricuspid subvalvular vegetation and parenteral antibiotic therapy with ceftriaxone and gentamicin plus cloxacillin (5 weeks) was administered. Four weeks after discharge he was readmitted with low grade fever and joint pain. Blood analyses revealed microcytic anemia, raised CRP (35 mg/L) and *S. hominis* was identified in 4 blood cultures using conventional techniques. Echocardiography confirmed the persistence of the tricuspid subvalvular wart. 4/4 serial blood cultures were positive and classified as *S. caprae* using MALDI-TOF mass spectrometry. Antimicrobial susceptibility was identical (oxacilline-sensitive) to the previously identified *S. hominis* isolate. 16s PCR-sequencing confirmed the presence of *S. caprae* andtreatment with cloxacillin plus rifampicin (8 weeks) and gentamicin (2 weeks) resulted in a complete clinical recovery including normal echocardiography.

Learning Points/Discussion

S. caprae is an unusual cause of endocarditis in children. It is important to highlight the potential indolent course of the infection and recurrence, despite appropriate antibiotic management, as it was in our case. MALDI-TOF spectrometry allows reclassification of *S. hominis* as *S. caprae* demonstrating the usefulness of molecular techniques in the pediatric setting.

ESP16-0883
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

VANCOMYCIN-RESISTANT AND VANCOMYCIN -SUSCEPTIBLE ENTEROCOCCAL BACTEREMIA: A PROSPECTIVE STUDY COMPARING RISK FACTORS, CLINICAL FEATURE, AND OUTCOME.

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Background

Vancomycin-resistant enterococci(VRE) is increasingly reported as an important cause of serious infections like bacteremia worldwide.This study aimed to determine therisk factors, clinical characteristics and outcome associated with the acquisition of vancomycin-resistant *enterococcal* (VRE) and vancomycin-susceptible *enterococcal* (VSE) bacteremia at a teaching hospital in Riyadh during a 2-years period.

Methods

Over the 2 years, 79 patients with clinically significant *enterococcal* bacteremia were identified. Patients were divided into two groups, VRE and VSE. Risk factors, clinical characteristics and outcome were identified and compared for both group prospectively using medical records and computerized patients data. Minimum inhibitor concentration (MIC) of vancomycin, teicoplanin, linezolied, and gentamicin was determined by E-test method.

Results

There were 25 (31.6%) VRE and 54 (68.4%) VSE bacteremia.*E. faecalis* 50 (63%) was the most common isolate followed by *E. faecium* 26 (33%). Hematologic malignancy (*P*=0.0178), and Heart disease (*P*=0.0053) were significantly associated with VRE bacteremia. Vancomycin resistance was significantly more prevalent among *E. faecium* 17/25 (P<0.001), while *E. faecalis* was more likely to be vancomycin susceptible 5/25 (P<0.001). Almost half of the isolate 14(56%) among the 25 cases of VRE were isolated from patients admitted to the intensive care unit .The highest resistance pattern to ampicilin, vancomycin and ciprofloxacin was identified in *E. faecium.* VRE bacteremia was associated with higher mortality rate (P=0.0375).

Conclusions

VRE bacteremia is an important nosocomial infection. Overall, the clinical presentation was similar between the VRE and VSE groups. Risk factors for acquiring VRE bacteremia included hematologic malignancy, heart disease and admission to intensive care.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0121
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

RARE PRESENTAIONS OF BACTERIAL INFECTIONS

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Title of Case(s)

Rare presentations of bacterial infections in Childhood

Background

We report two rare presentations of bacterial infections in childhood caused by common bacterial pathogens.

Case Presentation Summary

1: A 7 year old boy presented with right shoulder and left knee pain associated with fever. There was no history of trauma. Neurological examination was normal and meningeal signs were absent. There was tenderness over the joints with restricted movements.

Investigations revealed raised inflammatory markers. Blood culture, throat swab, antistreptolysin O titre, and rheumatoid factor were negative. Fluid aspirated from both joints was blood stained and culture grew *Neisseria meningitidis*.

Immunological tests were within normal limits. He was treated with iv ceftriaxone to enable home therapy.

2: An 8 month old boy was admitted with a 2 day history of fever, cough and vomiting. He developed generalised seizures. He was drowsy and noted to have hypoglycaemia. His GCS gradually deteriorated and required ventilation. Subsequently he became oliguric.

He had raised inflammatory markers with low white cell response. A second CT scan on day 5 revealed bilateral subdural effusions. Blood investigations revealed a low platelet count with microangiopathic hemolytic anaemia, deranged clotting and worsening renal function confirming HUS. His blood and CSF culture grew *Streptococcus pneumoniae*. He was commenced on IV cefotaxime and completed 21 days. He recovered but continues to have ongoing complications.

Learning Points/Discussion

Primary arthritis is a rare manifestation of meningococcal disease in the paediatric population, and can easily be missed. Primary meningococcal arthritis should be considered in the differential diagnosis of any acute septic arthritis. HUS is a rare but a severe complication of invasive pneumococcal infection. A high index of suspicion is required in order to start early treatment and to improve the clinical outcome.

ESP16-0140
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

SEVERE EOSINOPHILIA WITH CONCOMITANT HEPATITIS IN A BARTONELLA HENSELAE-INFECTED INFANT

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Title of Case(s)

Severe Eosinophilia With Concomitant Hepatitis In A *Bartonella Henselae*-Infected Infant

Background

Bartonella henselae is a Gram-negative bacterium that causes infection in pediatric patients as a self-limited lymphadenopathy or less often as a disseminated disease. *Bartonella* hepatitis has seldom been described in infants. To our knowledge, severe eosinophilia has not been not reported in *Bartonella* infected children. Herein, we present a case of a *Bartonella*-infected infant with severe eosinophia and concomitant hepatitis.

Case Presentation Summary

A 13-month-old, previously healthy, male infant was admitted for acute onset of right inguinal lymphadenopathy. Cat scratches were observed on the right foot. Laboratory studies revealed severe eosinophilia (absolute eosinophil count = 2,860 x 10^3/ml) and elevated hepatic transaminases (AST: 172 U/L and ALT: 252 U/L). Ultrasound did not reveal liver abnormalities. Azithromycin, 10 mg/kg q24h loading dose and then 5mg/kg q 24h per os was initiated empirically for suspected *B. henselae* infection. *Bartonella* IgM serology later returned positive (>20 units). After 48h of receiving azithromycin, increasing fever and generalized fatigue developed. Surgical drainage of lymphadenopathy was then performed and rifampicin 10 mg/kg q12h *per os* was added. Following administration of azithromycin and rifampicin for 2 and 3 weeks, respectively, his clinical status improved, eosinophilia resolved, and elevated hepatic transaminases normalized.

Learning Points/Discussion

Severe eosinophilia can be observed in *B. henselae* infected infants, possibly representing an immune dysregulation at this young age. Hepatitis may also be a clinical manifestation of *B. henselae* infection not only in older children, but in infancy, as well. Surgical intervention of lymphadenopathy and a combination treatment with macrolides and rifampicin may be effective. However, the optimal duration and dosages of macrolides and rifampicin for treatment of *B. henselae* infection in infants remain to be established.

ESP16-0060
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

INVASIVE ACINETOBACTER INFECTION IN A PEDIATRIC POPULATION IN BRAZIL: A FIVE-YEAR HOSPITAL-BASED SURVEILLANCE STUDY

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Background

Invasive *Acinetobacter* infections are an important cause of mortality in children and of increasingly importance in health care-associated infections, due the emergence of strains that are resistant to most commercially available antibiotics. We retrospectively analyzed *Acinetobacter* bloodstream infections in a Pediatric Unit to determine antimicrobial susceptibility, risk factors for lethality, and outcomes

Methods

A retrospective surveillance study in children aged under 18 was conducted from January 1st, 2010, through November 30, 2015, where all positive blood cultures for *Acinetobacter* spp were identified. Patient's clinical and laboratorial data were extracted from digital medical records and comprised antimicrobial susceptibility, underlying condition, need of PICU, and final outcome. Children aged older than 18 years and duplicate blood cultures were excluded

Results

We analyzed 109 non-duplicate *Acinetobacter* spp. isolates during the studied period, of which one hundred (92%) were *A. baumannii* and nine *A. lwolfii* (8%). Fifty-eight percent were male and 42% were female; the mean age was 1.4 years. Base comorbidities were seen in 91.7% of the patients, of which cardiopathy (25,3%), oncologic/hematologic diseases (24,2%), prematurity (22,1%), neurologic (20%) and chronic pulmonary disorders (17,9%) were the most prevalent. Crude mortality rate was 28.4%, with higher rates among those with multidrug-resistant isolates (48.7%) than those with susceptible isolates (18.8%). The median hospitalization time was 40 days, during which 78.9% required intensive care. Resistance to amikacin (30.2%), ciprofloxacin (36.4%), ampicillin/sulbactam (34.3%) and meropenem (40.6%) were seen among 96 isolates with antibiogram. Multidrug-resistant isolates accounted for 40.6% of the strains

Conclusions

Acinetobacter invasive infection is an emerging and difficult-to-treat condition in pediatric hospitalized patients, especially in PICU. Risk factors for *A. baumannii* infections were presence of base comorbidity, need of invasive procedures and long periods of hospitalization

ESP16-0842
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

PYOMYOSITIS IN A NON-TROPICAL SETTING

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Title of Case(s)

PYOMYOSITIS IN A NON-TROPICAL SETTING

Background

Pyomyositis is a bacterial infection within skeletal muscles, which is common in tropical countries but rare in Spain. Our objective was to describe the cases diagnosed in our center and assess the yield of the different diagnostic tests.

Case Presentation Summary

Retrospective study of patients under 15 years diagnosed with pyomyositis during a 12-year period (2004-2015).

We included 15 patients (8 women) with a mean age of 5.35±4.3 years. Thirteen infections were primary and 2 secondary (1 to sacroiliitis and 1 to skin infection). Seven patients reported prior injuries of the affected area. The most common symptoms were pain (93%), fever (80%) and swelling (60%). The most frequently affected muscles were femoral quadriceps (33%) and iliopsoas (13%).One patient had multiple involvement. Ultrasonography was the most used technique (80%), allowing the diagnosis in 58% (7/12). Magnetic resonance imaging (MRI) was used in 53%, and was the most sensitive technique (100%, 8/8). Eleven patients (73%) presented with leukocytosis>15,000 cells/mm^3, and 1 with leukopenia. C-reactive protein was> 40 mg/L in 67% of patients. *S. aureus* (1 MRSA) was isolated in 8 patients, with a blood culture yield of 33% (3/9). Six cases (40%) underwent surgical drainage, with a culture yield of 83% (5/6). All received sequential IV-oral antibiotic therapy for a mean of 31.6±17.5 days.

Learning Points/Discussion

Pyomyositis should be considered in children with fever and limb pain, especially if there is history of prior trauma, even in non-tropical settings. *S. aureus* is the most common causative agent. The yield of blood and surgical drainage fluid cultures is very high. Diagnosis can be made by ultrasound, but MRI is the most sensitive test. Most cases have a good outcome with antibiotic-only treatment.

ESP16-0381
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

STAPHYLOCOCCUS AUREUS BACTEREMIA IN CHILDREN: CHANGES OVER THE LAST 18 YEARS

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Background

Staphylococcus aureus is a major cause of bacteremia in children and is associated with high morbidity; nonetheless, complete data are lacking on the incidence, related risk factors, and mortality due to this infection

Methods

Descriptive study including patients younger than 16 years admitted to a tertiary reference hospital, with blood cultures exclusively positive for *S. aureus.* Four study periods were established: period 1, 1995-1999; period 2, 2000-2002; period 3, 2006-2008; and period 4, 2010-2012

Results

In total, 269 episodes of *S. aureus* bacteremia (SAB) occurred in 242 patients. Over the total time studied, the incidence increased from 1.3 to 3.3 cases per 1000 patients hospitalized (RR=2.71; 95% CI 1.85-3.95) and mortality decreased from 18% to 6% (p=0.008). There were no differences in the resistance patterns of *S. aureus* strains. The prevalence of methicillin-resistant *S. aureus* (MRSA) increased from 3% to 13% between periods 1 and 2 and decreased from 14% to 3% between periods 3 and 4 (p=0.011). The 30-day cumulative mortality was 3.3% and the SAB-related mortality was 1.5%. Nosocomial acquisition and age 12 to 16 years were factors independently related with death on multivariate analysis.

Conclusions

The incidence of SAB tripled during the years studied, but remained stable in the last period. Antimicrobial resistances did not increase. Although a decrease in mortality was documented, around half the 30-day cumulative mortality was caused by SAB.

ESP16-0382
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

STAPHYLOCOCCUS AUREUS BACTERIEMIA IN NEONATES: CHANGES OVER 18 YEARS

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Background

Data are limited on the changes occurring in *Staphylococcus aureus* bacteremia(SAB) over time and the clinical impact of this condition on neonatal morbidity and mortality

Methods

Descriptive study including neonates admitted to a tertiary hospital with blood cultures exclusively positive for *S. aureus* during 4 periods of study—1, 1995-1999; 2, 2000-2002; 3, 2006-2008; and 4, 2010-2012—as part of an epidemiological surveillance program.

Results

In total, 71 SAB episodes occurred in 67 neonates. The incidence of this condition increased from 1.5 to 5.4 cases per 1000 hospitalized newborns (RR=3.48; 95% CI 1.85-6.55) and mortality decreased from 18% in period 1 to 9% in period 4, although differences were not significant, likely because of the small number of deaths (p=0.61). Five methicillin-resistant *S. aureus* (MRSA) strains were isolated, distributed among the 4 periods (p=0.18). In total, 61% of neonates showed signs of SAB sepsis, with an increase in the incidence rate from 0.54 (period 1) to 2.67 (period 4) per 1000 neonates. On multivariate analysis, factors related to the development of sepsis included nosocomial acquisition, prematurity, and a need for central venous catheter (CVC) removal.

Conclusions

The incidence of neonatal SAB almost quadrupled over the periods studied, but mortality has remained low and has shown a trend to decrease. The incidence of MRSA strains has held steady, despite changes in the patterns of resistance to antimicrobials other than methicillin.

ESP16-0513
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

RISK FACTORS FOR POST-OPERATIVE MEDIASTINITIS AFTER SURGERY FOR CONGENITAL HEART DEFECTS IN CHILDREN

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Background

The occurrence of a postoperative mediastinitis is due to several factors and its prevention relies on the knowledge and management of risk factors related to patients, to the surgery, and to the operating room environment. Risk factors for mediastinitis have been well documented in adults, but limited data have been reported in pediatric patients. This study investigates risk factors for mediastinitis after median sternotomy in children.

Methods

This was is a single-center retrospective 1:3 case-control study conducted within a cohort of 1570 patients, who underwent median sternotomy for treatment of congenital heart defect over a 5-year-period at a third level children’s hospital. Mediastinitis was defined as an infection involving the mediastinum, the sternum or both, according to specific criteria.

Results

Mediastinitis rate was 2.9% (51 mediastinitis/1732 surgical procedures). At the multivariable analysis, age <12 months, previous sternotomy, Risk Adjustment for Congenital Heart Surgery score ≥4, revision surgery, and postoperative blood transfusion were independently associated with increased risk of infection. The most common pathogens were coagulase-negative staphylococci and Staphylococcus aureus, with high rates of methicillin-resistance. Univariate analyses revealed that American Society of Anesthesiologists (ASA) score ≥4, preoperative mechanical ventilation and cardiopulmonary bypass time >105 min were associated with infection due to methicillin-resistant bacteria.

Conclusions

We found that age below 12 months, previous operations through midline sternotomy, RACHS score≥4, need for sternal re-exploration, and post-operative RBC transfusion were independently associated with increased risk fof mediastinitis. Unfortunately, the majority of risk factors identified in this and previous pediatric studies cannot be modified because strongly necessary to the management of patients. However, this study helps to select a high risk group of patients who may be offered specific and intensive prophylaxis measures before cardio-thoracic surgical procedures.

ESP16-0789
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

EVALUATION OF PNEUMOCOCCAL CONJUGATE VACCINATION IMPACT IN SEROPREVALENCE OF STREPTOCOCCUS PNEUMONIAE IN BRAZILIAN CHILDREN AT DIFFERENT AGE GROUPS

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Background

Pneumococcal conjugate vaccines (PCV) was introduced in Brazilian National Vaccination Program in 2010. Because this vaccine targets only a minority of pneumococcal serotypes, concerns that non-vaccine serotypes (NVTs) could increase in prevalence and reduce the benefits of vaccination are real. This ongoing study describes the evolution of the *S. pneumoniae* serotypes causing IPD from 2000 to 2013 in the cities of Sao Paulo and Uberlandia, Brazil.

Methods

We conducted a hospital-based surveillance study of IPD (defined as isolation of *S. pneumoniae* in blood, cerebrospinal fluid or any other sterile site) in children aged under 16 (further grouped into “under 2y”, “2-5y” and “over 5y” groups), from January 1st, 2000 through December 31st, 2013. Once the strain was isolated clinical and laboratory information were retrospectively extracted from medical records and analyzed according to pre-vaccination period (2000-2009) and post-vaccination period (2010-2013).

Results

A total of 445 IPD episodes in children under 16 were evaluated during the studied period. Results were similar at both hospitals. Overall pre and post-vaccination cases were respectively distributed as followed: 60% and 42% were aged under 2 years, 23% and 28% were between 2-5 years and 16% and 25% were over 5 years. The most prevalent serotypes over the pre-vaccination period were 14 (40%), 6B/D (10%), and 1 (7%), while 14 (18%), 19A (11%), and 6B/D (9%) were more seen during the post-vaccination period. NVT increased from 32% to 59% (p=0,001) as well as serotypes 3, 6A e 19A increased from 9,5% to 22,8% (p=0,05) after vaccination.

Conclusions

PCV markedly reduced the vaccine serotypes after vaccination, while there was relevant increase in NVTs and serotypes included in PCV13 but not in PCV10. Older ages were proportionally more affected in post-vaccination cases.

ESP16-0480
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

PREDICTORS OF BLOOD STREAM INFECTION IN SEVERELY MALNOURISHED MALAWIAN CHILDREN

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Background

Children with complicated severe acute malnutrition (SAM) are at high risk of death. Blood stream infection (BSI) is a potential contributory factor. Identifying those children most at risk of BSI is important to target broad spectrum antibiotic use appropriately. We investigated the predictive factors for BSI in children presenting to a nutritional rehabilitation unit (NRU) in Malawi.

Methods

Routine bacteraemia surveillance was enhanced by collection of blood cultures from both febrile and afebrile children admitted to the NRU of Queen Elizabeth Central Hospital, Blantyre from June 2011 to March 2012. Logistic regression was used to identify risk factors associated with community acquired BSI.

Results

205 blood cultures from 178 children with SAM were included. 11 (5.4% of cultures, 6.2% of children) grew pathogens. Of these, six were resistant to both chloramphenicol and gentamicin and four were resistant to ceftriaxone. BSI was associated with chest signs (adjusted OR 10.23 [95% CI 1.36-76.95]), but not abnormal temperature (adjusted OR 1.85 [95%CI 0.18-19.16]) or shock at presentation (adjusted OR 0.32 [95% CI 0.01-11.59]).

Conclusions

BSI prevalence was low among children admitted with SAM, although the pathogens that were isolated displayed a high frequency of anti-microbial resistance. The presence of chest signs on examination was associated with the presence of BSI. This is consistent with findings from other cohorts. Respiratory signs could prove a useful indicator to increase the index of suspicion of BSI in children with SAM.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0626
E-POSTER DISCUSSION SESSION 15 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 2 (station 9)

EPIDEMIOLOGY OF BLOOD CULTURE-PROVEN ESCHERICHIA COLI SEPSIS IN CHILDREN IN SWITZERLAND - RESULTS OF THE SWISS PEDIATRIC SEPSIS STUDY

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Background

Gram-negative sepsis is a serious disease carrying significant mortality. *E. coli* is one of the main Gram-negative pathogens causing sepsis during childhood. Here we describe the characteristics of *E. coli* sepsis in a large cohort of paediatric patients in Switzerland.

Methods

Prospective observational cohort study of newborns and children <17 years with blood culture-proven sepsis admitted to ten paediatric hospitals in Switzerland between September 2011 and November 2015. For this analysis we considered only children beyond the neonatal age.

Results

In the 4.2 years study period we recorded 738 sepsis episodes. In 285 (39%) episodes Gram-negative bacteria were isolated. *E. coli* was detected in 133 (18%) episodes, for an age-standardised incidence rate of 4.0 per 100'000 children (95CI 3.4-4.6). Fifty-nine (44%) *E. coli* sepsis episodes occurred in previously healthy children (n=359), 74 (56%) in children with comorbidities (n=379). In previously healthy children, median age at sepsis onset was three

months (IQR 2-9) compared to 53 months (IQR 14-126) in children with comorbidities (p<0.001). Urinary tract infection (UTI) (46, 78%) was the predominant infection type in previously healthy children, but not in children with comorbidities (17, 23%) (p<0.001). Extended-spectrum beta-lactamase production was only detected in children with comorbidities (10, 14%) (p=0.002). *E. coli* sepsis presented as severe sepsis in 20 (15%) episodes, three (5.1%) in previously healthy children and 17 (23%) in children with comorbidities (p=0.006). Case fatality rate was 3.8%, all five deaths occurred in children with comorbidities.

Conclusions

In previously healthy children *E. coli* sepsis mainly occurs as a consequence of UTI in infants, while children with comorbidities are older at sepsis onset and more often suffer from a severe disease course that may be fatal.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0315
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

COMMUNITY-ASSOCIATED EXTENDED-SPECTRUM β-LACTAMASE-PRODUCING ENTEROBACTERIACEAE IN CHILDREN. EVOLUTION FROM 2010 TO 2015 IN FRANCE

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Background

The emergence of extended-spectrum β-lactamase–producing *Enterobacteriaceae* (ESBL-E) in the community is an alarming epidemiologic change. The best example of antibiotic resistance spread is *E. coli* sequence type 131 (ST131), a multi-drug–resistant clonal group disseminated worldwide. It has contributed to the dissemination of resistance to third-generation-cephalosporins. However, few studies have assessed for long period intestinal carriage in community-based infants and toddlers in developed countries.

Methods

In this prospective study, rectal samples were obtained from children aged 6 to 24 months by community pediatricians between 2010 and 2015. Demographic characteristics and risk factors for ESBL-E carriage were collected (use of antibiotics, previous hospitalization, travel history…). Genetic characterization of the strains was performed with the determination of ß-lactamase genes, phylogenetic groups, sequence type 131 (ST131) and virulence factors of resistant *Escherichia coli.*

Results

We enrolled 1,886 children; 144 (7.6%) harbored ESBL-E, and this rate increased from 4.8% to 10.2% between 2010 and 2015. We observed an increase of phylogenetic group B2 from 5% to 48% mainly due to the increase of ST131 (5% to 37%).

Risk factors for ESBL-E carriage were being cared for at home (adjusted-OR [aOR]=1.8 [95% CI 1.1;2.9]), recent antibiotics use (aOR=1.5 [1.0;2.1]) and travel history (aOR=1.7 [1.1;2.6]). When focusing on ST131 strains comparing to non–ESBL–producing strains, ST131 carriage was associated with hospitalization in the last 6 months (aOR=3.5 [1.4;8.8]).**Conclusions**

Between 2010 and 2015, the carriage of ESBL-Ein community children doubled because of massive expansion of the *E. coli* ST131 clonal group. The risk for carrying ST131 was associated with previous hospitalization but not, contrary to the counterpart, antibiotic treatment, daycare attendance or travel history. These results suggest that infection control measures may be adapted to the genetic background of the strain.

ESP16-0324
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

GENOMIC EPIDEMIOLOGY OF MENINGOCOCCAL DISEASE IN THE UNITED KINGDOM AND IRELAND, 2010-2015 – APPLICATIONS FOR THE CLINICIAN

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Background

Invasive meningococcal disease continues to afflict children and adults worldwide. In the United Kingdom and Ireland the major burden of disease remains serogroup B, which can occur in clusters. Further, the rapid increase of serogroup W disease in England led to implementation of adolescent ACWY vaccination in 2015. Genomic epidemiological surveillance, pioneered by the Meningitis Research Foundation Meningococcus Genome Library, is a powerful tool to monitor disease-causing *Neisseria meningitidis* population structure.

Methods

N. meningitidis disease isolate data for epidemiological years 2010-11 to 2014-15 (n=2428) were analyzed from PubMLST.org embedded genome comparator module, SplitsTree version 4.14.2, R version 3.2.2 and MEGA 6.

Results

Serogroup B outbreaks 2010-11

Using sequence data alone, 62 putative outbreaks were identified, defined as ≤20 non-identical loci from the 1605 loci in the meningococcal core genome version 1.0. 22 putative outbreaks had ≤12 loci differences. In 15 putative outbreaks, both isolates were within the same UK geographical region. Genes that differed within outbreak isolates included glycosyltransferases, rotamases and outer membrane peptidases.

Serogroup W disease 2014-15

Analysis of all isolates identified a grouping of isolates ~60 non-identical loci from 1605, predominantly serogroup W ST11. Genome comparison produced two previously undescribed clusters (termed cluster A and B), both belonging to sublineage 11.1. Neither group possessed *fhbp* allele 9 (Hajj strains) and were not differentiated by PorA/FetA typing. Phylogenetic analysis with allele-based neighbour-net trees and concatenated aligned nucleotide sequences identified the same two clusters A and B.

Conclusions

Applications of genomic epidemiology for clinicians range from bedside to public health, including bacterial typing, virulence factors, antibiotic susceptibility, outbreaks and with

Bexsero® implementation, vaccine antigens. The utility of functional analysis platforms enables those without a bioinformatics background to rapidly access and analyse data that influences patient management.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0875
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

JUVENILE RECURRENT RESPIRATORY PAPILLOMATOSIS IN PORTUGAL – BURDEN OF DISEASE OVERVIEW BETWEEN 2005 AND 2009

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Background

Juvenile-Onset Recurrent Respiratory Papillomatosis (JORRP), a benign larynx neoplasm in children, is caused by the Human Papillomavirus (types 6 and 11). Although a rare condition, disease morbidity in children is significant. Besides clinical consequences, the medical costs associated to disease management are considerable.

Methods

A clinical characterization of hospital admissions due to JORRP was performed regarding information collected through the Diagnosis-Related Groups (DRGs) national database from 2005 to 2009, which includes anonymized information regarding hospitalizations and ambulatory treatment performed at Portuguese Health System's hospitals. The ICD-9 codes used were 212.1 benign neoplasm of larynx, 212.2 benign neoplasm of trachea and 212.9 benign neoplasm of respiratory and intrathoracic organs. The costs analysis associated to disease management regarding the same period was based on 2013 DRGs' national requirements and took into account an average inflation rate of 2.16%.

Results

From 2005 to 2009, 46 JORRP cases were observed, which corresponded to 56 hospital admissions (mean hospital admissions per patient of 1.3). The number of cases by year is increasing: 4 cases were observed in 2005 and in 2009 10 cases were registered. No statistical difference between genders were observed. Moreover, the majority of hospital admissions (94.9%) have lasted less than 8 days. The total JORRP management costs between 2005-2009 was 94,407€, and the annual costs ascended from a minimum of 6,436€ in 2005 to a maximum of 26,766€ in 2008.

Conclusions

Despite the low number of cases, hospital admissions JORRP-related are increasing and, consequently, the burden of disease in Portugal is becoming heavier. The inclusion of the quadrivalent HPV vaccine in the National Vaccination Calendar in 2008 is expected to have a significant impact in JORRP national cases incidence, once vaccinated girls reach child-bearing age.

ESP16-0732
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

THE NASOPHARYNGEAL CARRIAGE RATE AND SEROTYPE DISTRIBUTION OF STREPTOCOCCUS PNEUMONIA IN CHILDREN WITH CHRONIC DISEASES

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Background

Invasive pneumococcal infections (IPI) are seen more frequently when there are certain coexisting conditions such as: primary and secondary immunodeficiencies, chronic lung and renal diseases, congenital heart diseases, type 1 diabetes mellitus and nephrotic syndrome.

The aim of this study is to evaluate and to compare the nasopharyngeal (NP) carriage rate and serotype distribution of *S. pneumonia* (SP) in children with chronic diseases that predispose to IPI with healthy children.

Methods

NP swabs were collected from children 1–277 months of age in outpatient clinics, pediatric wards and emergency department from January 2015 to December 2015 in Marmara University Pendik Research and Training Hospital, Istanbul, Turkey.

Results

NP swabs were collected from 394 healthy children and 1024 children with chronic diseases. The carriage rate of SP among the healthy children was 8.4% and among the children with chronic diseases was 10.3%. The rate of SP carriage in patients with different comorbidities are as following; asthma 13.5 %, chronic lung disease 8.6%, solid organ tumors 6.7%, leukemia 8.6%, primary immunodeficiency 17.5%, type 1 diabetes mellitus 4%, nephrotic syndrome 8%, chronic renal failure 10.5% and congenital heart diseases 9.3%. Pneumococcal immunization rate was 50% in children with chronic diseases and 52% in healthy children. The most common isolated serotypes in healthy children are serotype 6A/B/C (18%), 35B (9%), 34 (9%), 19F (6%), 15B/C (6%), 22F/A (6%), 7F/A (6%) and 23A (6%). Among the children with chronic diseases the most common isolated serotypes are 19F (15%), 6A/B/C (14%), 15B/C (8%), 22F/A (7%), 23F (7%), 23A (6%) and 14 (5%).

Conclusions

As a conclusion the carriage rates of SP among the children with asthma, primary immunodeficiency and chronic renal failure were higher than the healthy children.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0969
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

MENINGOCOCCAL C CONJUGATE VACCINE IMPACT: ROUTINE IMMUNIZATION IN SAO PAULO STATE, BRAZIL

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Background

Meningococcal disease (MD) occurs as sporadic cases or in endemic form all over the world. The attack rates in Sao Paulo State were highest in infants under 2-years-old (2005-2009 mean incidence of 24.2 cases/100,000 inhabitants/year). Approximately 70% of all cases were from serogroup C. In 2010, the Brazilian Healthy Minister recommended meningococcal C conjugate vaccine in routine immunization schedule for children under 2-years-old. Therefore, this study evaluated vaccine impact in MD incidence in Sao Paulo State.

Methods

A cross-sectional study comparing MD cases in children under 2-years-old in the prevaccine period (2005-2009) with the postvaccine period (2011-2014). The year of 2010 was excluded from analysis since vaccine was gradually introduced for children under 1-year-old and afterwards for children under 2-years-old. Statistical analysis used the Kruskall-Wallis test and a p-value < 0.05 was considered significant.

Results

MD cases in infants under 2 years-old in the prevaccine period were 1,538 versus 610 in the postvaccine period (median 302 vs 140 cases, p=0.01). The incidence also significantly decreased after vaccination (median 24.5 vs 13.1 cases/100,000 inhabitants/year, p=0.01) as well as the mortality (median 5.6 vs 2.1, p=0.01). Regarding MD from serogroup C, there were 498 cases in the prevaccine period versus 113 after vaccine was introduced (median 97.0 vs 22.5 cases, p=0.01). Incidence significantly decreased (median 7.7 vs 2.1 cases/100,000 inhabitants/year, p=0.01) as well as mortality (median 1.3 vs 0.28, p=0.1) in the postvaccine period.

Conclusions

Meningococcal C conjugate vaccine routine immunization for children under 2-years-old led to significant reduction of MD incidence and mortality not only for serotype C, but also for the whole MD cases in Sao Paulo State.

ESP16-0768
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

STRENGHTENING THE REPORTING OF OBSERVATIONAL STUDIES IN EPIDEMIOLOGY FOR NEWBORN INFECTIONS: AN EXTENSION OF THE STROBE STATEMENT FOR NEONATAL INFECTION RESEARCH

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Background

Neonatal infections are estimated to account for a quarter of the 2·8 million annual neonatal deaths, as well as approximately 3% of all DALYs. Despite this Neonatal infections are estimated to account for a quarter of the 2·8 million annual neonatal deaths, as well as

approximately 3% of all DALYs. Despite this burden, data are limited on incidence, aetiology and outcomes, particularly regarding impairment. We aimed to develop guidelines for improved scientific reporting of observational and interventional neonatal infection studies, to increase comparability and to strengthen research in this area. This statement, Strengthening the Reporting of Observational Studies in Epidemiology for Newborn Infection (STROBE-NI), is an extension of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

Methods

STROBE-NI was developed following systematic reviews of published literature (1996-2015), compilation of over 130 potential reporting recommendations, and circulation of a survey to relevant professionals worldwide, receiving responses from 147 professionals from 37 countries. An international consensus meeting of 18 participants (with expertise in infectious diseases, neonatology, microbiology, epidemiology and statistics) identified priority recommendations for reporting, that were additional to the STROBE statement.

Results

The final STROBE-NI checklist is an extension of the 22 item STROBE list, with 28 additional parameters relating to neonatal infection, including a suggested flow diagram for the recruitment and follow up of mothers and newborns (Figure 1).

Conclusions

Implementation of these STROBE-NI recommendations, and linked checklist, aims to improve scientific reporting of neonatal infection studies, increasing data utility and allowing meta-analyses and pathogen-specific burden estimates to inform global policy and new interventions, including maternal vaccines.

ON BEHALF OF: The SPRING (Strengthening Publications Reporting Infection in Newborns Globally) Group**Systematic Review Registration (Please input N/A if not registered)**

N/A

ESP16-0890
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

WHOLE GENOME SEQUENCING OF CARRIAGE AND DISEASE ISOLATES OF STREPTOCOCCUS PNEUMONIAE SEROTYPE 22F REVEALS LINEAGE SPECIFIC DIVERGENCE AND NICHE ADAPTATION

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Background

Streptococcus pneumoniae is a major cause of meningitis, sepsis and pneumonia worldwide. Pneumococcal conjugate vaccines (PCV) were added to the UK's childhood immunisation programme in 2006 and led to a reduction in the incidence of disease. Serotype replacement has been observed and necessitates vigilance and study of emerging serotypes. Serotype 22F is one such example that has been observed in our Southampton paediatric pneumococcal carriage study as well as in European Centre for Disease Control's (ECDC) annual surveillance of invasive bacterial diseases.

Methods

Two clones of 22F (an emerging serotype of clinical concern, multi locus sequence types (MLST) 433 and 698) were isolated and underwent whole genome sequencing and comparative analysis. The four isolates were paired by ST, with one of each pair being derived from carriage and the other disease (sepsis).

Results

The most compelling observation was of non-synonymous mutations in *pgdA*, encoding peptidoglycan *N*-acetylglucosamine deacetylase A, which were found in the carriage isolates of both ST433 and 698. Deacetylation of pneumococcal peptidoglycan is known to enable resistance to lysozyme upon invasion. Whilst no other clear genotypic signatures related to disease or carriage could be determined, additional intriguing comparisons between the two STs are possible. These include the presence of an intact prophage, in addition to numerous additional phage insertions, within the carriage isolate of ST433. Contrasting gene repertoires related to virulence and colonisation, including bacteriocins, lantibiotics and toxin-antitoxin systems were also observed.

Conclusions

S. pneumoniae causing invasive disease remains a significant global challenge and it is vital to continue to explore the genome repertoire of emerging serotypes. Using comparative genomic approaches we have shown a number of serotype 22F lineage specific characteristics of potential significance to disease and carriage.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1001
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

REVIEW OF 3,756 SERIOUS ACUTE RESPIRATORY INFECTIOUS (SARI) CAUSED BY INFLUENZA VIRUS IN SÃO PAULO STATE – BRAZIL, 2013-2015

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Background

Influenza has been associated with large number of serious acute respiratory infection (SARI) and deaths. This study aims at describing the SARI infections caused by influenza virus in SP during three seasons.

Methods

We reviewed the SINAN influenza web database for all SARI cases registered from Jan/2013 to Dec/2015 and analyzed the influenza confirmed cases by type/subtype, age group, presence of underlying diseases and outcome.

Results

From 23,447 SARI cases registered in this period, 3,756 (16.0%) were caused by influenza virus (92.3% detected through PCR). There was large variation on influenza circulation from year to year. Influenza A (H1N1)pdm09 was the predominant one (2,135), followed by influenza A(H3N2) (728), influenza B (734) and influenza A subtype not performed (161). About 25% of SARI cases were confirmed in person < 20 years, and in this age group, the predominant strains were influenza A(H1N1)pdm09 (45.4%) and B (31.6%). At least one comorbidity was reported in 326 children (34.8%) and in 1,509 adults (53.5%). The fatality rate in children was 6.5% and in adults, 21.5%, but was 24.6% in all persons with at least one reported comorbidity.

Table 1: Fatality rate of SARI confirmed cases by influenza virus according to age group and outcome, São Paulo/Brazil, 2013-2015.

Age group	Cure	Death	Total	Fatality (%)
< 20 years	877	61	938	6.5
≥ 20 years	2,213	605	2,818	21.5
Total	3,090	666	3,756	17.7

Conclusions

Influenza caused serious complications and deaths in people of all age groups, with high case fatality rates, even in children without any reported comorbidity. Influenza A and B virus co-circulate in the last three seasons.

ESP16-1106
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

DETECTION OF INFLUENZA B LINEAGES FROM 2013 TO 2015 AT THE SENTINEL SURVEILLANCE OF INFLUENZA IN PARAGUAY

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Background

Since 1983, 2 lineages of Influenza B (Victoria and Yamagata) have been isolated in different countries, but the information about mismatch between B strains and the B lineage included in trivalent influenza vaccines (which corresponded to the Yamagata lineage for the years 2013 to 2015) is scarce for Southern Hemisphere countries.

The objective of this study was to describe the influenza B lineages identified in Paraguay between 2013 - 2015, and compare them with the vaccine strain for those seasons

Methods

Between 2013 and 2015, respiratory specimens from sentinel surveillance of Influenza Like Illness (ILI) and Severe Acute Respiratory Infection (SARI) in Paraguay, were analyzed at the National Influenza Centre. A total of 18250 samples, were screened for influenza A and B viruses, both lineages of influenza B and subtypes of influenza A were identified using real-time RT-PCR.

Results

From all respiratory samples collected, 2,894 (15.8%) were positive for influenza: 2,211 (76. 4%) tested positive for influenza A, and 683 (23.6%) for Influenza B. Among 604 B strains with lineage identification, 277 (45.9%) were Victoria and 327 (54.1%) were Yamagata. The median age of influenza B infected patients was 16 years, while for Influenza A was 23 years. 55% of confirmed cases of influenza B and 57% of influenza A were classified as SARI.

Conclusions

During the study period in Paraguay, both lineages co-circulated in similar proportions over the whole year, and 45.9% of the circulating influenza B belonged to the lineage not included in the vaccine strain. Considering the high percentage of mismatch with B lineage included in TIV (Yamagata), we estimate that the quadrivalent influenza vaccines licensed for Southern Hemisphere could provide better protection as compared with TIV.

ESP16-0292
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

ACUTE NOROVIRUS GASTROENTERITIS IN CHILDREN IN A HIGHLY ROTAVIRUS-VACCINATED POPULATION IN NORTHEAST BRAZIL

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Background

Gastroenteritis is one of the most important causes of morbidity and mortality in children and an important etiological agent is norovirus. We describe the occurrence and characteristics of norovirus diarrhoea in children from Sergipe, Northeast-Brazil, over two consecutive periods of three years following rotavirus vaccine introduction.

Methods

A cross sectional hospital-based survey was conducted from October-2006 to September-2009 and from July-2011 to January-2013. Acute diarrhoea cases had a stool sample collected and tested for norovirus by RT-PCR. Positive samples were sequenced.

Results

In total 280 (19.6%) of 1432 samples were norovirus positive, including 204 (18.3%) of 1,113 samples collected during the first period and 76 (23.9%) of 318 collected during the second period ($p < 0.01$). Norovirus was detected all year-round, without clear seasonality and peaks occurring in different months each year (Figure 1A). The proportion of children with norovirus infection increased significantly through the second study period and was more frequent in rotavirus vaccinated and in younger children. Of 280 norovirus-positive specimens, 188 (67.1%) were sequenced. Of these, 12 were genogroup I and 176 genogroup II. The main genotype was GII.4 (149/188, 79.3%), followed by GII.2 (6, 3.2%) and GII.6 (5, 2.6%). Phylogenetic analysis demonstrated the predominance of GII.4_New Orleans variant from January 2011 to May 2012 and its replacement with GII.4_Sydney from May to August 2012 (Figures 1B).

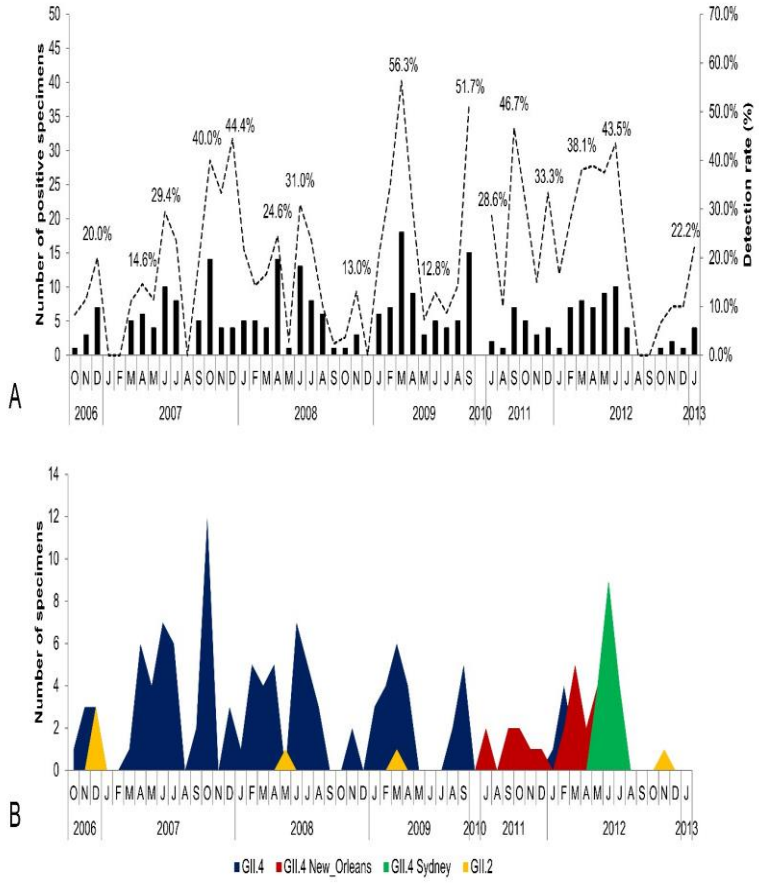

Figure 1. A. Number (bar) and percentage (line) of samples positive for norovirus by month. B. The stacked area represents the norovirus specimens most frequently genotyped during the study.

Conclusions

Norovirus annual detection rates increased over the study period. The detection of norovirus was higher among young and rotavirus vaccinated children. This increase was only partially explained by the younger age of vaccinated children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1008
E-POSTER DISCUSSION SESSION 16 - EPIDEMIOLOGY AND PUBLIC HEALTH 2 (station 10)

NEONATAL INFECTIONS IN GREECE - DATA FROM A EUROPEAN INFECTION SURVEILLANCE NETWORK

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Background

Data on the pathogens causing infections in the Neonatal Units (NNUs) in Greece are limited and the emergence of multi-drug resistant pathogens is an important public health concern. This study aims to describe the epidemiology of neonatal infections in Greek NNUs as captured in the neonIN database (www.neonin.org.uk).

Methods

neonIN is an international web-based infection surveillance network for culture proven neonatal infections. Data from participating Greek NNUs between January 2012 and August 2015 were extracted. Early-onset sepsis (EOS) was defined as occurring within 48 hours of birth. Repeated growth of the same organism within 7 days was considered to be the same episode (or 10 days for Coagulase-negative Staphylococci and fungi).

Results

459 episodes (involving 418 infants) were recorded in 16 NNUs in Greece with a median gestational-age of 33.5 (29-38) weeks, median birth-weight of 1910 (1176-3030) grams and an overall incidence of 50/1000 NNU-admissions. The majority of episodes were late-onset sepsis (LOS) (413, 90%). *Coagulase-negative Staphylococci* (CoNS) (80%) were the most common Gram-positive organisms causing LOS and *Klebsiella spp* (39%) the most common Gram-negative. Resistance among *Enterobacteriaceae* to aminoglycosides was 27% (46/172), to 3rd generation cephalosporins 34% (48/143) and to carbapenems 7% (10/147). Details of the pathogens are shown in the table.

Pathogens	EOS 46 (10 %)	LOS 413 (90 %)
Gram positive (GP)	28 (60.9%)	162 (39.2%)
Gram negative (GN)	17 (37.0%)	207 (50.1%)
Fungi	1 (2.1%)	44 (10.7%)
Most common GP pathogen	CoNS (28.6%)	CoNS (80.3%)
Most common GP pathogen (CoNS excluded)	GBS (30.0%)	*E. faecium* (37.5%)
Most common GN pathogen	*E.coli* (47.1%)	*Klebsiella* sp. (38.7%)
Most common fungi	-	*Candida parapsilosis* (52.3%)

Table Pathogen distribution
EOS: Early-onset sepsis, LOS: Late-onset sepsis, GP: Gram-positive bacteria, GN: Gram-negative bacteria, CoNS: Coagulase-negative staphylococci, GBS: Group-B streptococcus

Conclusions

This is the largest collection of data on the epidemiology of neonatal infections in Greece and will guide the development of evidence-based national guidelines on the management of neonatal sepsis. Continuous surveillance at a national level will facilitate better understanding of the disease and antibiotic resistance burden.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1061
E-POSTER DISCUSSION SESSION 17 - IMMUNOPATHOGENESIS AND NUTRITION (station 2)

CHRONIC MALNUTRITION IS ASSOCIATED WITH INCREASED RESPIRATORY PATHOGEN CARRIAGE IN VENEZUELAN INDIGENOUS CHILDREN

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Background

Malnutrition is rampant in indigenous children. Although the relationship between respiratory infections and acute malnutrition has been well established, few studies have investigated the relationship between nutritional status and nasopharyngeal colonization with potential pathogens.

Methods

Nasopharyngeal swabs were collected from 504 indigenous pneumococcal vaccine-naïve Warao children < 5 years of age. Both weight-for-height and height-for-age Z scores were calculated, indicating acute malnutrition, i.e. wasting, and chronic malnutrition, i.e. stunting, respectively. A multivariable logistic generalized estimation equation regression analysis was performed to assess the influence of nutritional status on nasopharyngeal carriage with potential respiratory pathogens. The multivariable analysis included other factors known to be associated with colonization, such as crowding and age.

Results

Nasopharyngeal colonization rates for *S. pneumoniae*, *S. aureus*, *H. influenzae* and *M. catarrhalis* were 73%, 6%, 1% and 22% respectively. A multivariable analysis was performed for all bacteria except *H. influenzae*, due to low carriage rates. Over one-third of children was stunted with height-for-age Z scores < - 2 standard deviations. In multivariable analysis we observed that better chronic nutritional status (i.e. higher height-for-age Z scores) was associated with less S. pneumoniae and M. catarrhalis carriage (odds ratios 0.81 (95% CI 0.76 - 0.87) and 0.88 (95% CI 0.78 - 0.99), respectively).

Univariate and multivariable analyses of factors associated with nasopharyngeal carriage of potential pathogens in 504[#] Venezuelan Warao children

Characteristic	n (%)	*S. pneumoniae*	univariate	multivariable	*S. aureus*	univariate	multivariable	*M. catarrhalis*	univariate	multivariable
		% carrier	p-value	OR (95% CI)	% carrier	p-value	OR (95% CI)	% carrier	p-value	OR (95% CI)
Sex										
Male	249 (49)	48	0.34	1		0.65	1		0.55	1
Female	255 (51)	52		1.3 (0.97 - 1.79)			0.85 (0.38 - 1.9)			1.1 (0.61 - 2.0)
Age (years)										
0 - 1	188 (37)	78			5			32		
2 - 3	205 (41)	70	0.18*	**0.90 (0.83 - 0.97)***	4	0.09	1.2 (0.88 - 1.7)*	19	**<0.01**	**0.73 (0.64 - 0.84)***
4	110 (22)	69			9			12		
Cooking method										
Woodsmoke	425 (84)	87	0.16	1	85	1.0	1	82	0.31	1
Gas	74 (16)	14		0.72 (0.41 - 1.3)	15		0.81 (0.16 - 4.1)	18		1.4 (0.68 - 3.0)
Wall status of house										
Without walls	148 (30)	71	0.89	1	4	**<0,01**	1	27	0.59	1
With walls	354 (70)	29		1.1 (0.68 - 1.8)	96		**12.1 (1.9 - 78.3)**	73		1.2 (0.61 - 2.3)
Tobacco smoke exposure in household										
No	267 (53)	51	0.11	1	54	0.95	1	51	0.56	1
Yes	234 (47)	49		1.4 (0.9 - 2.2)	46		1.1 (0.48 - 2.7)	49		1.2 (0.65 - 2.1)
Total number of people in household										
≤ 5	121 (24)	22			19			20		
6 to 10	295 (59)	51	0.09	1.0 (0.93 - 1.1)*	59	0.79	1.0 (0.84 - 1.2)*	51	0.26	1.0 (0.96 - 1.1)*
>10	83 (17)	27			22			30		
Total number of children < 5 years of age in household										
1	137 (27)	25			19			24		
2	210 (42)	43	0.07	1.2 (0.85 - 1.7)*	52	0.66	1.1 (0.75 - 1.6)*	44	0.36	1.1 (0.82 - 1.4)*
≥3	156 (31)	32			30			32		
Nutritional status[$]										
Height-for-age Z score										
< - 2 SD	193 (38)	43	**<0.01***	**0.81 (0.76 - 0.87)***	29	0.93	1.0 (0.79 - 1.3)*	47	0.09	**0.88 (0.78 - 0.99)***
≥ - 2 SD	311 (62)	57			71			53		
Weight-for-height Z score										
< - 2 SD	24 (5)	5	0.97	1.0 (0.85 - 1.2)*	7	0.08	0.79 (0.60 - 1.0)*	7	0.08	**0.84 (0.72 - 0.99)***
≥ - 2 SD	480 (95)	95			93			93		

[#] For some characteristics there were missing values (maximum n=5 per characteristic); therefore, not all numbers in the second column sum up to 504.

* These variables were evaluated as continuous variables in univariate and multivariable analysis. This number reflects the mean increase/decrease in no. of children carrying the specific pathogen.

[$] An increase in Z score indicates an improved nutritional status. Odds ratios < 1.0 thus indicate that better nutritional status was associated with less nasopharyngeal carriage.

Conclusions

The highest carriage rates in Venezuelan indigenous children < 5 years of age were found for *S. pneumoniae* and *M. catarrhalis* which were strongly associated with chronic malnutrition. Longitudinal studies are needed to determine whether malnutrition is a risk factor for carriage or whether nasopharyngeal colonization affects growth. In addition to programs focusing on prevention of acute malnutrition during disease episodes, targeting chronic malnutrition may directly affect colonization with disease-causing pathogens.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0355
E-POSTER DISCUSSION SESSION 17 - IMMUNOPATHOGENESIS AND NUTRITION (station 2)

CLINICO-LABORATORY AND INFECTION PROFILE OF CHILDREN ADMITTED WITH SEVERE ACUTE MALNUTRITION AT MALNUTRITION TREATMENT CENTRE IN DEPARTMENT OF PEDIATRICS, S.P.MEDICAL COLLEGE, BIKANER (NORTHWESTERN INDIA)

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Background

Severe acute malnutrition (SAM) among children below five years of age remains a major impediment to optimal human development. This study describes clinico-epedemiological and infection profile of severely acute malnourished children.

Methods

This prospective observational study was conducted in children, 0-60 month of age group, admitted with SAM at malnutrition treatment centre in department of pediatrics, S.P.Medical College, Bikaner (northwestern India). Children were defined for SAM according to WHO standards. These children were examined clinically and investigated thoroughly for evidence of any cause of malnutrition. Data were analysed by student *t*-test and ANOVA test.

Results

Out of total 828 children of malnutrition, 388 were categorized into SAM. The gender proportion was 1.8 (male: female). Most of children were in 6–12 months age (43.1%) followed by 12-18 months age (23.8%) and 0-6 months age (13.6%). These SAM children had clinical manifestations of diarrhea (45.4%), pneumonia (36.3%), CNS infection (9.09%), and urinary infection (4.5%). Tubercular infection was diagnosed in 13.9% children; measles were associated with 11.9% children; and none of the child had HIV infection. Celiac disease was found in 8.5% children. Major causes for SAM were poor faulty feeding (86.2%), low socioeconomic status (78.6%), and female illiteracy (69.7%). The mean hospital stay was 8 days. All these children were treated for infection and supplemented with diet according to standard malnutrition treatment protocol. Most of children (75%) had satisfactory weight gain on follow up.

Conclusions

This study showed that most vulneralble age for SAM was 6-12 months. Gastrointestinal and respiratory infections are the most common cause of hospitalisation and morbidity in SAM. Government has to make policy to strengthen the nutrition at this age.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0415
E-POSTER DISCUSSION SESSION 17 - IMMUNOPATHOGENESIS AND NUTRITION (station 2)

VACCINE EFFECTIVENESS AND GENETIC SUSCEPTIBILITY TO ROTAVIRUS GASTROENTERITIS IN TAIWANESE CHILDREN

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Background

It has been proposed that human rotavirus recognizes the histo-blood group antigens (HBGAs) as ligands to establish infection. The diversity of HBGAs phenotypes in distinct ethic groups may influence the susceptibility to rotavirus acute gastroenteritis (AGE) and vaccine effectiveness. The aim of this study was to evaluate the effectiveness of rotavirus vaccine and associations between the susceptibility to rotavirus AGE and the HBGAs among Taiwanese population.

Methods

A case-control study was conducted in northern Taiwan from April to December in 2015. Cases were children < 18 years old who were hospitalized because of diarrhea and found to have laboratory-confirmed rotavirus infection. Controls were healthy children matched to cases by age and gender. The distributions of HBGAs including secretor status, Lewis antigen and ABO blood types were determined by molecular methods.

Results

A total of 52 cases and 136 healthy controls were included. Rotavirus immunization was identified in 5 (10.0%) case and 79 (58.1%) controls, which gave a vaccine effectiveness of 92.3% (95% confidence interval 79.5% - 97.1%). The secretor and Lewis-positive genotype were more commonly identified in cases than in controls (98.1% versus 77.9%, P<0.001, and 100% versus 89.0%, P=0.013, respectively) but not significantly different between cases with severe diseases and those with mild/moderate diseases (P > 0.05 for both). The distribution of ABO blood types did not differ significantly between cases and controls (P=0.541).

Conclusions

Secretor and Lewis-positive genotypes were significant parameters associated with increased risk of severe rotavirus infections in Taiwanese children. The illness can be prevented by vaccination with an effectiveness of more than 90 percent.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0922
E-POSTER DISCUSSION SESSION 17 - IMMUNOPATHOGENESIS AND NUTRITION (station 2)

GENE POLYMORPHISMS IN THE PROTEIN C AND FIBRINOLYTIC PATHWAY: RELEVANCE FOR SEVERITY AND OUTCOME IN PAEDIATRIC SEPSIS

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Background and Objective

The overwhelming pro-inflammatory host response in severe sepsis affects coagulation and fibrinolysis, resulting in a net pro-coagulant state. Individual responses to infection vary widely and are partly explained by genetic polymorphisms. Our objectives are to give an overview of polymorphisms in the protein C (PC) and fibrinolytic pathway which are associated with susceptibility to or severity of paediatric sepsis. Secondly, to report PC and fibrinolytic pathway polymorphisms associated with other thromboembolic disease in children, which might be candidates for future genetic research in paediatric sepsis.

Methods

A systematic literature search was performed, on 22 April 2014 and repeated on 25 August 2015, for English language, patient-control studies which studied genetic polymorphisms in the PC or fibrinolytic pathway in association with susceptibility to or severity of sepsis or other thromboembolic disease in previously healthy children. References of selected papers were screened for missing papers. 53 papers were selected for this review.

Learning Points Discussion

The high producer *plasminogen-activator-inhibitor-1* 4G/4G genotype is most significantly associated with sepsis mortality. From studies in other thromboembolic disease in children, we hypothesize that *Factor II* G20210A or A19911G polymorphisms, both increasing prothrombin levels, could potentially contribute to the pro-coagulant state in paediatric sepsis. Also genetic polymorphisms associated with the extent of tissue-type or urinary-type plasminogen activator levels might be interesting for future studies. The selected studies for this review included relatively small patient cohorts (median 86 patients, IQR 44-172 patients). Future genetic studies in paediatric sepsis should include large-scale cohorts of homogeneous patients. Newly identified polymorphisms or combination of polymorphisms in hemostatic genes could help to better understand coagulation and fibrinolysis in sepsis, and could eventually contribute to tailor-made therapy.

ESP16-0956
E-POSTER DISCUSSION SESSION 17 - IMMUNOPATHOGENESIS AND NUTRITION (station 2)

MOLECULAR RESEARCH OF ROTAVIRUS GENOTYPES IN CHILDREN HOSPITALIZED IN 2011-2013- SUMMARY REPORT

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Background

Rotavirus is characterised by great geographical and seasonal diversity**.** The G1P[8], G2P[4], G3P[8], G4P[8], G9P[8] and more recently G12P[8] have been defined as the most common human rotavirus strains. Nevertheless, other genotypes are seen more frequently in different parts of the world.Prospective surveillance is needed to monitor and to allow the identification of potentially epidemic and emerging strains. The aim of this study was to present molecular predominance of rotavirus genotype inthe Department of Pediatrics of Bielanski Hospital.

Methods

In 2011-2013, there were 7590 hospitalized children including 18.2% (1379/7590) of gastroenteritis (GE) diagnosis. The main cause of GE was rotavirus infection, detected in 36% (500/1379) of samples. Genotypes of rotaviruses were determined in randomly selected samples 150 (50 per year) by a reverse transcription-polymerase chain reaction, according to their protein capsids VP6, VP4, VP7 and NSP4.

Results

The genotyping of 150 rotaviruses showed a predominance of the G9 – 30%, followed by the G2 – 15,3%, the G4 – 8,6%, the G1 – 4%, and a high coexistence of strains – 31.3%, including the emerging G12. Most G-strains were associated with the P[6] – 46%, followed by the P[8] – 12% and the co-infections – 31,3%. The rotavirus group A (human) was found in 78% and NSP4 in 28% of samples.

Conclusions

The most common rotavirus strain was the G9 and P[6], not included in the current rotavirus vaccines. During the study period, we noticed a molecular changeability of certain genotypes, which differed within our geographic area from year to year.

Clinical Trial Registration (Please input N/A if not registered)

MCPE grant 502-1-20-19/15

ESP16-0170
E-POSTER DISCUSSION SESSION 17 - IMMUNOPATHOGENESIS AND NUTRITION (station 2)

ASSOCIATION OF UNDERNUTRITION, VITAMIN A AND IRON DEFICIENCY WITH IMPAIRED INTESTINAL MUCOSAL PERMEABILITY IN YOUNG BANGLADESHI CHILDREN ASSESSED BY LACTULOSE/MANNITOL TEST

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Background

Lactulose/mannitol (L:M) test has been used as a non-invasive marker of intestinal mucosal -integrity and -permeability (enteropathy). There is insufficient information on L:M and its association with micronutrient status and markers of inflammation. We conducted this study to investigate the association of enteropathy with anthropometrics, micronutrient- status, and morbidity in young Bangladeshi children.

Methods

During November 2009 through April 2013 the study was conducted among residents (poor and middle class families) of an under-privileged community in Dhaka, Bangladesh. The average family income was Tk.4200 (~US $68) per month. Using standard procedures urine and blood samples were collected from 483 underweight (weight-for-age (WAZ) <-2) and 442 well-nourished (WAZ >-1) children aged 6-24 months. L:M test and micronutrient status were assessed in the laboratory of International Centre for Diarrhoeal Diseases Research, Bangladesh (icddr,b) following standard procedure.

Results

Mean±SD age of the children was 13.2±5.2 months and 47.8% were female. L:M of underweight- and well nourished- children were 0.122±0.207 and 0.095±0.071 respectively ($p>0.05$). An overall negative correlation (Spearman's-rho) of L:M was found with age (r_s= -0.087; p =0.004), WAZ (r_s= -0.077; p=0.010), weight-for-height (r_s= -0.060; p=0.034), mid-upper-arm-circumference (r_s= -0.098; p=0.001) and serum-retinol (r_s= -0.105; p=0.002); and a positive correlation with serum C-reactive-protein (r_s=0.126; p<0.001). Approximately 44% of children had enteropathy as reflected by L:M of ≥0.09. Logistic regression analysis revealed that younger age (infancy) (adjusted odds ratio (AOR)=1.35; p=0.027), diarrhea (AOR=4.00; p=0.039) or fever (AOR=2.18; p=0.003) within previous three days of L:M test were the risk factors of enteropathy (L:M of ≥0.09).

Conclusions

Enteropathy (high L:M) is associated with younger age, undernutrition, low vitamin A and iron status, and infection particularly diarrhea and fever.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0828
E-POSTER DISCUSSION SESSION 17 - IMMUNOPATHOGENESIS AND NUTRITION (station 2)

STUDY OF SERUM ZINC, COPPER,MAGNESIUM AND PHOSPHORUS IN CHILDREN WITH SEVERE ACUTE MALNUTRITION

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Background

Protein energy malnutrition is one of the major public health problems and is one of the leading causes of morbidity and mortality in Bangladesh.Malnutrition is widely prevalent among hospitalized children in most developing countries. Though malnutrition accounts for the high rate of under 5 mortality sometimes it is overlooked. So the present study was designed.Objective of the study is to estimate the level of serum zinc, copper, magnesium and phosphorus in children of severe acute malnutrition& compare with that of healthy children

Methods

Comparative cross sectional study in tertiary care hospital. Duration: 1st October 2009 to 31st May 2011. Children aged 1- 5 years with presence of one or more criteria WHM<70%,WH Z-score <-3SD, Bipedal edema MUAC <110mm were taken as study group.ii) Children aged 1-5 years in between 3rd and 97th centile curve (CDC growth chart, USA,2000) as reference group.Serum Zinc, Copper Magnesium and Phosphorus level were determined by Atomic Absorption Spectrometry .Statistical significance of difference between two groups were evaluated by using students unpaired 't' test.

Results

Total 120 study populations were taken .90 Out of 150 were taken as a study group (SAM) & 60 were reference group. In reference group serum Zn , Cu, Mg, P value were103.80±8.86 µg/dl, 135.92±13.57 µg/dl, 2.31±0.18mg/dl, 3.96±0.22mg/dl respectively In study group serum Zn , Cu, Mg, P value were 60.33±11.08 µg/dl, 80.60±15.46 µg/dl, 80.60±15.46 mg/dl, 2.00±0.52mg/dl respectively. This results shows that there is significant difference between study group & reference group.

Conclusions

In Present study shows, significant decrease in serum zinc, copper, magnesium and phosphorus was observed in children with SAM. Considering the decreased level of these parameters, close biochemical monitoring and follow up should be emphasized for the children with SAM.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0615
E-POSTER DISCUSSION SESSION 17 - IMMUNOPATHOGENESIS AND NUTRITION (station 2)

MALNUTRITION, PHYSICAL GROWTH, AND COGNITIVE DEVELOPMENT ASSOCIATED WITH CHILDHOOD DIARRHEA: AN ASSESSMENT OF DIARRHEA DISABILITY-ADJUSTED LIFE YEARS

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Background

The global burden of childhood diarrhea remains substantial despite tremendous decline over the last several decades. The Global Burden of Disease Study (GBD), a systematic, scientific effort to measure the comparative magnitude of health loss by age, sex, and population over time, quantifies diseases using disability adjusted life years (DALYs) lost where DALYs are the sum of mortality and morbidity. DALYs due to diarrhea have traditionally been dominated by childhood deaths, but in light of current evidence, the diarrhea DALYs may be underestimated.

Methods

We have conducted a systematic review of published and unpublished data and performed separate meta-analyses of the impact of childhood diarrhea on physical growth and cognitive development.

Results

Our results show that days of diarrhea significantly increases the risk of subsequent physical growth and cognitive development. Each day of diarrhea was associated with a decrease in height-for-age z-score of 0.003 and a weight-for-age z-score of 0.006. Further, physical growth is significantly associated with cognitive development. Each unit increase in height-for-age z-score was associated with an increase in standardized intelligence scores by 0.08. However, diarrhea was not significantly associated with cognitive development in our analysis, suggesting that malnutrition may be a modifier in this relationship.

Conclusions

Our findings call for including long-term sequelae and better quantifying the non-fatal consequences of childhood diarrhea for a complete understanding of the burden of diarrhea.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESP16-0960
E-POSTER DISCUSSION SESSION 18 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 3 (station 3)

UNUSUAL PRESENTATIONS OF INVASIVE GROUP A STREPTOCOCCAL INFECTION IN CHILDREN FROM 2015

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Title of Case(s)

INVASIVE GROUP A STREPTOCOCCAL INFECTION IN CHILDREN

Background

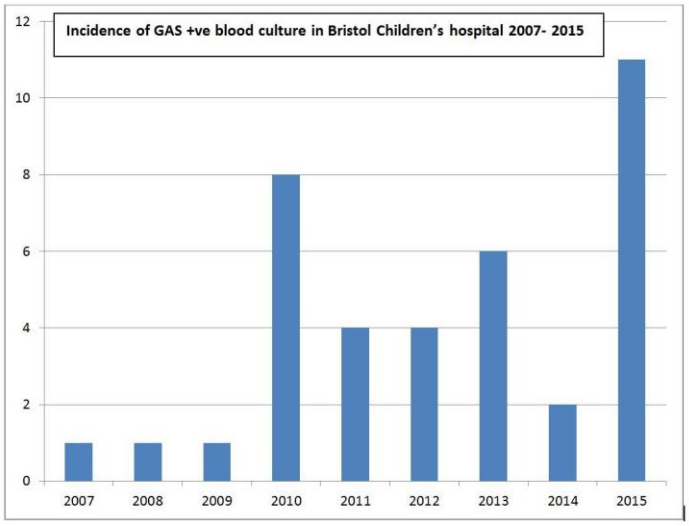
In 2015, there was a significant rise in cases of culture-confirmed invasive group A streptococcal infections (iGAS) at Bristol Children's Hospital compared to previous years (Figure 1), coupled with seemingly more aggressive disease. We review three cases of invasive GAS, illustrating the unusual disease pattern and severity.

Case Presentation Summary

Case 1: A 3 year old boy presented with fever, headache, left-sided third nerve palsy and fluctuating conscious level. Urgent neuro-imaging showed left mastoid and middle ear opacification, enhancement of several cranial nerves and leptomeningeal enhancement. He had multiple seizures and required intensive care management. GAS was isolated from blood culture and 16S rDNA PCR identified GAS in cerebrospinal fluid. He was treated with 3 months IV ceftriaxone and required prolonged neuro-rehabilitation for polycranial neuropathy and behavioural difficulties.

Case 2: A 3 week old girl presented septic with swollen cheek, leg and arm, requiring inotropic support in PICU. Whole bodyMRI confirmed multi-focal septic arthritis and soft tissues collections; GAS was grown from multiple sites. Once clinically stable on ceftriaxone, she continued to develop collections requiring multiple surgical interventions more than 3 weeks later.

Case 3: A 2 year old boy presented with testicular pain and swelling. Surgery revealed an epididymal abscess which was drained, growing GAS. He developed peritonitis and following exploratory laparotomy GAS was also isolated from peritoneal fluid and blood. No source was identified and he recovered completely.



Learning Points/Discussion

GAS can cause severe invasive disease in unusual sites and needs to be considered as a potential causative agent in severe infections, including meningitis. Management should be prompt, aggressive and prolonged. Further research into the change in epidemiology is required.

ESP16-1072
E-POSTER DISCUSSION SESSION 18 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 3 (station 3)

POTT'S PUFFY TUMOUR IN CHILDREN - IS IT REALLY RARE?

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Title of Case(s)

Pott's Puffy Tumour in Children - Is it really rare?

Background

Pott's puffy tumour (PPT) is characterised by osteomyelitis of frontal bone and subperiosteal abscess formation. It is reported to be rare in paediatrics, hence not commonly considered as a differential in children presenting with features of sinusitis.

We describe 4 cases that were referred to the paediatric department at St George's University hospital, London.

Case Presentation Summary

4 cases (ages 8-15 years) were admitted via referral to ENT/Neurosurgery services. Presenting features included fever, headache and facial / forehead swelling. 3 cases had history of multiple presentations during the same illness. All received antibiotics on decision to admit. Time to surgical intervention (frontal extradural drainage, sinus surgery) varied between 1 to 8 days. 2 cases required a second surgical procedure. 2 cases developed venous thrombus one of whom required anticoagulation.

Empirical antibiotics included Coamoxiclav, Flucloxacillin, Ceftriaxone and Metronidazole. S Milleri was isolated from pus sample of 2 cases and Group A Streptococcus from 16sPCR on pus sample on one case. One case had no organism isolated. All received 6-8 IV therapy with Ceftriaxone and 2-4 weeks of Metronidazole (oral + IV)

All cases made complete clinical recovery with ongoing radiological changes in keeping with persistent sinus disease (2 cases) and post infectious brain changes (all cases)

Learning Points/Discussion

Cases of PPT have been increasingly reported suggesting that the condition is commoner than previously thought. Severe complications may arise possibly related to delayed recognition and intervention. Clinicians should be aware of this entity and have a low threshold to seek PID and surgical input. There is currently a lack of data to inform consensus on early treatment of sinus disease or length of therapy for PPT.

ESP16-0788
E-POSTER DISCUSSION SESSION 18 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 3 (station 3)

BURDEN OF TYPHOID AND INVASIVE NONTYPHOIDAL SALMONELLA DISEASE IN MALAWIAN CHILDREN UNDER 4 YEARS

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Background

In a resource-limited setting where antimicrobial resistance is rising, characterisation of the common causes of fever is needed to inform empirical antimicrobial therapy. Blood culture surveillance at Queen-Elizabeth-Central-Hospital (QECH) in Blantyre has identified sequential outbreaks of *Salmonella Enteritidis* (SEN), *Typhimurium* (STM) and *Typhi* (STY). We investigated the hypothesis that the burden of invasive *Salmonella* disease (iSD) in young Malawian children is underestimated by blood culture alone.

Methods

We recruited 465 febrile children under 4 years and a comparative group of 50 children aged 4-15years with suspected Typhoid fever presenting to QECH from August 2014 to December 2015. In addition to blood cultures, EDTA-Blood was incubated in tryptone-soy broth containing ox-bile overnight prior to DNA extraction. Quantitative Real-time-PCR was performed using primers targeting pan-Salmonella, STY and STM. PCR results were classified as positive for STY or STM when a cycle threshold(ct)-value below 20 was reached for both pan-*Salmonella* and the species-specific primer and positive for Salmonella if the pan-Salmonella ct-value was below 20.

Results

Across all ages, blood cultures identified 38/515 (7.3%) children with iSD (23STY/14STM/1SEN). 26/37 (70%) of blood culture positive STY/STM cases were also blood PCR positive. PCR identified Salmonella in additional 12/515 (2%) cases (4STY/5STM/3Salmonella species). Among children under 4 years, prevalence of blood culture-confirmed iSD was 25/465 (5.3%; 11STY/13STM/1SEN). PCR identified 11/465 (2.4%) additional cases (4STY/5STM/2Salmonella species). Compared to blood cultures (median age 5.2 years and 1.5 years for STY and STM), PCR tended to be positive in younger children (3.7 and 1.45 years respectively).

Conclusions

These data suggest that blood PCR may be useful in identifying additional cases of invasive Salmonella disease, even in young children. Further evaluation of the PCR is required exploiting novel serological diagnostic approaches.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0809
E-POSTER DISCUSSION SESSION 18 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 3 (station 3)

DISTRIBUTION OF STREPTOCOCCUS PNEUMONIAE SEROTYPES BEFORE AND AFTER NATION-WIDE PNEUMOCOCCAL CONJUGATE VACCINATION IN CHILDREN IN NORTHERN TAIWAN

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Background

Pneumococcal conjugate vaccine (PCV) has been introduced to Taiwan since 2005 and the nation-wide 13-valent PCV immunisation program started from 2013. We continuously monitored the distribution of capsular serotypes of isolated *Streptococcus pneumoniae* to know the changes before and after the nation-wide immunisation program with particular attention to invasive pneumococcal disease.

Methods

S. pneumoniae strains isolated from children were collected from 2010 to 2015 in two medical centres in Northern Taiwan. Polysaccharide capsule types were determined using Quellung test. Demographic data, vaccine status, serotypes and antibiotic susceptibility were recorded and analyzed.

Results

A total of 548 isolates were serotyped with 132 (24.1%) of them derived from patients with invasive pneumococcal diseases (IPD). Serotype 19A (43.1%), 19F (17.0%) and 15A (9.3%) were the most prevalent serotypes. Both percentage and patient number of 19A decreased by year, while 15A only increased in percentage without significant difference in patient number. Percentage of IPD-isolates from patients not received PCV (non-PCV group) was higher than those received at least one dose of 13-valent PCV (PCV13 group) (45.8% v.s. 14.3%, p=<0.001). PCV13 group had lower percentage of 19A than non-PCV group (p=0.004), while percentage of 15A was higher in PCV13 group than in either non-PCV group (6.0% v.s. 18.4%, p=0.02) or those only received 7-valent PCV patients (2.8% v.s. 18.4%, p=0.0037). There was no significant difference in serotype 19F in terms of vaccination status.

Conclusions

Serotype 19A is declining in the post-vaccination era that contributed the higher percentage in serotype 15A. Patients received at least one dose of PCV13 had lower percentage of serotype 19A and higher rate of 15A. Percentage of serotype 19F was not influenced by the vaccination status.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1075
E-POSTER DISCUSSION SESSION 18 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 3 (station 3)

DESCRIPTIVE STUDY AND EVALUATION OF RISK FACTORS FOR INVASIVE STREPTOCOCCUS PYOGENES INFECTION IN CHILDREN IN MADRID COMMUNITY

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Background: Invasive Group A Streptococcal infection (iGASi) may be a severe disease with increased incidence in recent studies. Aim: to evaluate the incidence of iGASi and possible risk factors associated to this disease in children in Madrid, Spain.

Methods: Medical records from children with iGASi diagnosed in 8 hospitals of Madrid between 2005-2015, were evaluated. Demographic, clinical, diagnostic and treatment parameters, and outcome, were analyzed. Two periods of time were compared: 2005-June 2010(P1) and July 2010-2015(P2).

Results: One hundred and fifty-five children with iGASi were evaluated. Median age was 32 months; 52% female. Most common clinical syndromes were cellulitis/skin abscess(20%), pneumonia(14%), primary bacteremia(12%) and mastoiditis(9%). Sixty seven percent of children underwent surgery and 27% were admitted to PICU. Mean duration of admission and antibiotic therapy were 13 and 19 days, respectively. Resistance to clindamycin/macrolides were unusual. There was a non-significant increase in the number of cases from P1 to P2 (11 vs 18 cases/year;p=0.12). Only the number of diagnosis by PCR and surgical procedures at diagnosis were different between periods (OR 13 [1,71-101] and 3 [1,1-10]). Children >2 years underwent surgery more frequently (OR 2[1,1-3,97]) and those admitted to PICU were younger (41 vs 51 months; p=0.05) and also required more surgical procedures. Developing pneumonia increased the risk of PICU admission (OR:16 [5,3-47,8]). These children were mostly >2 years (74%) and underwent surgery (96%; OR 12 [1,7-98.5].

Conclusions: According to this study, there has been an increase in the number of iGASi in children in our area, which may be due, in part, to a more aggressive approach and new diagnostic tools. Younger children and those with pneumonia had more severe disease whereas older children required surgery more frequently.

ESP16-0105
E-POSTER DISCUSSION SESSION 18 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 3 (station 3)

EBOLA VIRUS DISEASE IN CHILDREN IN SIERRA LEONE: A RETROSPECTIVE COHORT STUDY

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Background

The West African Ebola virus disease (EVD) outbreak claimed over 11300 lives with >28600 cases. Little is known about disease manifestations and the impact of clinical and operational factors on outcomes in children.

Methods

We undertook a retrospective cohort study of children <13 years admitted to 11 Ebola Holding Units (EHUs) in the Western Area, Sierra Leone from August 2014 to March 2015. Primary outcome was death or discharge from care after transfer to specialist Ebola Treatment Centres (ETCs). Retrospective data were collected from paper records at sites, cross-referenced with district-wide laboratory results, burial records, staff interviews and follow-up telephone calls to guardians.

Results

309 children aged 2 days to 12 years testing positive for EVD were included. Outcomes were available for 282 (91%). Case-fatality was 57%: 55% of deaths occurred at EHUs and 45% at ETCs. Age <5y predicted mortality (adjusted OR 1.74, 95% CI 1.04 – 2.93 compared to older children), and death occurred swiftly (median time from admission to death 3 days, IQR 1-5).

Blood test results showed marked derangement of organ function and inflammatory markers with significant hypoglycaemia. 37% were admitted unaccompanied, and 56% were transferred to an ETC 5-380km away.

Conclusions

This is the most comprehensive paediatric cohort of EVD to date, and the only one in adults or children to incorporate data from EHUs and ETCs. Mortality was high and progression to death rapid. As no potentially modifiable factors were identified, prevention must be the primary objective of future strategies.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0794
E-POSTER DISCUSSION SESSION 18 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 3 (station 3)

A GEOSTATISTICAL INVESTIGATION OF VEROTOXIGENIC E. COLI (VTEC) O157 INFECTION IN CHILDREN <5 YEARS IN THE REPUBLIC OF IRELAND, 2008–2013

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Title of Case(s)

A GEOSTATISTICAL INVESTIGATION OF VEROTOXIGENIC *E. COLI* (VTEC) O157 INFECTION IN CHILDREN <5 YEARS IN THE REPUBLIC OF IRELAND, 2008–2013

Background

Ireland has the highest incidence of VTEC infection in the European Union; incidence rates of confirmed infection have increased ten-told over the past decade. Moreover, 3-5% of infections occurring among those aged <5 years are associated with haemolytic uremic syndrome (HUS).Geostatistical analyses and GIS have been employed in the current study to examine associations between geo-coded primary paediatric (<5 years) infections and both agricultural and infrastructural risk factors. All domestically-acquired sporadic or outbreak index cases of VTEC O157 infection during the period 2008–2013, were geo-referenced by to one of >18,000 census enumeration areas and spatially matched with GIS derived explanatory variables including population density, livestock densities, private wells per population, septic tank density and social deprivation score.

Case Presentation Summary

Overall, 78.1% of cases (N = 407) during the reference period were associated with children <5 years. Bivariate analyses indicate an association with lower population densities ($p < 0.001$), higher cattle densities ($p < 0.001$), high private groundwater reliance ($p < 0.001$), and marginally lower socioeconomic status ($p < 0.001$). Logit modelling indicates that cattle density (OR = 1.001, 95% CI 1.001–1.003) and private well reliance (OR = 4.026, 95% CI 1.167–13.89) are the primary pathogen source and pathway, respectively.

Learning Points/Discussion

Paediatric VTEC O157 infection in the Republic of Ireland is a characteristically rural disease. Accordingly, a health inequality currently exists within the context of residential classification or “place”.

ESP16-0413
E-POSTER DISCUSSION SESSION 18 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 3 (station 3)

PRESENT - DAY MULTILOCUS SEQUENCE TYPES OF INVASIVE S. PNEUMONIAE ISOLATES FROM INDIAN CHILDREN UNDER FIVE AND THEIR CORRELATION TO ANTIBIOTIC RESISTANCE

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Background

Molecular epidemiology data is essential to understand the population dynamics of *S. pneumoniae* in India before the introduction of pneumococcal vaccines in NIP. The aim of this study was to evaluate the genotypic and phenotypic characteristics of *Streptococcus pneumoniae* isolates. MLST was used to determine clonality, to establish genetic relatedness, and sequence types (STs). Serotype and antibiotic resistance characters were analyzed

Methods

Seventy six Invasive pneumococcal isolates collected during 2013-15 from children < 5yrs were characterized. The organism was characterized by optochin sensitivity, bile solubility and capsular typing with Quellung Reaction. The analysis of the genotypic characteristics included autolysin, pneumolysin and psaA detection by PCR and MLST using seven housekeeping genes (aroE, gdh, gki, recP, spi, xpt, ddl). STs were analyzed for clonality using an eBURST algorithm. Antibiotic susceptible profile was generated using microdilution method

Results

Fifty Three novel STs were identified which had known alleles but in new combinations. The novel STs are being submitted to MLST database. One clonal complex was found among 76 isolates. The Most common serotypes were 1, 6B, 19A and 19F. Antibiotic resistance for Penicillin, Erythromycin, Levofloxacin, Tetracycline and Cotrimoxazole was 12%, 31%, 8%, 40% and 60% respectively. 29% of the isolates had multidrug resistance. Among MDR isolates, 7 isolates had reported STs and 15 isolates had novel STs. 7 MDR isolates belong to reported ST groups and remaining 15 to novel ST groups

Conclusions

This study reports a significant number of novel STs, in addition to internationally recognized strains circulating in India, highlighting the geographical variation in pneumococcal STs. High MDR in novel STs is a matter of concern which needs to be monitored.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0750
E-POSTER DISCUSSION SESSION 19 - VIRAL INFECTIONS (station 4)

IMPACT OF HCV CO-INFECTION ON THE EVOLUTION OF VERTICALLY ACQUIRED HIV INFECTION DURING CHILDHOOD

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Background

Although HCV co-infection is a well-known prognostic factor in HIV-infected populations, few studies have described the effects of HCV on the evolution of vertically acquired HIV infection in children and adolescents.

Methods

Cross-sectional study among vertically HIV-HCV and HIV-infected patients registered in the Spanish Cohort of HIV-infected Children (CoRISpe) that were transferred to Adult Units (AU) before December 2014. The clinical situation of both groups of patients when transferred to AU was analyzed.

Results

Up to December 2014, 444/1165 (38.1%) vertically HIV-infected patients registered in CoRISpe were transferred to AU, 56 (12.6%) of whom were HIV-HCV co-infected. There were no differences in the proportion of HIV/HCV and HIV-infected women (55.3% vs. 55.7%). The age of transition was not different (18[16.8-18.8] *vs.* 18.1[16.8-19.1]), neither the %CD4 nadir (12.7[7-19] *vs.* 13[6-19], nor the number of ART regimens received (5.6 *vs*. 5.8). CD4 counts (cell/mm^3) were good: 681[436-881] within the co-infected group and 715[458-927] within HIV-infected patients. Co-infected patients presented a better virological control (HIV-ARN<50cop/mL): 61.8% *vs.* 52.7% (p=0,27) and 14.4% *vs.* 27.7% (p= 0.05) were on stage C. Moreover, 3.6% *vs.* 11.4% (p=0,13) were transferred to AU without ART and 34% *vs*. 26.5%

(p=0,35) were receiving QD regimens. Over half (58.8%) of HIV-HCV patients were transferred to AU without fibrosis (F0-1); 6(10.7%) patients were unsuccessfully treated against HCV during pediatric care using interferon and ribavirin.

Conclusions

HIV-HCV co-infected patients tend to present a better clinical and virological condition at the time of transition and are more frequently on ART. Most co-infected patient were transferred to AU without liver fibrosis. This unique population now has an opportunity to receive new drugs developed for treating HCV and be cured from the infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0301
E-POSTER DISCUSSION SESSION 19 - VIRAL INFECTIONS (station 4)

UNIQUE CHARACTERISTICS OF ENTEROVIRUS D68 IN CHILDREN IN SOUTHERN ISRAEL

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Background

Clusters of Enterovirus D-68 (EV-D68) infections have emerged globally since 2004, such as the 2014 outbreak in North America. EV-D68 affects mostly children with comorbidities, causing mainly respiratory manifestations. EV-D68 is also related to neurologic morbidity resembling poliovirus. Our objective was to compare laboratory confirmed EV-D68 associated morbidity with other EV strains, in hospitalized patients in southern Israel.

Methods

This was a retrospective study. The Soroka University Medical Center serves the entire population of southern Israel composed of two ethnic groups - Bedouins and Jews. All laboratory samples from November 2013 to October 2015, positive for EV were further tested for EV-D68 by specific qRTPCR (quantitative real time PCR). Clinical data were obtained from the hospital's computerized records for all patients positive for any EV with an upper respiratory or CSF sample, which are specific for acute infection. Positive rectal swabs were attributed to colonization

Results

A total of 3676 samples from children and adults were tested, 695 were found to be positive for EV. 22/695 (3.2%) of EV positive patients were EV-D68 (8 nasopharyngeal washes and 14 rectal swabs). No sociodemographic differences were noted between the 2 groups. The most common clinical manifestation of EV-D68 positive patients was respiratory distress. One child presenting with myocarditis died. **Table 1** shows the comparison of clinical manifestations of EV-D68 positive patients with other EV-strains.

Table 1

	EV-D68 positive (n=8) NPW=8	Other EV strains (n=293) NPW=157 CSF=123 NS-=13	P value
Age in month (Average ± SD)	30.5 ± 22	30.13 ± 73.7	0.98
Male (n, %)	4 (50%)	170 (58%)	0.72
Bedouin (n, %)	6 (75%)	170 (58%)	0.47
Respiratory manifestations (n, %)	5 (62.5%)	38 (12.9%)	**0.002**
Neurologic manifestations (n, %)	1 (12.5%)	148 (50%)	0.06
Oxygen (n, %)	5 (62.5%)	31 (10.5%)	**<0.001**
ICU (n, %)	5 (62.5%)	36 (12.3%)	**0.001**
Mortality (n, %)	1 (12.5%)	4 (1.36%)	0.12

NPW, Nasopharyngeal Wash; CSF, Cerebrospinal Fluid, NS-Nasal Swab; ICU, Intensive Care Unit

Conclusions

EV-D68 is mainly a respiratory pathogen with more severe manifestations and pediatric intensive care unit admissions rates compared with other EV-strains. No polio-like illness related to EV-D68 was noticed in southern Israel.

ESP16-0604
E-POSTER DISCUSSION SESSION 19 - VIRAL INFECTIONS (station 4)

CHRONIC HEPATITIS E TREATED WITH RIBAVIRIN IN A KIDNEY TRANSPLANT CHILD
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Title of Case(s)

Chronic hepatitis E treated with ribavirin in a kidney transplant child.

Background

Chronic hepatitis E is described in adults and children immunosuppressed patients, with potential progression to fibrosis. Treatment with Ribavirin has been described as effective in adults.

Case Presentation Summary

A ten-year-old boy has had a kidney transplant at the age of one year for severe malformative uropathy complicated by chronic humoral rejection with severe chronic renal failure.
While he was treated by tacrolimus, mycophenolate mofetil and steroids, chronic hepatitis E was diagnosed on elevated liver enzymes (5xN), anti HEV Ig M +, Ig G -, PCR Hepatitis E + in blood and feces for more than six months.
Given the chronic nature and the inability to reduce immunosuppression, initiation of ribavirin treatment with dosage adjustment at renal clearance. Treatment was well tolerated under regular control of the ribavirin blood level, and efficient with normalization of liver function tests in six weeks and PCR negativity in blood and stool after one month. Discontinuation of ribavirin three months after PCR negativation in blood and feces (four months of treatment in total). The negativity of the PCR was maintained at over six months of stopping treatment.

Learning Points/Discussion

Chronic hepatitis E in a pediatric kidney transplant and immunocompromised patient can be effectively treated with ribavirin.

ESP16-0343
E-POSTER DISCUSSION SESSION 19 - VIRAL INFECTIONS (station 4)

EFFECTIVENESS OF NON-SPECIFIC HUMAN IMMUNOGLOBULIN AS POSTEXPOSURE PROPHYLAXIS AGAINST VARICELLA ZOSTER

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Background

The use of immunoglobulin for post-exposure prophylaxis to prevent chickenpox in children under 1 year old and other susceptible patients is based on evidence from studies with hyperimmune immunoglobulin. This drug is not available for this indication in Spain and other countries, where non-specific human immunoglobulin is used instead. However, there is no direct evidence for the effectiveness of this measure.

Methods

An analytical cohort study was performed with a retrospective data collection to assess the effectiveness of intramuscular non-specific immunoglobulin administration as post-exposure prophylaxis against varicella zoster in susceptible contacts of a confirmed case. Vaccination must be contraindicated (pregnant women, children younger than 12 months, immunocompromised patients) and time between exposure and administration of immunoglobulin should be less or equal to 5 days. Patients treated between 2003 and 2013 were included.

Results

From 53 contacts receiving non-specific immunoglobulin intramuscularly, 13 (25%) developed varicella. All these cases were mild (fewer than 50 lesions) and without complications. The effectiveness of non-specific immunoglobulin to prevent chickenpox in postexposure prophylaxis of susceptible contacts was 71.8% (95%CI 56.0 - 84.1). The effectiveness of this measure by risk group was 72.3% (95%CI 50.0 - 88.1) in children under 1 year and 71.3% (95%CI 34.3 - 93.7) in pregnant woman and immunosuppressed patients. The effectiveness of immunoglobulin in the first 72 hours was 71.3% (95%CI 43.6 - 90.1).

Conclusions

Non-specific immunoglobulin for post-exposure prophylaxis against chickenpox is a good therapeutic option for contacts with contraindications to the vaccine. The effectiveness to prevent the disease or lessen its course towards milder forms was complete for the studied cohort. No statistically significant differences between the effectiveness of the measure were found according to the risk group or time from exposure.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0078
E-POSTER DISCUSSION SESSION 19 - VIRAL INFECTIONS (station 4)

HUMAN BOCAVIRUS INFECTION IN ACUTE LOWER RESPIRATORY TRACT INFECTION IN CHILDREN

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Background

There were a few study of Human bocavirus(HBoV) infection in acute lower respiratory tract infection (ALRTI) in children. The aims of this study is to investigate the roles of HBoV on ALRTI and to outline the clinical features of ALRTI associated with HBoV infection in children.

Methods

Total 4370 children with clinical diagnosis of ALRTI from March 2007 to February 2015 were enrolled. One nasopharyngeal aspirate specimen was collected from each patient when admission. Multiplex RT-PCR were performed to detect 15 common respiratory viruses including RSV, HRV, IFV, PIV type 1-4, ADV, HCoVs, EV, hMPV and HBoV. Epdemiological features, Clinical manifestation and laboratory findings of ALRTI with HBoV were analyzed. The clinical features of single HBoV infection and single RSV infection were compared.

Results

The overall positive rate of HBoV infection was 7% (308/4370), and 78.9% (243/308) of cases with HBoV infection co-infected with at least one other respiratory virus. The positive rates of HBoV infection were 6.4%, 17.4%, 4.3% and 2.4% in group of <1 year old, 1 - <3 years old, 3 - <6 years old and ≥6 years old, respectively. There were total 11 ALRTI patients with single HBoV infection, including 8 bronchial pneumonia and 3 bronchitis. The most common clinical manifestations included cough in 11 patients, abnormal chest x-ray in 11 patients, fever in 9 patients, dyspnea in 1 patient. There was no significant difference between the clinical manifestations or severity of ALRTI with single HBoV infection and single RSV infection.

Conclusions

HBoV is correlated with ALRTI in young children. The severity of ALRTI associated with HBoV infection was comparable to that of ALRTI with RSV infection in children.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0515
E-POSTER DISCUSSION SESSION 19 - VIRAL INFECTIONS (station 4)

CLINICAL AND EPIDEMIOLOGIC CHARACTERISTICS OF NOROVIRUS GASTROENTERITIS IN LEBANON AND THE MIDDLE EAST AND NORTH AFRICA (MENA) REGION AMONG CHILDREN LESS THAN FIVE YEARS OLD

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Background

Norovirus (NoV) is responsible for at least 50% of all gastroenteritis outbreaks worldwide. NoVs are classified into six different genogroups (GGI- GGVI) based on the viral capsid protein with NoV genogroup II genotype 4 (GGII.4) being the predominant strain causing human diseases. This study aims to determine the incidence of Norovirus gastroenteritis and the distribution of their genotypes among hospitalized children less than 5 years old in Lebanon and to compare results to those reported by countries of the MENA region.

Methods

Stool samples were collected from six major hospitals in different regions of Lebanon during a period of 30 months. A total of 739 samples were tested for NoV by RT-PCR. Nucleotide sequencing of the major capsid protein gene was performed and phylogenetic tree was inferred to determine the extent of diversity and evolution among detected viruses.

Results

11.2% of our samples tested positive for NoV with the highest number of cases detected during the hot months. 68% of positive cases were attributed to GII.4 and specifically the JB-15/KOR/2008 Apeldoorn variant strain circulating in 2011 and replaced between 2012 and 2013 by a variant sharing homology with Sydney/ NSW0514/2012/AUS GII.4 Sydney 2012 and the Sydney 2012/FRA GII.4. We also report non-GII.4 genotypes among hospitalized children in Lebanon.

Conclusions

Our results are compatible with globally reported ones whereby the majority of viral gastroenteritis outbreaks are attributable to GII.4. Few studies reported on NoV in the MENA region among hospitalized children less than 5 years old with GII.3 being more prevalent. There is a clear lack of data on the clinical diagnosis and genetic relatedness of NoV in the MENA region and further studies are needed in order to support intervention strategies.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0076
E-POSTER DISCUSSION SESSION 19 - VIRAL INFECTIONS (station 4)

THE EPIDEMIOLOGIC FEATURES OF JAPANESE ENCEPHALITIS IN TAIWAN FROM 2000 TO 2014

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Background

Japanese encephalitis (JE) is one of the severe vector-borne viral encephalitis worldwide. With the establishment of JE surveillance and vaccine use in Taiwan, the JE incidence rate has decreased; however, cases with JE still occur. Understanding the characteristics of JE cases and identifying the circulating JE virus genotype will improve JE prevention and control. The purpose of this study was to explore the epidemiologic characteristics and risk factors of JE in Taiwan.

Methods

We analyzed data reported as part of surveillance programs run by the Taiwan Center for Disease Control (Taiwan CDC).

Results

Between 2000 and 2014, a total of 379 confirmed JE were reported to Taiwan CDC. The annual incidence rate of JE cases was from 0.07 per 100,000 in 2000 to 0.18 per 100,000 in 2007 (0.13 on average). The epidemic season appeared from May to October, with a peak in July and August. The age distribution shifted from mainly children to adults, with 90% of confirmed JE cases older than 20 years (range, 20-70 years). Male to female ratio was 1.5:1. Most JE cases occurred in Eastern, Central, and Southern regions in Taiwan. Mosquito surveillance showed that *Cx tritaeniorhynchus* and *Cx annulus* were the most important JEV vectors to human and domestic animals.

Conclusions

The JE remains a prominent public health problem in Taiwan. To strengthen surveillance systems of JE and implementation of national JE vaccination program are needed for prevention and control of JE.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0360
E-POSTER DISCUSSION SESSION 19 - VIRAL INFECTIONS (station 4)

TENOFOVIR IN UTERO EXPOSURE - DENSITOMETRIC AND BIOCHEMICAL STUDY OF BONE METABOLISM IN PRESCHOOL CHILDREN

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Background

Incidence of vertical transmission of HIV has declined in recent years due to the implementation of measures such as combine antirretroviral treatment (cART) in pregnant women and newborn. Tenofovir disoproxil fumarate (TDF) is considered a first line ART drug, however during pregnancy TDF has been associated with potentially teratogenic effects (animal studies): impaired bone mineralization, small for gestacional age (SGA) and congenital abnormalities. Human experience is controversial.

Methods

Prospective cohort study of non-infected children, born to mothers with HIV infection receiving cART. Patients were divided into TDF exposed or not during pregnancy. GA and antropometrics data at birth, posterior weight and height/length were collected. Bone mineralization density (z score) through Dual-energy X-ray absorptiometry (DXA) of lumbar region and biomarkers of bone turnover were determined.

Results

10 babies (5 exposed; 5 not exposed) were included. The incidence of SGA was equal in both groups. Anthropometric measurements were within normal range at birth in both groups (table 1). Two of five patients of the TNF exposed group had short stature postnatal growth and none of the not TNF exposed group. All subjects had normal values of biochemical parameters, however bone alkaline phosphatase (BAP) and cross linking telopeptide of tipe 1 collage CTX (increased bone remodeling) values were higher in the TNF exposed group. Lower weight percentile suposes higher values of P1NP (p=0,0142), pointing an increased osteogenesis at aerlier ages. None of subjects had osteopenia at DXA study, BMD and z

score being similar in both

	TDF (n = 5)	No TDF (n = 5)	p Value
Age (months) (median, IQR)	42 (34,5)	54 (26,5)	0,056
Prematurity¶ (n)	0	1	-
SGA§ (n)	1	1	-
Birth Weight percentile (median, IQR)	21 (84)	14 (35,5)	0,905
Birth Length percentile (median, IQR)	19 (52,5)	44,5 (61,5)	0,556
Birth Craneal Perimeter percentile (median, IQR)	50 (58,5)	36 (19)	1
Last Weight percentile (median, IQR)	37 (18)	47 (51,5)	0,421
Short Stature¥ (n)	2	0	-
Last height percentile (median, IQR)	41(64)	28 (54)	1
BAP (UI/L) (median, IQR)	187,5 (49)	267 (122)	0,2
PTH (pg/mL) (median, IQR)	20 (13)	22 (1)	0,786
P1NP (ng/mL) (median, IQR)	697 (679)	570 (149)	0,841
CTX (pg/mL) (median, IQR)	838,8 (6165)	978,5 (399)	1
BMD (gr/cm2) (DXA) (median, IQR)	0,539 (0,2345)	0,498 (0,1049)	0,4
Z score (DXA) (median, IQR)	-0,75 (0,7)	-0,3 (-1,4)	0,786
Osteopenia$ (n)	0	0	-

¶Prematurity = < 37 weeks gestacional age. §SGA = small for gestacional age (birth weight <p3 or -2SD). ¥Short Stature= height <p10. BAP = bone alkaline phosphatase. P1NP = procollagen I A-terminal propeptide. CTX = cross linking telopeptide of tipe 1 collage. BMD = bone mineral densit. DXA = Dual energy X-ray absorptiometry. $Osteopenia = DXA z score < -2SD.

groups.

Conclusions

In this small study no differences in prevalence of SGA, bone mineralization and/or anthropometric data between children exposed in utero to TDF compared to non-exposed subjects were found.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1035
E-POSTER DISCUSSION SESSION 20 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 4 (station 5)

B. PERTUSSIS INFECTIONS IN A TERTIARY HOSPITAL IN SEVILLE BETWEEN 2011-2015 PRIOR TO SYSTEMATIC INTRODUCTION OF PERTUSSIS VACCINE IN PREGNANT WOMEN

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Background

To describe epidemiological, clinical, laboratory characteristics and mortality of patients hospitalized with *B. pertussis* at the University Hospital Virgen del Rocío in Sevilla before systematic introduction of pertussis vaccine in pregnant women in 2016.

Methods

Retrospective study of infants admitted with microbiological diagnosis *B. pertussis* using PCR technology between 2011 and 2015.

Results

Series of 87 infants, of whom 18 were admitted to ICU and 6 died. The range of annual frequency of cases admitted was 13 (2011) to 25 (2014). The median age was 61 days (range 12-500). Vaccination status (number of doses administered) against *B. pertussis* prior to hospital admission, were as follows: 0 (54%), 1 (36%), 2 (8%), 3 doses (3%). There was evidence of co-infection by RSV in 6 (7%) infants. Patients admitted to the ICU were less likely to have a presumed diagnosis of *B. pertussis* at time of admission (39% vs 74%, p=0.007) and had less frequently signs of whooping cough (33% vs 87%, p<0.001). However, they suffered more frequently from apneas (50% vs 23%, p<0.001), respiratory distress (39% vs 5%; p<0.001) and pneumonia (56% vs 5%; p<0.001), and had higher WBC (x10e9/L; 63.13 ±35.86 vs 29.54 ±15.17, p=0.0002), CRP (mg/L; 61.6 ±66.5 vs 10.4 ±5.1; p=0.005) and more days of hospital admission (13.8 ±12.9 vs 6.5 ±4.02; p=0.037).

Conclusions

Pertussis continues to be associated with significant morbidity and mortality over the last 5 years in our center. These data provide the basis for future studies in order to assess the impact of the now launched pertussis vaccine for pregnant women in Andalucía.

ESP16-0128
E-POSTER DISCUSSION SESSION 20 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 4 (station 5)

NEUROLOGICAL INFECTIONS BY ENTEROVIRUS AND BACTERIAL COINFECTIONS IN VERY YOUNG INFANTS WITH FEVER.

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Background

Very little information exists on simultaneous infections from viruses and bacteria in infants with fever without source (FWS). Our aim was to investigate viral-bacterial coinfections in those infants diagnosed of viral meningitis or systemic infection.

Methods

Prospective study (funded PI12-00904 AES) performed during 18 months in infants less than 3 months of age admitted to two hospitals in Spain with FWS. We included the infants in which lumbar puncture was done to perform a viral screening and bacterial infection study through blood, CSF and urine cultures. Viral EV and HPeV detection in CSF was performed using a PCR assay.

Results

A total of 119 infants <90 days were included. A virus was detected in CSF in 45 of them (38%); 33 EV (27.7%), 11 hPeV (9.2%) and 1 HV6 (0.8%). Mean age was 33 + 22 days and 63% were males. Among the 45 infants wiht a virus in CSF, 8 of them had also a bacterial infection. That means that there are 17.7% of coinfections in infants with neurological viral infection. All of these cases were in the EV group (none in hPeV infections). Bacterial infections were urinary tract infections (*E.coli)* 7 cases and one sepsis by *P.multocida.*

Conclusions

Neurological infections by EV and hPeV are very frequents in infants less than 90 days with FWS. Coinfections in young infants between EV in CSF and bacterial infections, especially urinary tract infections are common. It is unclear the role of viral infection in these patients, but the finding of a viral infection in young infants, does not rule out a bacterial infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0648
E-POSTER DISCUSSION SESSION 20 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 4 (station 5)

MANAGEMENT OF CHILDREN WITH SUSPECTED MENINGITIS – ROOM FOR IMPROVEMENT: A MUTICENTRE PROSPECTIVE COHORT STUDY

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Background

The incidence of bacterial meningitis has significantly decreased since the introduction of bacterial conjugate vaccines. Viral pathogens are now the commonest cause of childhood meningitis in the UK, but delays in treatment of bacterial meningitis are associated with poorer outcomes. Incomplete microbiological investigation may increase the proportion of children without a pathogen identified.

Methods

The study was undertaken at 3 UK hospitals. Inclusion criteria were: child <16 years; new hospitalisation with suspected meningitis or having an LP as part of a sepsis screen. Clinical data were collected from hospital records and parental interview. Pearson's chi-squared tests were used to compare categorical variables and student's t-tests to compare continuous variables.

Results

388 children were recruited; 70 had meningitis. 220/388 (57%) were seen by a medical professional before hospitalisation (134/220 by their GP). The median time between initial hospital assessment and LP was 4.8 hours and between assessment and first dose of antibiotics was 3.1 hours, with 62% of children having an LP after antibiotics. Children ≥3 months experienced longer delays until both LP ($p<0.0001$) and antibiotics ($p<0.0001$) than those <3 months. When no pathogen was identified, hospital stay was longer if LP was performed after antibiotics (median 13 days vs 5 days, $p=0.0334$). In meningitis of unknown cause, CSF PCR was performed for meningococcus in 7%, for pneumococcus in 11% and for enterovirus in 79%.

Conclusions

There are significant delays in early hospital management of children with suspected meningitis. Many children are seen by a GP before hospital admission, providing a potential opportunity for earlier referral. Currently available investigations are under-utilised, and increasing their use could reduce the number of children who do not have a pathogen identified.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0834
E-POSTER DISCUSSION SESSION 20 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 4 (station 5)

SEVERE ENTEROVIRUS INFECTIONS REQUIRING INTENSIVE CARE ADMISSION IN THE UNITED KINGDOM AND IRELAND

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Background

Enterovirus and human Parechovirus infections are prevalent in paediatric population and generally associated with mild to moderate upper respiratory and gastrointestinal symptoms. Rarely, they may also cause severe illnesses, including meningo-encephalitis, myocarditis, septic shock. This study describes the burden of severe Enterovirus and Parechovirus infections in children admitted to Paediatric Intensive Care Units (PICUs) in the UK and Ireland during 2010-14.

Methods

Anonymised data on all children aged 0-16 years, admitted in Paediatric Intensive care unit (PICU) in the UK and the Republic of Ireland with Enterovirus or human Parechovirus infection diagnosed between 01 January 2010 and 31 December 2014 were obtained from PICANet (Paediatric Intensive Care Audit network) in July 2015.

Results

In total, 104 children were admitted to PICU with Enterovirus or human Parechovirus infections during 2010-14. Annual number of cases and incidence increased significantly over the five year period, from 0.6/1,000 PICU admission (12 cases) in 2010 to 1.8/1,000 (36 cases). The male-to-female ratio was 1.7 and infants (aged <1 year) accounted for 83% (86/104 cases) of admissions. There was a bi-modal seasonal distribution, peaking in June-July and again in November-December. Most children had a severe course of illness in PICU, with 77% (80 cases) requiring invasive ventilation, 40% (42 cases) inotropic support, 4% (4 cases) renal dialysis, and 3% (3 cases) extra-corporeal membrane oxygenation. Eight children died in PICU (case fatality rate, 7.7%).

Conclusions

We have estimated the minimum incidence of Enterovirus and human Parechovirus infections in children admitted to PICU in the UK and Ireland. The rapid and continuing increase in incidence suggests that the true burden of disease is likely to be substantially higher that our estimates.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1030
E-POSTER DISCUSSION SESSION 20 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 4 (station 5)

CLINICAL BURDEN OF ENTEROVIRUS AND PARECHOVIRUS MENINGITIS IN INFANTS YOUNGER THAN 90 DAYS OLD IN THE UNITED KINGDOM AND REPUBLIC OF IRELAND

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Background

Enterovirus (EV) meningitis accounts for over 90% of all cases of viral meningitis in young infants. This study aimed to prospectively collect detailed clinical information for all confirmed cases of EV and human parechovirus (HPeV) meningitis in in infants younger than 90 days in the United Kingdom and Ireland over a 13-month period.

Methods

Prospective national surveillance study during June 2014 – June 2015 through the British Paediatric Surveillance Unit (BPSU). All consultant paediatricians reporting a case were asked to complete a detailed clinical questionnaire.

Results

During the 13-month surveillance period, 388 cases of EV (n=366) and HPeV (n=22) meningitis were identified through the BPSU surveillance. The majority presented between 15 and 89 days of age (77%, 299/388) and only 6% (22/388) had been born prematurely (<37 weeks gestation). The three commonest clinical presentations for EV meningitis were fever (85%, 310/366), irritability (64%, 234/366) and reduced feeding (53%, 194/366).

10% (37/366) and 23% (5/22) of EV and HPeV meningitis cases respectively were admitted to PICU/NICU.

In 97% (375/388) of cases, the virus was confirmed in the CSF by PCR. Of these, only 58% (216/375) had a CSF white cell count (WCC) >20ml. The majority (74%, 287/388) had a CRP level <20mg/L. None of the cases had a secondary bacterial infection. One child (0.3%) died and six of the survivors (1.6%) had significant neurological impairment secondary to EV/HPeV meningitis at discharge.

Conclusions

The great majority of infants with EV/HPeV meningitis are diagnosed through CSF PCR, highlighting the importance of lumbar punctures when evaluating febrile infants with non-specific clinical presentations. A small proportion have significant long-term neurological complications. Future studies should evaluate long-term neurodevelopmental outcomes and define targets for future antiviral therapy.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0374
E-POSTER DISCUSSION SESSION 20 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 4 (station 5)

PROSPECTIVE STUDY OF ENTEROVIRUS AND PARECHOVIRUS INFECTIONS IN CHILDREN UNDER 3 YEARS-OLD IN SPAIN

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Background

Human enteroviruses (EV) and more recently parechoviruses (HPeV) have been recognized as important viral causes of severe infections in children. Our aim was to investigate the epidemiology of EV/HPeV infections and their clinical association in children over a 3-y study period in Spain.

Methods

Prospective study (2013-2015) performed in 12 hospitals in Spain (Grant PI12-00904). EV and HPeV infections were investigated in cerebrospinal fluid, sera or throat swab from children < 3y of age admitted with fever without source, clinical sepsis or meningitis/encephalitis. Clinical data were recorded. Viral detection in clinical samples was performed by RT-PCR and further genotyping.

Results

A total of 750 patients were included in the study. Of them, 391(52%) were EV-positive and 42(6%) were HPeV-positive. 26 different EV types were identified while 95% of HPeV were type 3.

So far, data of 448 cases have been analyzed, comparing EV and HPeV infections clinically (170 vs 24). EV-infections were associated with pleocytosis (40% vs 4%,p=0.001) and meningitis (28% vs 0%,p=0.0001), and higher leucocytes (10200+5000 vs 7200+3800 cells/mm3,p=0.04) in blood. HPeV infections were associated with younger age (24+15 vs 137+273 days,p=0.04) (100% children <2 months), with irritability (50% vs 20%,p=0.005), clinical sepsis (28% vs 5%,p=0.0001), antibiotic treatment (100% vs 70%,p=0.002), and PICU admission (30% vs 9%,p=0.004).

Both groups had similar proportion of fever symptoms 93% vs 100%, and exanthema 18% vs 14%. Only 1 child died in EV-positive group and 2 had sequelae (1 EV and 1 HPeV-positive).

Conclusions

Significant differences in clinical data were observed between EV and HPeV infections. EV are associated to meningitis and HPeV to clinical sepsis in infants < 2 months. Initially the process is more severe in children HPeV-positive, although prognosis is good in general.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0400
E-POSTER DISCUSSION SESSION 20 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 4 (station 5)

DETECTION OF ENTEROVIRUS BY REAL-TIME PCR OF STOOL, SERUM, AND RESPIRATORY SAMPLES IN CHILDREN WITH SUSPECTED OR CONFIRMED VIRAL MENINGITIS – FINDINGS FROM UK-CHiMES

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Background

The majority of aseptic (bacterial culture negative) meningitis is caused by enteroviruses when a pathogen is identified, but in approximately half of cases no cause is found. Early identification of enterovirus (EV) in meningitis could reduce unnecessary hospitalisation and antibiotic treatment. The aim of this study was to examine the presence of EV in non-CSF samples in children who had a lumbar puncture for suspected meningitis.

Methods

Stool, serum, throat swab and nasopharyngeal aspirate samples were collected from children <16 years with suspected or confirmed meningitis in 4 groups: CSF EV PCR+ at hospital laboratory with and without pleocytosis (CSF WBC >4/μL); aseptic meningitis with no pathogen identified; suspected meningitis with normal LP. Children with a confirmed alternative diagnosis were excluded. RNA was extracted using the QIAamp Viral RNA Mini kit. Enterovirus RT-PCR was performed using the Enterovirus R-gene® kit.

Results

Of 25 children with CSF EV+ and pleocytosis, EV PCR was positive in 15/15 stool, 2/9 throat and 1/1 NPA samples. Of 17 children with CSF EV+ without pleocytosis, 13/13 stool, 1/3 throat, 1/2 NPA and 2/2 serum samples were EV PCR+. Of 29 children with aseptic meningitis and no CSF pathogen identified, 7/19 stool, 0/11 throat and 0/6 serum samples were EV PCR+. Of 18 children with normal LP results, 0/11 stool, 1/10 throat, and 0/8 serum samples were EV PCR+. 31 serum results were invalid likely due to presence of PCR inhibitors.

Conclusions

In confirmed enteroviral meningitis, enterovirus was detected in all stool samples. In children with aseptic meningitis and no CSF pathogen identified, enteroviral meningitis may be considered the diagnosis if there is a stool EV PCR+ result. Testing of throat and serum samples has lower yield than stool.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0462
E-POSTER DISCUSSION SESSION 20 - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS 4 (station 5)

BACTERIAL MENINGITIS COMPLICATED WITH SUBDURAL EFFUSION IN INFANTS YOUNGER THAN ONE YEAR OLD : A RETROSPECTIVE STUDY IN A FRENCH TERTIARY CARE CENTRE

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Background

Bacterial meningitis is associated with an important morbi-mortality. The occurrence of a sub-dural effusion (SDE) is associated with a poor prognosis. Few paediatric data are available. Our study describes the clinical and biological characteristics of meningitis complicated by a SDE.

Methods

We included in a retrospective study all children younger than one year admitted for a confirmed bacterial meningitis between 2004 and 2014 at the University Hospital Robert Debré in Paris, France.

Results

Sixty-four infants, among which 16 newborns, were included. Fifty had a brain imaging: 20 (40%) were normal, 16 (32%) revealed a SDE, 14 (28%) an isolated cerebral infarction and 3 (6%) a cerebral venous thrombosis. The isolated bacteria in cases of SDE was *Streptococcus agalactiae* (N=9), *Streptococcus pneumoniae*(N=4), *Escherichia coli* (N=2) and *Neisseria meningitidis* (N=1). Upon diagnosis, the occurrence of a SDE was associated with hemodynamic disorders (56% vs 18% in the group with normal brain imaging, p=0.06) and to behaviour disorders (94 % vs 50%, p=0.09). Six infants with SDE had seizure, 5 had persistant or relapsing fever and 3 required a neurosurgical drainage. They required intensive care more frequently than those with normal imaging (75% *vs* 35%, p=0.03). Their mortality was 6%, while morbidity (neurodevelopmental delay and/or epilepsy) tended to be higher than for those without SDE (43% vs 20 %, p=0.08). Rifampicin or ciprofloxacin were added to conventional antibiotics for bacterial meningitis in 10 and 6 patients with SDE, respectively.

Conclusions

The occurrence of SDE during a bacterial meningitis in infants younger than one year is associated with intensive care requirement. Morbidity tended to be higher than for those with normal imaging. The impact of combined antibiotic treatment needs to be precised.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1014
E-POSTER DISCUSSION SESSION 21 - EPIDEMIOLOGY AND PUBLIC HEALTH 3 (station 6)

INFLUENZA A AND B STRAINS CIRCULATION IN CHILE: REVIEW OF 4 SEASONS (2012-2015)

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Background

Information on circulating influenza strains is essential to update vaccines. Limited information on influenza B is available in Latin America. The aim of this study is to review the influenza A and B strains circulation in Chile during 2012-2015 and to describe the frequency of mismatch between the predominant lineage B and that included in influenza trivalent vaccine (TIV) recommended for the Southern Hemisphere.

Methods

Data were obtained from the Ministerio de Salud, Instituto de Salud Publica of Chile from Jan 01/ 2012 to Aug 25/2015 and were reviewed according to year, age group and compatibility of B strain with TIV. Instituto de Salud Pública is the reference laboratory in the country for cell cultures, real time polymerase chain reaction and genotyping studies for influenza.

Results

A total of 6,337 influenza strains were isolated; out of these, 4,873 (77.0%) were influenza A and 1,464 (23.0%) were influenza B. In the pediatric age group (0-19 years of age), influenza B was more prevalent in individuals < 10 years. Influenza B lineages Yamagata and Victoria were detected in all seasons, and the frequency of mismatch with TIV was higher than 50% in 2012 and 2013 (Figure).

Conclusions

Influenza B burden in Chile was substantial, especially in pediatric age groups. Mismatch with the lineage B included in the TIV was observed in 50% of seasons. It is expected that the introduction of new quadrivalent influenza vaccines could be more effective in reducing the burden of the disease.

ESP16-0321
E-POSTER DISCUSSION SESSION 21 - EPIDEMIOLOGY AND PUBLIC HEALTH 3 (station 6)

ROTAVIRUS VACCINES EFFECTIVENESS AGAINST ROTAVIRUS INFECTION AND HOSPITALIZATION IN LATIN AMERICA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background

Rotavirus was the leading cause of hospitalisation and mortality in children prior to the introduction of rotavirus vaccines in Latin America. In this study, we describe the effectiveness of rotavirus vaccines to prevent rotavirus infection and hospitalizations and the frequency of circulating rotavirus strains before and after vaccine introduction.

Methods

We performed a systematic review and meta-analysis of published studies between 1990 and 2014. After screening titles and abstracts, 592 full-text articles were assessed for eligibility, resulting in 203 studies to estimate the proportion of rotavirus and 10 studies on impact of rotavirus vaccine. Of the 46 studies conducted in the post-vaccination period, 41 were used for meta-analysis of genotypes, eight for the meta-analysis of vaccine effectiveness (VE) against hospitalisation and seven for the VE against severe rotavirus-diarrhoea.

Results

The proportion of cases of diarrhoea due to rotavirus pre- and post-vaccination was 24.3% (95%CI 22.1-26.5) and 16.1% (95%CI 13.2-19.3), respectively. The most prevalent G types circulating post-vaccine introduction were G2 (51.6%, 95%CI 38-65), G9 (14.5%, 95%CI 7-23) and G1 (14.2%, 95%CI 7-23). The P genotypes, most common after vaccine introduction were P[4] (54.1%, 95%CI 41-67) and P[8] (33%, 95%CI 22-46). G1P[8] was the most frequent genotype before vaccine introduction, compared to G2P[4] after vaccine introduction. Vaccines had similar effectiveness, with 73% (95% CI, 66-78) against hospitalisations and 74% (95% CI, 68.0-78.0) for severe diarrhoea. Reductions in hospitalisations and mortality due to diarrhoea were observed in countries that adopted universal rotavirus vaccination.

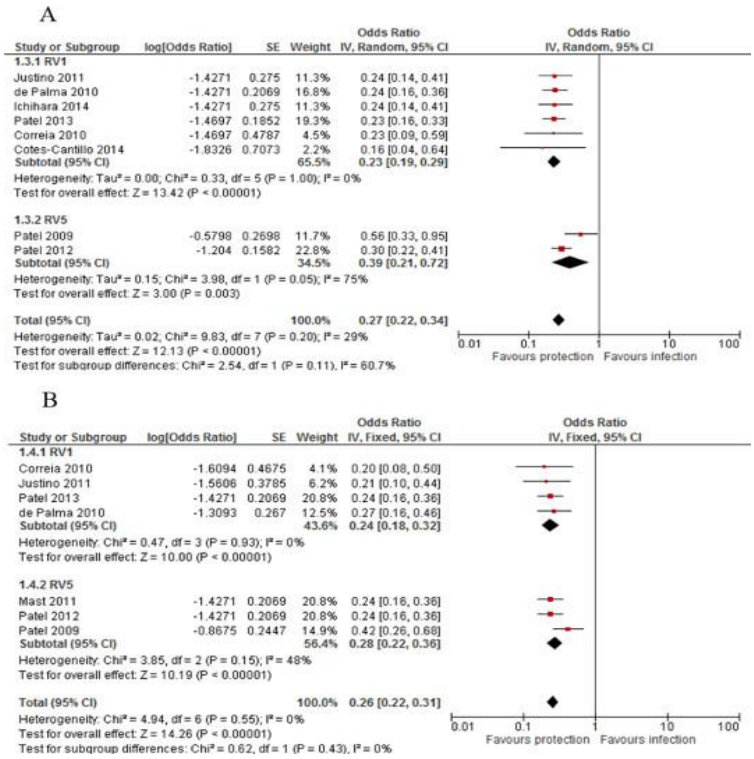

Figure 1. Effectiveness of rotavirus vaccines against rotavirus hospitalisation (A) and severe rotavirus-diarrhoea (B).

Conclusions

Rotavirus vaccines are effective in preventing rotavirus-diarrhoea in children in Latin America. Vaccine introduction was temporally associated with changes in genotype distribution.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESP16-0671
E-POSTER DISCUSSION SESSION 21 - EPIDEMIOLOGY AND PUBLIC HEALTH 3 (station 6)

CLONAL PROFILE AND RESISTANCE OF STAPHYLOCOCCUS AUREUS ISOLATES IN CHILDREN IN CRETE

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Background

Methicillin-resistant *Staphylococcus aureus* (MRSA) carriage and infection has been increasingly reported both in healthcare and community settings worldwide over the last decades. The spread of MRSA has been attributed to several clones globally.

Methods

This study investigated 86 *S. aureus* isolates (51 MRSA and 35 MSSA) from children hospitalized between 2008 and 2014 in the Heraklion General University Hospital, the referral centre in Crete. Molecular typing of the isolates was done using MLST and spa, and were characterised for the presence of PVL toxin genes, mecA gene and TssT1 toxin gene.

Results

A decline in overall MRSA rates was observed during the study period from 58.4% (66/113) in 2008-2010 to 37.7% (43/114) in 2012-2014 (OR 2.31; 95% CI 1.36-3.95; p 0.001). The predominant clone ST80 was more common among MRSA (26/46, 56.5%) than MSSA (11/24, 45.8%) isolates) and was followed by ST7 in MRSA (3/46, 6.5%) and ST30 (4/24, 12.5%) in MSSA. The incidence of ST80 decreased over the study period (12/17 vs 25/53 in 2008-2010 and 2012-2014 respectively; OR 2.69, 95% CI 0.83-8.70, p 0.079). The predominant spa type t044 was more common in MRSA than MSSA isolates (25/51, 49% versus 10/24, 42%). The incidence of spa t044 decreased over the study period (12/18 vs 23/57 in 2008-2010 and 2012-2014 respectively; OR 2.96, 95% CI 0.97-9.00, p 0.046). The prevalence of Panton-Valentine leukocidin (PVL)-positive isolates was higher in MRSA (35/39, 90%) than MSSA (2/17, 12%) isolates (p <0.0001).

Conclusions

In the study area and over a 7-year period, a decrease in MRSA rates was observed alongside with changes in *S. aureus* clonal profile. Further molecular surveillance will better illuminate the MRSA trends.

Clinical Trial Registration (Please input N/A if not registered)

n/a

ESP16-0742
E-POSTER DISCUSSION SESSION 21 - EPIDEMIOLOGY AND PUBLIC HEALTH 3 (station 6)

ACUTE HEPATITIS IN HOSPITALISED CHILDREN IN UNITED KINGDOM AND REPUBLIC OF IRELAND. A PROSPECTIVE EPIDEMIOLOGICAL STUDY

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Background

Hepatitis remains a key public health priority in most industrialised countries. Most childhood cases of acute hepatitis are caused by viruses, with Hepatitis A and B being the commonest causes. The aims of this study were to estimate the burden of acute infectious hepatitis in hospitalised children, and to describe their clinical characteristics and outcomes.

Methods

Prospective surveillance through the British Paediatric Surveillance Unit (BPSU) whereby paediatricians in the United Kingdom and Ireland reported cases of acute infectious hepatitis in hospitalised children aged 1 month and over during January 2014-January 2015 and completed a detailed clinical questionnaire. Confirmed cases were followed-up at six months with a second questionnaire.

Results

A total of 81 children were hospitalised with acute infectious hepatitis (annual incidence, 0.5/100,000). Of these, 46% (37/81) had hepatitis A, 6% (5/81) had acute hepatitis B, and 20% (16/81) were caused by other viruses; for 28% (23/81), an aetiological agent was not isolated. Of the 37 hospitalised hepatitis A cases, 70% of children had travelled abroad but only 8% had been vaccinated. Similarly, three of the five children with acute hepatitis B cases had not received any vaccination despite being a household contact of a confirmed hepatitis B case. All patients with hepatitis A recovered completely. In contrast, of the 5 patients with acute hepatitis B, three developed acute liver failure, including two who required a liver transplant.

Conclusions

Acute infectious hepatitis is rare and, although it is reassuring that none of the children died, children with acute hepatitis B had poor outcomes and 3 of the 5 cases (of whom, 2 underwent liver transplant) could have been avoided with an appropriate screening and immunisation.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0972
E-POSTER DISCUSSION SESSION 21 - EPIDEMIOLOGY AND PUBLIC HEALTH 3 (station 6)

EVALUATION OF ACUTE ROTAVIRUS GASTROENTERITIS SEVERITY IN HOSPITALIZED CHILDREN IN PRE-VACCINATION PERIOD

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Background

Purpose of this study was to determine severity of rotavirus gastroenteritis (RVGE) episode in hospitalized children and assess parents' opinions on vaccination. In Latvia no other research of such scale has been made.

This is a part of the study "Clinical peculiarities of rotaviral infection, molecular epidemiology and heath associated life quality for hospitalized children and their family members", financially supported by Riga Stradins University.

Methods

Study was conducted in Children Clinical University Hospital in Latvia from February 2014 till December 2014, including children with positive rotavirus antigen in their stool sample and negative rotavirus vaccination status.

Symptoms were graded by Vesikari 20-point scoring system and parent thoughts were assessed during interview.

Results

Total 235 patients with mean age of 25.1 months were enrolled into study; 51.1% (n=120) were males. Median age was 19.0 months. 61.3% (n=144) were in age group < 24 months.

Mainly patients had ≥ 6 diarrheic stools/24 h 63.8% (n=150) and it lasted for 1-4 days 55.1% (n=131). Mostly patients had 2-4 episodes of vomiting/24 h 46.4% (n=109) with a duration of 2 days 46.4% (n=109). Most of the children had axillary temperature of 37.1^{o}c-38.4^{o}c 45.1% (n=106) and moderate dehydration 69.4% (n=163). In 94.0% (n=221) of cases RVGE episode was graded as severe.

No statistically significant correlation was observed between gender (p=0.117), age groups (p=0.812) and the severity of the episode.

77.9% (n=183) of parents' had heard about rotavirus vaccine. 18.3% (n=43) were against vaccination, predominantly in families where one of the parents' had highest education (p=0.035), mostly stating that vaccine cannot guarantee 100% protection against rotavirus infection 61% (n=25).

Conclusions

More than 90% of patients had severe episode of RVGE. Parents lack information on true purpose of rotavirus vaccine.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0427
E-POSTER DISCUSSION SESSION 21 - EPIDEMIOLOGY AND PUBLIC HEALTH 3 (station 6)

DETECTING PARENT-REPORTED ACUTE OTITIS MEDIA EPISODES USING A MOBILE DEVICE APPLICATION

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Background

Acute otitis media (AOM) is a common childhood infection. For 30-50% of AOM, no healthcare is sought. Quantifying population AOM disease burden therefore requires comprehensive assessment of both healthcare-attended and parent-reported AOM. Previous studies used paper diaries to detect parent-reported AOM episodes. These are prone to non-compliance and hamper real-time detection of disease occurrence to allow proper assessment. This study determined performance of a user-friendly mobile device application (App) for AOM symptom recording and real-time disease detection in comparison with conventional methods.

Methods

During four consecutive months in 2013 and 2015, respectively, parents of 162 and 69 children aged 0-3 years participated. In 2015, parents used an AOM diary App, daily marking presence or absence of listed AOM symptoms in their child. Automated detection of AOM from parent-reported symptoms triggered an App-notification and additional questionnaire detailing AOM symptom burden. Risk-factor exposure was assessed in a monthly App-based questionnaire. In 2013, a similar design used conventional paper questionnaires and diaries instead.

Results

During conventional (2013) and App-based (2015) recording, 84% and 90% of the symptom-diaries were completed, respectively and the detected incidence of parent-reported AOM episodes was 715/1000 and 849/1000 child-years. Disease questionnaires were completed for 59% of the episodes when using conventional, compared to 100% for the App-based recording and automated detection.

Conclusions

A mobile device Diary-App for symptom recording and automated disease detection improves case-finding and disease questionnaire completeness. This is important for quantifying disease burden and incidence, especially for diseases that often remain undetected by healthcare systems, such as AOM.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0849
E-POSTER DISCUSSION SESSION 21 - EPIDEMIOLOGY AND PUBLIC HEALTH 3 (station 6)

FREQUENCY, SEVERITY AND DIRECT MEDICAL COSTS OF INFLUENZA-ASSOCIATED HOSPITALIZATIONS (IAH) BY INFLUENZA SUBTYPE IN CHILDREN AND ADULTS AT A TERTIARY CARE HOSPITAL IN GERMANY, 2010-2013

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Background

The burden of IAH and related direct costs may vary considerably in different age groups and relate to specific influenza subtypes. We therefore initiated a retrospective study in a large tertiary care University Hospital (Würzburg, Germany).

Methods

All patients with any ICD-10 discharge diagnosis for influenza (J09-J11), hospitalized for at least one day during the years 2010 to 2013, were identified from the hospital routine documentation database and demographic data, all ICD-10 and procedural codes, and costs per patient were extracted. IAH were verified by medical chart review and laboratory confirmation.

Results

A total of 247 IAH were identified; 151 (61%) were children (median age 3 years; 5% were immunocompromised; 2% needed intensive care; median length of stay was 4 (IQR 3-9) days). In children, the influenza subtypes A(H1N1)pdm09/A(H3N2)/B accounted for 30/67/54 IAH, with average per-patient costs of 2,579/2,378/1,673 EUR ($p<0.001$).
In 73 adults 18-65 years of age, 44% were immunocompromised; 7% were pregnant; 47% needed intensive care, 16% ECMO; 13 (18%) died; median length of stay was 12 days (IQR 5-20). A(H1N1)pdm09/A(H3N2)/B accounted for 53/11/9 IAH. Per influenza subtype, 57%/27%/11% needed intensive care ($p=0.015$); 23%/0%0% ECMO ($p=0.067$); 23%/9%/0% died ($p=0.186$); average per-patient costs were 23,527/8,148/4,828 EUR ($p=0.044$).
In 23 patients >65 years of age, 44% were immunocompromised; 26% needed intensive care; 3 (13%) died. Median length of stay was 10 days (IQR 6-17); A(H1N1)pdm09/A(H3N2)/B accounted for 7/6/10 IAH, with average per-patient costs of 14,760/7,877/5,520 EUR per subtype ($p=0.831$).

Conclusions

The majority of IAH occurred in children at toddler age, with few complications. In adults 18-65 years of age, complications, ECMO and fatalities were more frequent and often associated with A(H1N1)pdm09, resulting in high per-patient costs.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0248
E-POSTER DISCUSSION SESSION 22 - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS (station 7)

IMMUNOGENICITY AND SAFETY OF THE INACTIVATED HEPATITIS A VACCINE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS ON IMMUNOSUPPRESSIVE TREATMENT; A MATCHED CASE-CONTROL STUDY

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Background

Children with Juvenile Idiopathic Arthritis(JIA) are at increased risk of infection nonetheless data regarding vaccination in this population are scarce. Hepatitis A is an indolent disease with a varying clinical spectrum and consequences and also a vaccine preventable disease. The aim of this study was to describe the immunogenicity and safety of immunization against Hepatitis A virus(HAV) in JIA patients on immunosuppressive treatment, who have not been previously exposed to HAV.

Methods

Matched case-control study performed in JIA patients and healthy controls. The subjects received two doses of inactivated anti-HAV vaccine (720mIU/ml) intramuscularly at 0 and 6 months. Seroconversion, seroprotection rates and anti-HAV-IgG titers were measured at 1, 7 and 18 months. Children were actively monitored for adverse events for 7 days and for novel autoimmune disease or JIA flare for 3 months. Statistical significance was set at $p<0.05$ and analyses were conducted using SPSS(version 19.0).

Results

83 JIA patients and 76 controls were enrolled in the study. Seroprotection rates were 48.2% in the JIA vs. 65% in the control group ($p=0.05$) and rose to 94% and 91.6% at 7 months and 98.7% and 96.1% at 18 months for the two groups respectively. Significantly lower anti-HAV-IgG-levels were found in the JIA group at all time points($p<0.001$). Vaccines were well tolerated. No serious adverse event or death was reported. None of the subjects in the control or the patient group developed a novel autoimmune disease. No-JIA flare was reported.

Conclusions

Two doses of the inactivated HAV vaccine are safe and effective in immunosuppressed children with JIA; a single dose of HAV was insufficient to induce seroprotection in half of the patients. Further studies are required to analyze the long-term immunity against HAV in this population.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0808
E-POSTER DISCUSSION SESSION 22 - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS (station 7)

NOVEL PNEUMOCOCCAL VACCINES: THE CHALLENGE OF DISTINCT FRAGMENTS AND B-CELL EPITOPES WITHIN PNEUMOCOCCAL VIRULENCE PROTEINS (PNVPS)

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Background and Objective

Due to limitations of current polysaccharide-based pneumococcal vaccines (serotype-specific coverage, low effectiveness against mucosal disease and serotype-replacement), the alternative of universally expressed PnVPs has emerged. However, shortcomings regarding manufacture instability, sequence and level of expression variability led several research groups towards the identification of highly-conserved antigenic regions/B-cell epitopes within PnVPs. This review discusses the up-to-date progress on the identification of such antigenic regions/epitopes and their evaluation as pneumococcal vaccine candidates.

Methods

Peer-reviewed papers in English reporting immunogenicity and protective efficacy data of protein fragments or epitopes were retrieved through a PubMed search using the terms 'protein fragments', 'protein epitopes', 'pneumococcal vaccines'.

Learning Points Discussion

Overall, 18 studies were included concerning various regions/B-cell epitopes within PnVPs (i.e. PspA, PhtD, pneumolycin, CbpA, PsaA, PspC). Eight studies demonstrated that protein fragments protected mice against invasive pneumococcal disease (IPD); three studies reported that such fragments are immunogenic in mice and/or IPD patients. Four studies demonstrated that distinct protein B-cell epitopes offered protection against IPD in mice. Three studies combined whole proteins with either protein fragments or B-cell epitopes and successfully demonstrated the protective efficacy of such formulations against multiple diseases in mice (sepsis, pneumonia, meningitis), while one of the latter also showed efficacy against nasopharyngeal carriage in mice.
There are several promising protein fragments/B-cell epitopes undergoing pre-clinical evaluation, alone or in combination with whole PnVPs. Such formulations may retain the benefits of protein antigens (natural serotype-independent "priming/boosting", immune memory, immunogenicity in infants); besides, their low-cost and stable construction permits the combination of several highly-conserved antigens that impair different stages of pneumococcal disease and offer even wider serotype coverage. Therefore, further research is warranted on the identification of such antigens and their pre-clinical and clinical evaluation as vaccine candidates.

ESP16-0348
E-POSTER DISCUSSION SESSION 22 - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS (station 7)

ANTIBODY PERSISTENCE 12 MONTHS AFTER A BOOSTER DOSE OF PFIZER'S PCV13 IN CHILDREN PRIMED WITH 2 OR 3-DOSES OF PHID-CV OR PCV13

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Background

Pneumococcal serotype distribution and the proportion of emerging serotypes, particularly 19A, differs among countries. 10-Valent Pneumococcal Non-Typeable Haemophilus Influenzae Protein D-conjugate vaccine (PHiD-CV) and 13-Valent Pneumococcal Conjugate Vaccine (PCV13) are broadly used PCVs. Interchangebility of vaccines from clinical trials on mixed schedules has been investigated in UK and Mexico recently. We presented one month data after booster dose at ESPID 2015.

Methods

Two phase III, open-label, multicenter studies were conducted. In the Czech Republic (CZ), 12-15-month-old children received booster dose of PCV13 after 3-dose-priming with either PHiD-CV or PCV13. In Slovakia (SK) 11-12-month-old children received PCV13 following 2-dose-priming with either PHiD-CV or PCV13.
AIM: To assess antibody persistence of Pfizer´s PCV13 12 months after the booster dose. Primary objective was to assess non-inferiority of one-month post-booster OPA response for serotype 19A.

Results

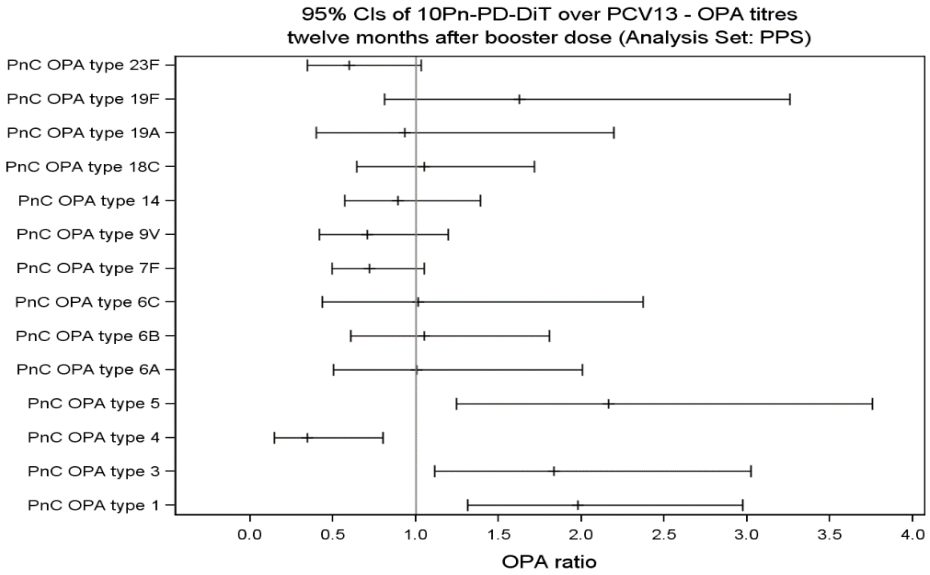
98 subjects were enrolled in CZ, 89 subjects in SK.

Table 1: Antibody Persistence: OPA GMT twelve months after booster dose

Country/Serotype	Treatment	N	G_Mean	95% CI
SK/19A				
	Schedule 2+1			
	PHiD-CV	38	239.6	(141.2, 406.5)
	PCV13	49	289,6	(181.0, 463.3)

CZ/19A				
	Schedule 3+1			
	PHiD-CV	47	266.9	(150.0, 475.2)
	PCV13	44	355.8	(219.9, 575.6)

Graph 1. OPA GMTs ratios and 95% CIs twelve months after PCV13 booster dose in the Czech Republic



Conclusions

Mixed schedules induced robust immunological response for serotype 19A both in OPA and ELISA which persisted 12 months after booster dose. As observed in exploratory analyses, PCV13 booster in PCV10 primed subjects elicited non-inferior persistence of immune response to majority of vaccine serotypes. Mixed schedules may offer reasonable alternative in setting with higher occurrence of 19A.

Clinical Trial Registration (Please input N/A if not registered)

CZ: EudraCT: 2012-005366-35, SK: EudraCT: 2012-005367-27

ESP16-0350
E-POSTER DISCUSSION SESSION 22 - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS (station 7)

IMMUNOGENICITY/SAFETY OF A HEXAVALENT DTAP-IPV-HB-HIB VACCINE VERSUS INFANRIX®HEXA CONCOMITANTLY ADMINISTERED WITH PREVENAR13® AND ROTATEQ® AT 2, 3, 4 MONTHS OF AGE IN EUROPEAN INFANTS

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Background

Assess immunogenicity/safety of a fully liquid, ready-to-use, hexavalent DTaP-IPV-HB-Hib vaccine (Hexaxim®/Hexacima®/Hexyon®) administered in a 3-dose primary immunization at 2, 3, 4 months of age.

Methods

Phase III, randomized, active-controlled, observer-blind, multicenter study. Infants randomized to receive one of the two licensed hexavalent vaccines (DTaP-IPV-HB-Hib: N=266; Infanrix® hexa: N=262), and concomitantly administered with 13-valent pneumococcal conjugate and rotavirus vaccines. Blood samples collected pre-Dose 1, 1-month post-Dose 3 and analyzed via validated serological assays. Non-inferiority of DTaP-IPV-HB-Hib to control vaccine tested by comparison to predefined seroprotection (HepB, PRP) and vaccine response rates (PT, FHA). Safety assessed via study site observation and parental monitoring/reporting of solicited/unsolicited adverse events.

Results

Non-inferiority of DTaP-IPV-HB-Hib to control one-month post-Dose 3 demonstrated for Hep B, PRP, PT,FHA antigens.

Primary Objective: **Non-inferiority of seroprotection/vaccine response rates of DTaP-IPV-HB-Hib vs. Infanrix hexa (one month post-Dose 3) - Per-protocol analysis**

		DTaP-IPV-HB-Hib(N=237)		Infanrix hexa (N=239)		DTaP-IPV-HB-Hib minus Infanrix hexa (i.e. Test - Reference)			
Component	**Criteria**	**n/M**	**%**	**n/M**	**%**	**%**	**2-sided[95% CI] †**	**d%**	**Conclusion‡**
Anti-PT(EU/mL)	**Vaccine response***	225/229	98.3	225/230	97.8	0.4	(-2.51; 3.44)	10	Yes
Anti-FHA(EU/mL)	**Vaccine response***	229/231	99.1	217/229	94.8	4.4	(1.23; 8.12)	10	Yes

Primary Objective: **Non-inferiority of seroprotection/vaccine response rates of DTaP-IPV-HB-Hib vs. Infanrix hexa (one month post-Dose 3) - Per-protocol analysis**									
		DTaP-IPV-HB-Hib(N=237)		**Infanrix hexa (N=239)**		**DTaP-IPV-HB-Hib minus Infanrix hexa (i.e. Test - Reference)**			
Component	**Criteria**	**n/M**	**%**	**n/M**	**%**	**%**	**2-sided[95% CI] †**	**d%**	**Conclusion‡**
Anti-Hep B(mIU/mL)	**≥ 10 mIU/mL**	221/231	95.7	228/231	98.7	-3.0	(-6.59; 0.11)	10	Yes
Anti-PRP(µg/mL)	**≥ 0.15 µg/mL**	204/224	91.1	195/226	86.3	4.8	(-1.12; 10.74)	10	Yes
* Vaccine response (PT , FHA): post-Dose 3 Ab concentrations ≥ 4×LLOQ, if pre-Dose 1 Ab concentrations < 4×LLOQ; Post-Dose 3 Ab concentrations ≥ pre-Dose 1 Ab concentrations, if pre-Dose 1 Ab concentrations ≥ 4×LLOQ ‡ If lower bound of 95% CI was greater than -d, the null hypothesis H0 was rejected and we could conclude for the non-inferiority									

High response rates observed for D, T, Polio 1, 2, 3 in both groups one month post-dose 3. PCV13 antigens: seroprotection rates were high in both groups for most of the pneumococcal serotypes. Anti-rotavirus GMCs were higher in DTaP-IPV-HB-Hib than in Infanrix hexa Group.

No safety concern was observed. No death or adverse event leading to study discontinuation was reported.

Conclusions

DTaP-IPV-HB-Hib vaccine in a 3-dose primary immunization at 2, 3, 4 MoA elicits protective responses against 6 targeted diseases, with no safety concern.

Clinical Trial Registration (Please input N/A if not registered)

EudraCT#:2012-001055-39; UTN:U1111-1122-2329

ESP16-0472
E-POSTER DISCUSSION SESSION 22 - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS (station 7)

THE CONSEQUENCES OF CHILDHOOD PNEUMOCOCCAL CONJUGATE VACCINATION - SEROTYPE REPLACEMENT IN IRELAND, 2008-2014

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Background

Streptococcus pneumoniae is a major cause of life-threatening infections, including meningitis and bloodstream infections. The population groups at highest risk of infection are young children and the elderly. The 7- and 13-valent pneumococcal conjugate vaccines (PCV7/13) provide protection against the predominant serotypes associated with invasive pneumococcal disease (IPD). Uptake of the vaccines has been approximately 90% since the introduction of PCV7 in 2008 and PCV13 in 2010.

Methods

This study includes national typing data from invasive pneumococcal disease isolates from children aged between 0-15 years. Typing was performed using capsular co-agglutination and a multiplex-PCR. Reduced susceptibility to antimicrobials were interpreted using CLSI meningitis breakpoints. Incidence rates were calculated based on census data.

Results

Between January 2008 and December 2014, isolates from 303 of 390 confirmed cases of IPD were referred for serotyping. Eighty-two per cent of isolates were from children <5 years of age (*n*=248); among whom PCV7 serotypes fell significantly from 2008 to 2014 (*n*=46, *n*=0; *p*<0.001). The additional serotypes in PCV13 alone also fell. However, the number of non-PCV serotypes increased (*n*=7, *n*=17; *p*=<0.001). The rate of reported cases has decreased in children <5 years of age, from 24.1 to 12.9/100,000. A similar trend was observed in other paediatric cases. The number of penicillin non-susceptible strains decreased in children <2 years of age but remained high in older children due to the prevalence of serotype 19A.

Conclusions

Following the introduction of PCVs there has been a significant decrease in the number of paediatric IPD cases. However, the proportion of non-PCV serotypes has also increased during this period. This highlights the need to continued monitoring of serotype data to identify trends and serotype replacement which may inform future national vaccine strategies.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0845
E-POSTER DISCUSSION SESSION 22 - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS (station 7)

EVALUATION OF IMMUNOGENICITY AND PROTECTIVE EFFICACY OF IMMUNODOMINANT B-CELL EPITOPES WITHIN VIRULENT SURFACE PROTEINS OF S. PNEUMONIAE IN A MURINE MODEL FOR PNEUMOCOCCAL SEPSIS

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Background

Characterization of antibodies against previously identified B-cell epitopes, located within pneumococcal surface proteins, CbpD-pep4,PhtD-pep19,PhtE-pep40 and ZmpB-pep125 revealed that they were specifically detected in patients' sera recovering from invasive pneumococcal disease and exhibited consistent surface binding and Osponophagocytic activity against various Pneumococcal Serotypes. We further evaluated their immunogenicity and protective efficacy in vivo, in a murine model for pneumococcal sepsis.

Methods

Four groups (G1-G4) of mice were immunized with peptides CbpD-pep4,PhtD-pep19,PhtE-pep40 and ZmpB-pep125 respectively, whereas G5group was immunized with a mixture of all peptides and the control group(G6) received only Freud's Adjuvant. Sera were collected every 2 weeks after the 1st booster. Two weeks after the last bleeding, mice were challenged intraperitoneally with a lethal dose of S.Pneumoaniae serotype3(SP3) and the survival time was recorded. The kinetics of anti-peptides antibodies development and avidity enhancement were evaluated by appropriately ELISAs.To confirm that the observed protection was antibody-mediated we passively immunized mice with hyperimmune serum taken from G5group and challenged them with a lethal dose of SP3.

Results

G1-G5 groups elicited gradually higher antibody concentrations and avidity index between the 1st and last bleeding($p < 0.0001$). Immunogenicity of PhtD-pep19 and its specific antibodies' avidity were superior compared with the others peptides($p<0.05$). G1-G5 groups survived significantly longer than G6 group ($p < 0.0001$).Remarkably, G5group had a survival time significantly longer that those of individual groups ($p <0.05$). Among single groups there is only a significant enhance in the survival time of G2group over G1 group($p <0.05$). In addition, mice immunized with hyper-immune serum survived significantly longer than controls($p =0.001$).

Conclusions

All tested peptides were immunogenic and exhibited significant protective activity against SP3. Further experiments should be performed to improve their immunological characteristics for their use as potential vaccines candidates.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0987
E-POSTER DISCUSSION SESSION 22 - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS (station 7)

REDUCED CARRIAGE OF VACCINE TYPE PNEUMOCOCCI IN HEALTHY CHILDREN FOLLOWING VACCINATION WITH THE 10-VALENT PNEUMOCOCCLA VACCINE

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Background

Vaccination with the 10-valent pneumococcal conjugate vaccine (PCV-10) was initiated in Iceland in 2011 for children born in 2011 and later (2+1 schedule without catch-up).

Aim: To determine the impact of PCV-10 on nasopharyngeal carriage of pneumococci.

Methods

An ongoing, repeated cross-sectional study where nasopharyngeal swabs were collected in March every year from 2009, from children attending 15 DCCs in the Reykjavik capital area. Isolates were cultured selectively for pneumococci and serotyped with PCR and/or latex agglutination. To attain compatible age distribution, only children < 3 years of age were included and the Non-Vaccine Eligible cohorts (NVEC, born ≤2010) compared with the Vaccine Eligible Cohorts (VEC, born ≥2011). To exclude possible herd effect bias NVECs sampled in 2013 and later were excluded.

Results

There were 464 children in the NVEC and 234 in the VEC group. Dual carriage rate occurred in 4.7% and 7.5%, giving a total of 362 and 176 pneumococcal isolates in the NVEC and VEC respectively. There were no significant differences in average age (2.39 vs 2.44), carriage (70.5% in both groups) or sex (53.9% vs 56.8% males) between the NVEC and VEC respectively. Vaccine types represented 51.1% and 4.5% of the pneumococcal isolates for NVEC and VEC respectively. Pooled vaccine efficacy for acquisition of vaccine types for the VEC compared to the NVEC was 94% (CI:90-97%). For the vaccine-associated serotypes (6A and 19A) a 43% (7%-66%) reduction was found. There was a significant increased prevalence of the non-vaccine serotypes 23B, 6C, 11, 23A and 15 (all $p<0.05$) in the VEC.

Conclusions

Vaccine serotypes were almost eliminated from carriage following the vaccination. In addition, a reduction of vaccine-associated serotypes (6A,19A) was seen, indicating possible cross-reactivity.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0994
E-POSTER DISCUSSION SESSION 22 - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS (station 7)

EFFECT OF PCV-10 ON OUTPATIENT ANTIMICROBIAL PURCHASES FOR CHILDREN IN ICELAND

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Background

The PCV-10 was introduced in the Icelandic paediatric vaccination schedule in 2011. A significant reduction in invasive pneumococcal disease and hospital visits due to AOM and pneumonia has previously been reported. Our aim was to assess whether outpatient antimicrobial purchases for children have decreased following PCV-10 vaccination.

Methods

Data on outpatient antimicrobial purchases were extracted from the National Drug Prescription Database and analysed using an interrupted time-series analysis. Purchases during post-vaccination years (2012-2014) were compared to predicted values using data from pre-vaccination years (2008 – 2010). The year of vaccine introduction was excluded. The main outcome was daily purchases of antimicrobials used in the treatment of upper respiratory tract infections in children <36 months of age. Non-respiratory antimicrobial purchases in the same age group, and purchases for older children and adults were analysed using the same methods as a comparison.

Results

The number of seasonally-adjusted mean daily purchases of respiratory antimicrobials were reduced from 467.6 (95% CI 445.5 – 489.7) purchases per 100.000 children per day in 2008, to 415.5 (95% CI 395. 4 – 435.6)/100.000 per day, at the end of the post-vaccination period. This mean daily decline of 50.2 purchases per 100.000 children/day translates to 1832 fewer respiratory antimicrobial purchases in 2014. A non-significant increase in non-respiratory antimicrobial purchases was observed in the same age-group. Rates of antimicrobial purchases remained unchanged in other age-groups.

Conclusions

There was a significant reduction in outpatient purchases of antimicrobials used in the treatment of respiratory tract infections in children following PCV-10 introduction. No such reduction was evident in purchase rates of non-respiratory antimicrobials in the same age-group or the rest of the population.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0729
E-POSTER DISCUSSION SESSION 23 - DIAGNOSTICS (station 8)

IMPROVING DIAGNOSTIC YIELD IN LEMIERRE'S SYNDROME USING 16s rDNA PCR: A CASE SERIES

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Title of Case(s)

IMPROVING DIAGNOSTIC YIELD IN LEMIERRE'S SYNDROME USING 16s rDNA PCR: A CASE SERIES

Background

Lemierre's Syndrome (LS) is an oropharyngeal infection with secondary septic thrombophlebitis of head and neck veins, complicated by dissemination of septic emboli to pulmonary and systemic sites. It is typically caused by *Fusobacterium necrophorum*. The use of 16s rDNA polymerase chain reaction (PCR) in the diagnosis of fastidious organisms (including *Fusobacterium*) is becoming increasingly common.

We present a case series of four young children with LS diagnosed using 16s rDNA PCR between September 2014 and December 2015 at a large London Children's Hospital.

Case Presentation Summary

Three cases occurred in male infants (<1year) and one in an 18 month-old male. All patients were previously well and were fully immunised according to the UK vaccination schedule. All children completed a 4 to 8 week course of antibiotics, with a minimum of 2 weeks intravenous therapy. All children were anticoagulated with heparin for a period of 3-6 months (see Table 1).

Table 1. Clinical features, radiological and microbiological findings in 4 cases of Lemierre's Syndrome presenting to a London Children's Hospital between Sept 2014 and December 2015

Case	Age at presentation	Clinical presentation	Brain imaging findings	Complications	Organism	Identification
1	18 months	Ear discharge, mastoiditis	CT: non-occlusive right sigmoid sinus thrombus.		Fusobacterium	16s rDNA PCR
2	8 months	Intercurrent chickenpox infection. Ear discharge, mastoiditis and sepsis (PICU admission)	MRI: venous sinus thrombosis, occlusion of the right ICA and white matter infarcts in the right cerebral hemisphere.	Tibial osteomyelitis Cerebral infarcts	Fusobacterium S. aureus S. pneumoniae	Ear discharge: polymicrobial culture Bone sample: 16s rDNA PCR Fusobacterium
3	9 months	Ear erythema and fever	MRI: extensive left-sided otomastoiditis with ipsilateral sigmoid-transverse sinus thrombosis.		Fusobacterium	16s rDNA PCR
4	10 months	Mastoiditis	MRI: thrombosis of the right sigmoid/jugular vein.		Fusobacterium	16s rDNA PCR

Learning Points/Discussion

· Paediatricians need tobeware of complications of oropharyngeal infections including Lemierre'sSyndrome.

· Early diagnosis includingimaging and aggressive management may prevent complications. Repeat imaging andsurgery may be needed in non-responsive cases.

· Increase in diagnosismay be related to improved detection of *Fusobacterium*using 16s rDNA PCR and/or changes in antibiotic prescribing for oropharyngealinfections.

ESP16-0516
E-POSTER DISCUSSION SESSION 23 - DIAGNOSTICS (station 8)

PROFILING OF SERUM CYTOKINES IN HEALTHY CHILDREN: DOES AGE MATTER?

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Background

Cytokine-based immunodiagnostic tests for tuberculosis measuring IFN-y release show poor performance in young children. Limited current evidence suggests that cytokine release is influenced by age, however normal values of cytokines in children are lacking.

Methods

Healthy children aged 0-12 years undergoing elective/diagnostic procedures were eligible for inclusion. Children with a history of chronic disease, immunomodulatory medication, recent infection or immunisation were excluded. Whole blood was stimulated with SEB, PHA, *C. albicans*, or left unstimulated and concentrations of cytokines were analysed.

Results

A total of 271 children were included in the final analysis: median age 5.2 (IQR 3.4; 7.8) years and 74% male; 33% had circumcisions, 21% ENT-interventions, 11% orchidopexia, 6% herniotomia and 29% other interventions.

In unstimulated samples, 70% of IL-6, 40% of IFN-γ and 8% of TNF-α concentrations were below limit of quantification (BLQ), and 3% of IP-10 concentrations were above limit of quantification (ALQ) (Table).
IFN-γ and IL-6 concentrations were not associated with age.
IP-10 and TNF-α concentrations showed a median decrease of 19 pg/mL/year and 1 pg/mL/year of age, respectively.

In stimulated samples; SEB stimulation resulted in the highest median concentrations for all four cytokines, followed by PHA- and *C. albicans*- stimulated samples. The influence of age on cytokine concentration was best quantifiable in C. *albicans*-stimulated samples and showed the following increase per year of age: IFN-γ: 5.8 pg/mL/year, IL-6: 11 pg/mL/year,

TNF-α 2.6 pg/mL/year of age

Table: Summary of cytokine concentrations after stimulation in SEB-, PHA-, *C. albicans*- and unstimulated samples from 271 healthy children

	IL-6	IFN-γ	IP-10	TNF-α
unstimulated				
Quantifiable (%) < 3.2 pg/mL > 10 000 pg/mL	83 (31) 188 (69) 0 (0)	165 (61) 106 (39) 0 (0)	262 (97) 1 (0.4) 8 (3)	254 (94) 17 (6) 0 (0)
Median in pg/mL **IQR** in pg/mL	1.6 1.6; 4	4.7 1.6; 14	905 645; 1527	9.6 6.7; 14
Range in pg/mL	<3.2 - 768	<3.2 - 535	<3.2 - 61760	< 3.2 – 484
SEB-stimulated				
Quantifiable (%) < 32 pg/mL > 100 000 pg/mL	270 (99.7) 1 (0.4) 0 (0)	253 (93) 1 (0.4) 17 (6.3)	33 (12) 0 (0) 238 (88)	271 (100)
Median in pg/mL **IQR** in pg/mL	3368 1761 ; 5 237	28 964 13 484 ; 49 364	191 911 137 147 ; 255 704	7903 4995 ; 10 826
Range in pg/mL	<31 – 13 046	<32 – 348 112	11 100 – 1 717 000	33 – 30 503
PHA-stimulated				
Quantifiable (%) < 32 pg/mL > 100 000 pg/mL	255 (94) 16 (6) 0 (0)	267 (99) 4 (1) 0 (0)	131 (48) 0 (0) 140 (52)	266 (98) 5 (2) 0 (0)
Median in pg/mL **IQR** in pg/mL	1776 844; 3197	771 362; 1401	102 852 59 012; 162 812	553 294; 1278
Range in pg/mL	<32 – 19 944	<32 – 9 507	894 – 9 613 370	<32 – 7 696
***C. albicans*-stimulated**				
Quantifiable (%) < 3.2 pg/mL > 10 000 pg/mL	228 (84) 42 (15.5) 1 (0.4)	256 (94) 15 (6) 0 (0)	146 (54) 0 (0) 125 (46)	267 (99) 4 (1) 0 (0)
Median in pg/mL **IQR** in pg/mL	64 7.7; 342	40 15; 97	8 518 3690; 18 571	36 16; 81
Range in pg/mL	0.06 – 15 310	<3.2 – 4 057	35 – 127 700	<3.2 – 1 468

Conclusions

In healthy children the background concentration of TNF-α and IP-10 decreases in the first 12 years of life. Following stimulation, cytokine concentration increases and the extent of increase is positively correlated with age. Additional cytokines and co-variates will be evaluated in a next step.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0271
E-POSTER DISCUSSION SESSION 23 - DIAGNOSTICS (station 8)

UTILITY OF THE LAB-SCORE AND THE CLINICAL PREDICTION MODEL FOR PREDICTING SERIOUS BACTERIAL INFECTIONS IN FEBRILE CHILDREN ADDRESSING THE EMERGENCY DEPARTMENT

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Background

The Lab-score combines C-reactive protein, Procalcitonin and urinalysis for identifying serious bacterial infections (SBI) in febrile children. The Clinical Prediction Model (CPM) combines several clinical variables and the value of C-reactive protein, for the same purpose. This survey aimed to evaluate and compare the utility of the two new tools for predicting SBI in young febrile children addressing the emergency department (ED).

Methods

This survey is part of a prospective observational study aiming to identify children with fever without source (FWS) at risk for SBI. Children aged 1 to 36 months with FWS, who visited the ED during January until September 2013, were included. C-reactive protein, Procalcitonin and urinalysis were available for all patients. SBI diagnosis was supported by presence of positive cultures and chest radiographs. Subsequently, the Lab-score and the CPM were calculated for every patient.

Results

From 134 patients analysed, 31 (23.1%) had SBI, 11 pneumonia and 20 other SBI. For detecting pneumonia the Lab-score [AUC 0.87 (95%CI: 0.80-0.92)] modestly outperformed the CPM [AUC 0.81 (95%CI 0.73-0.87)]. For a low risk threshold of 2.5% used for ruling out pneumonia, CPM had a sensitivity of 90.9% (95%CI: 58.7 – 99.8) and a negative LR of 0.1 (0.02-0.8). For diagnosing other SBI, both the Lab-score [AUC 0.89 (95%CI: 0.82-0.93)], and the CPM [AUC 0.89 (0.83-0.94)] were similar predictors.

Conclusions

The Lab-score and the CPM are easy-to-use models in clinical practice for identifying SBI in febrile children and proved strong and similar prediction value.

ESP16-0484
E-POSTER DISCUSSION SESSION 23 - DIAGNOSTICS (station 8)

ENHANCED NUCLEIC ACID EXTRACTION USING A NOVEL BEAD-BASED METHODOLOGY TO IMPROVE QPCR FROM LOW TARGET SAMPLES

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Background

Molecular diagnostic and next-generation sequencing (NGS) technologies continue to improve early detection of infectious diseases. However, detection is limited by the initial quality and concentration of nucleic acids (RNA/DNA) from collected specimens. PrimeStore MTM® (PS-MTM) is a specimen collection and transport medium that kills microbes and preserves nucleic acids at elevated temperature to maintain high quality RNA/DNA for PCR and NGS. A novel extraction procedure was developed using optimized buffers and chemically coated magnetized beads for concentrating and subsequently purifying nucleic acids from samples to enhance quantitative PCR (qPCR) microbial detection.

Methods

Ten-fold serial dilutions of influenza A H3N2 (10^5 to 10 $TCID_{50}$/mL), adenovirus type 5 (10^5 to 1 $TCID_{50}$/mL), and *Mycobacterium tuberculosis* (10^5 to 1 CFU/mL) were prepared in PS-MTM and analyzed using an ABI-7500 instrument. Prior to amplification triplicate nucleic acid extractions were performed for each dilution using bead-based extraction and compared to commercial extraction using Qiagen QIAamp DNA Mini.

Results

According to qPCR, bead-based extraction was more sensitive, *i.e.,* lower cycle threshold (C_T) values at each dilution for all test pathogens. At 1 CFU/mL, MTB was detected (Avg C_T=35.6; S.E. =1.4) using bead-based extraction but not detected (C_T=40) from extractions using Qiagen. Furthermore, qPCR efficiencies were improved using bead-based nucleic acid extraction (96.8-97.2%) compared to qPCR efficiencies obtained using Qiagen extraction (96.8-110%).

Conclusions

This novel bead-based approach offers a concentration factor to detect low level RNA/DNA. Magnetized beads and optimized chemistry produce cleaner extraction preparations yielding high purity RNA/DNA from a wide range of clinical matrices. This methodology may be important for improving qPCR detection and next-generation sequencing of pathogens directly from low target clinical specimens.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0491
E-POSTER DISCUSSION SESSION 23 - DIAGNOSTICS (station 8)

DIAGNOSTIC TOOLS TO DIFFERENTIATE BETWEEN CLOSTRIDIUM DIFFICILE COLONIZATION AND INFECTION: EXPERIENCE IN A PEDIATRIC COHORT

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Background

Clostridium difficile (CD) diarrhoea is one of the most common nosocomial infections, often caused by prolonged courses of antibiotics. The production of Toxin A and B are the main pathogenic mechanisms. However, up to 80 % of children under the age of 2 years may be colonized with CD without a real infection. The determination of Toxins A and B in stool samples is thus of crucial importance for the diagnosis and treatment.

Methods

The Microbiology Laboratory of the Bambino Gesù Children's Hospital in Rome for research of toxigenic *CD* used bacterial culture from stool specimen and in case of a bacteriological positivity toxin B was investigated by PCR (Cepheid®.USA). Since May 2015 we added a rapid immuno-assay that detects both glutamate dehydrogenase (GDH) antigen and toxins A&B (TOX) of *CD* in fecal specimens (Alere™.USA).

Results

During the study period, 327 stool specimens were collected. 33 (10%) had a positive culture GDH and PCR. Among them, TOX turned positive only in 10 patients (30%). In the culture/GDH/PCR/TOX positive group, all the patients but one were treated with the appropriate antibiotics and resolved symptoms. The patient that did not receive any treatment improved after 48 hours, suggesting a false positive result. In the GDH+/PCR+/TOX- group, all the patients but two recovered without any antibiotic targeted on CD.

Conclusions

PCR testing seems to overestimate CD infections being responsible of many false positive results. Our study shows that the Toxin test is very useful to discriminate between colonization and infection, avoiding unnecessary courses of antibiotics in 70% of children in our cohort. Further study are needed to better define the best diagnostic approaches to distinguish children with CD infections vs colonization.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0574
E-POSTER DISCUSSION SESSION 23 - DIAGNOSTICS (station 8)

ELISPOT IGRA WITH PPD STIMULATION – A PROMISING DIAGNOSTIC TEST FOR CHILDHOOD NONTUBERCULOUS MYCOBACTERIAL CERVICAL LYMPHADENITIS

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Background

Childhood nontuberculous mycobacterial (NTM) lymphadenitis is a diagnostic challenge because fast and reliable diagnostic method is lacking. We present a novel modified T-SPOT®.TB test with purified protein derivative (PPD) as an additional antigen.

Methods

We reviewed retrospectively the hospital records of children diagnosed with cervical NTM lymphadenitis and tested with modified T-SPOT®.TB in the Hospital District of Helsinki and Uusimaa between October 2008 and September 2015.

Results

We found 37 children (22 girls and 15 boys). Age range was 16 to 73 months (median 36 months). All were non-BCG-vaccinated, presented typical NTM cervical lymphadenitis and in follow-up remained otherwise healthy. Culture specimens (n=26) yielded acid-fast bacilli in 58% with further molecular genetic identification of M. avium (11/15;73%), M. malmoense (2/15;13%), M. interjectum (1/15;7%) and one unspecified NTM (1/15;7%). Histological examinations (n=20) displayed inflammation with granulomata (14/20;70%) or with other cytopathology (6/20;30%). All diagnoses were supported by typical clinical presentation and course of the disease, and further supported by NTM growth in nine, typical histopathology in eight, and both in six patients. Duration of lymphadenitis from first parental observation to test date ranged from 9 to 252 days (median 45 days). PPD reactivities ranged from 22 to 678 spots/10^6 lymphocytes (median 170 spots/10^6 lymphocytes, **Figure**). With a cut-off ≥ 25 spots/10^6 lymphocytes, none were reactive to MTB specific antigens and all but one were reactive to PPD.

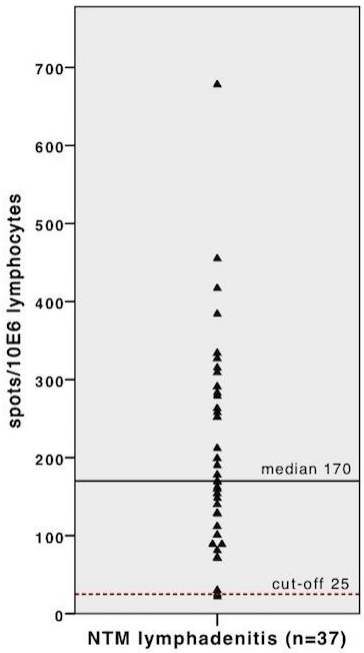

Figure.

The reactivities to PPD antigen mixture stimulation in the modified T-SPOT®.TB test.

Conclusions

The modified T-SPOT®.TB with PPD stimulation is a practical and promising non-invasive test. Further studies are needed to evaluate the sensitivity and specificity of the test. Due to rarity of NTM lymphadenitis, a prospective study requires multicentre collaboration.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1043
E-POSTER DISCUSSION SESSION 23 - DIAGNOSTICS (station 8)

CYTOKINE PROFILES IN CHILDREN WITH ACUTE LOWER RESPIRATORY TRACT INFECTIONS (LRTI)

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Background

The applicability of cytokines profiles to identify aetiology, severity of disease and need for antibiotic prescription in LRTI remains poorly defined.

Methods

Patients with a complete set of three consecutive blood samples (day 1, 3 and 5) from a randomised controlled trial (ProPAED) were included for analysis. Concentrations of serum cytokines (IFN-γ, IL-10, IL-1ra, IL-1β, IL-2, IL-4, IL-6, IP-10 and TNF-α) were measured using mulitanalyte panels on a Luminex instrument. Differences in cytokine concentrations were evaluated by Wilcoxon ranked test or by Holm test when multiple groups were compared.

Results

A total of 181 patients, median age of 6.5 years (range: 55 days – 17.5 years) were included, of which 44% were female and 40% received antibiotics. Serum concentrations of 6 cytokines (IFN-γ, IL-1RA, IL-6, IL-10, IP-10 and TNF-α) were elevated on day 1 and decreased subsequently, with the greatest decline between day 1 and 3 (56 – 94 %). PCT > 1 mcg/l and CRP > 100 mg/l were associated with a steep increase of concentrations of IL-1β, IL-1ra, IL-6, IL-10, IP-10, TNF-α and IFN-γ. Five patients were blood culture positive for *Streptococcus pneumoniae* (n=4) *or Streptococcus pyogenes* (n=1) and these had significantly higher concentrations of IL-1ra ($p < 0.01$), IL-6 ($p < 0.008$) on day 1. Chest radiography of these patients were classified as bronchopneumonia (n=2) and lobar pneumonia (n=3). Treatment with antibiotics was not associated with lower cytokine concentrations on day 3 or 5.

Conclusions

PCT > 1 mcg/l and CRP > 100 mg/l are indicative of a concomitant IFN-γ, IL-1ra, IL-1β, IL-6, IL-10, IP-10 and TNF-α stimulation. In our population, IL-1ra and IL-6 have a stronger association with bacterial LTRI as compared PCT, CRP or other cytokines.

Clinical Trial Registration (Please input N/A if not registered)

ISRCTN17057980

ESP16-0807
E-POSTER DISCUSSION SESSION 23 - DIAGNOSTICS (station 8)

MODERN ON-LINE DIAGNOSTIC TOOL IN STREPTOCOCCAL PHARYNGITIS - OLD DISEASE, NEW APPROACH

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Background and Objective

Streptococcal pharyngitis can be easily mistaken with viral infection, which still constitutes the vast majority of pharyngitis aetiology in children.

Methods

To help doctors in therapeutic decisions in acute pharyngitis we created our on-line application with the algorithm based on Centor/McIsaac Score and recent European and local guidelines. It requires input of basic patient information - age, weight, important medical history: risk factors and antibiotic allergy. By the input of presented symptoms the result of Centor Score is presented as well as the probability of diagnosis of streptococcal pharyngitis. The application includes indications to microbiological testing like pharyngeal swab or rapid strep tests. If antimicrobial therapy is necessary, it suggests the first line treatment, provides information about available drug forms on Polish market and adjusts doses to patients body weight. Exemplary prescription is also generated. The extraordinary situations like, for example, streptococcal carriage, treatment in case of allergy for beta-lactams are included.

Learning Points Discussion

The main purpose of this IT tool is the unification of management in acute pharyngitis according to current recommendations. We hope that it will increase the availability of reliable data for every healthcare professional as well as limit antibiotic misuse and development of drug resistance. It seems to be a handy, effortless form of e-learning using modern technology.

ESP16-0505
E-POSTER DISCUSSION SESSION 24 - CONGENITAL AND PERINATAL INFECTIONS 2 (station 9)

CHROMOSOMALLY INTEGRATED HUMAN HERPESVIRUS-6 AND CONGENITAL INFECTION

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Title of Case(s)

Chromosomally integrated human herpesvirus-6 and congenital infection: do we know enough?

Background

HHV6 congenital infection is defined as the presence of HHV6 DNA in an infant at birth, could originate from the transplacental passage of a new repeated HHV6 infection of the mother, from the reactivation of maternal endogenous (latent) HHV6, or by hereditary transmission of chromosomally integrated HHV6 (ciHHV6). We present the first case of congenital HHV6 infection originated from reactivation of hereditary transmission of ciHHV6.

Case Presentation Summary

A three-day-old male was admitted because hepatomegaly, jaundice, elevated transaminases, anemia and hyperferritinemia. A metabolic disease was excluded through aminoacids and enzymes dosage in urine and blood samples. A Torch screening was performed adding HHV6 research. HHV6 viral load in whole blood was 7.518.000 copies/ml. In the suspect of ciHHV6, newborn's hair follicle was undergone to quantitative HHV6-PCR, resulting positive and confirming ciHHV6. HHV6 was found in mother's blood sample with 26.698.000 copies/ml. HHV6 Immunoglobulin G were present in mother and her child. We hypothesized HHV6 congenital infection originated from a reactivation of hereditary ciHHV6 germline transmitted. Therefore, we opted to treat the newborn with ganciclovir (6 mg/kg twice daily) for six days and then valganciclovir (16 mg/Kg twice daily) for six days. After three days of ganciclovir clinical conditions improved and laboratory values normalized.

Learning Points/Discussion

Our experience suggests to research ciHHV6 in case of high HHV6-DNA load in whole blood and to not exclude a reactivation of hereditary ciHHV6, where an antiviral treatment might be warranted. A single quantitative PCR test on serum or plasma cannot prove whether a patient with ciHHV-6 has active HHV6 infection and no guidelines are present about treatment. Clinical judgment is the tool to decide to treat or not.

ESP16-0882
E-POSTER DISCUSSION SESSION 24 - CONGENITAL AND PERINATAL INFECTIONS 2 (station 9)

LATE-ONSET SENSORINEURAL HEARING LOSS IN INFANTS WITH CONGENITAL CYTOMEGALOVIRUS INFECTION AND PROLONGED ANTIVIRAL TREATMENT

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Title of Case(s)

Late-onset sensorineural hearing loss in infants with congenital cytomegalovirus infection and prolonged antiviral treatment

Background

Late-onset sensorineural hearing loss (SNHL) in congenital cytomegalovirus (cCMV) infection is rarely described in long-term treated patients. We report 4 children who deveoped late-onset NSHL after finishing prolonged antiviral treatment.

Case Presentation Summary

Since 2009, 27 infants with cCMV infection received antiviral treatment for at least 6 months and have been followed up for more than 2 years. Four (14.8%) developed late-onset SNHL. All were symptomatic at birth; three had abnormal central nervous system ultrasound (US) and one intrauterine growth restriction and unilateral hearing loss. All received ganciclovir (14-42 days) and valganciclovir (4.5-6 months). Hearing was assessed every 6-12 months by brainstem auditory evoked response (BAER). Patient 1: normal BAER at birth in left ear, no response in right ear (>90dB). At 2.4 years-of-age, no response bilaterally. Patient 2: normal BAER at birth. At 2.6 years-of-age, right ear responses at 60dB, no response in left ear (>90dB), at 3.2 years-of-age: no response bilaterally. Patient 3: BAER at birth 20 dB left ear, normal right ear. At 3 years 60 dB left ear, 20 dB right ear. At 6 years 60 dB left ear, 40 dB right ear. Patient 4: BAER at birth: normal left ear, 40-60 dB right ear. At 6 years 80 dB in right ear, and one year later drop of 35dB in left ear in high frequencies. Patients 1 and 2 had cochlear implants placed and the others use hearing aids.

Learning Points/Discussion

Late-onset NSHL can appear in congenital CMV infants after a prolonged course of antiviral treatment, even years after diagnosis. We recommend prolonged follow-up to identify these cases and larger studies to identify high-risk patients.

ESP16-0526
E-POSTER DISCUSSION SESSION 24 - CONGENITAL AND PERINATAL INFECTIONS 2 (station 9)

CHARACTERISING CLOSTRIDIUM PERFRINGENS COLONIZATION IN A COHORT OF PREMATURE NEONATES AND ITS ASSOCIATIONS WITH NECROTISING ENTEROCOLITIS

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Background

Necrotising enterocolitis (NEC) is a devastating gastrointestinal disease that mainly affects premature infants. The aetiology is unclear but is known to include the composition of the gut microbiota, and recent work has shown a potential role of *Clostridium perfringens* in some cases. We therefore set out to investigate the colonization and carriage of *C. perfringens* in a premature neonatal cohort.

Methods

Weekly faecal samples from a 2-year cohort of 348 premature neonates (from two Imperial College Healthcare Trust Neonatal Intensive Care Units) were cultured after alcohol shock, with surviving organisms grown under clostridium-selective anaerobic conditions. Microbes were then identified using Matrix Assisted Laser Desorption/Ionization Time-Of-Flight Mass Spectrometry.

Results

C. perfringens colonization was found to peak between weeks 2 and 4 of life. An initial statistical analysis of the two units independently has indicated a number of factors that may be relevant to *C. perfringens* colonization, including antibiotic treatment, feeds and birth weight. No correlation was found between incidence of *C. perfringens* colonization and incidence of NEC.

Conclusions

C. perfringens colonization of premature neonates is likely due to a complex interplay of different factors, especially when considering the requirement of potentially stochastic exposure to the organism. Further analysis will focus on the longitudinal aspect of colonization, with consideration given to the timing of colonization with regard to NEC. The isolates gathered are being characterized using whole-genome sequencing and a toxin-typing methodology (Cornwell et al. Abstract submitted).

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0097
E-POSTER DISCUSSION SESSION 24 - CONGENITAL AND PERINATAL INFECTIONS 2 (station 9)

A FIVE YEAR PROSPECTIVE OBSERVATIONAL ANALYSIS OF CONGENITAL PLASMODIUM VIVAX MALARIA IN LOW ENDEMIC REGION (BIKANER, NORTHWESTERN INDIA) FROM 2011 TO 2015

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Background

Congenital malaria is defined as malaria parasitaemia in the first week of life. Reports of congenital malaria in *P.vivax* are very scanty. The clinical presentation is not always classical, so routine screening should be essential for all neonates in endemic areas. This study describes the occurrence and clinical spectrum of congenital *vivax* malaria in Indian perspective.

Methods

This prospective study was conducted on admitted neonates from January 2011 to December 2015. The species diagnosis was done by peripheral blood smear examination, rapid diagnostic test and polymerase chain reaction analysis. The possibilities of other disease/infections causing similar illness were investigated thoroughly and stringently.

Results

A total of 2438 new born admitted in first week of life were screened. Out of them 66(2.70%) had evidence of parasitaemia (*P.vivax,*52 and *P.falciparum,*14). The criteria for admission in these 52 neonates with congenital vivax malaria were septicemia (46.15%), prematurity (38.46%), jaundice (21.15%), perinatal asphyxia (15.38%), and seizures (11.54%). The clinical malaria was seen in 46(88.46%) neonates in which spectrum was anemia (80.77%), thrombocytopenia (76.92%), poor feeding (75%), fever (61.54%) and hepatosplenomegaly (51.92%). Although the presence of parasitaemia didn't differ the proportion of neonates having fever (χ^2=0.238; p=0.52) and hypoglycemia (χ^2=0.117; p=0.63) from those without parasitaemia, but it was significantly associated with anemia (χ^2=14.676; p=0.001) and thrombocytopenia (χ^2=12.768; p=0.001). The mean Hb level was 8.8±2.7 gm/dl; mean platelet count was 126329.32±65324.56/µl; mean reticulocyte count was 3.8±1.2%; and mean parasite density was 12888.38±3733.21/mm^3. All these neonates were treated according to WHO guidelines and none of them expired.

Conclusions

This study emphasizes the occurrence of *P.vivax* congenital malaria without typical malaria manifestations, even in low transmission area, for awareness about this preventable and treatable disease.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0331
E-POSTER DISCUSSION SESSION 24 - CONGENITAL AND PERINATAL INFECTIONS 2 (station 9)

HIGH PREVALENCE OF MECA-POSITIVE COAGULASE-NEGATIVE STAPHYLOCOCCI (MR-CONS) IN BREAST MILK (BM) OF MOTHERS OF PRETERM NEONATES

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Background

Mothers of preterm neonates often require hospitalization or antimicrobial therapy. Therefore, BM may become colonized with resistant bacteria. We aimed to determine the presence of MR-CoNS in BM of mothers of preterm neonates.

Methods

Preterm neonates (gestational age [GA] <37wks; n=41) hospitalized to neonatal intensive care unit within the first week of life and healthy term neonates (GA >37wks; n=20), whose mothers had not been hospitalized or received antibiotics 3 months antepartum or 1 month postpartum, were studied. BM was collected weekly in the first month postpartum and cultured quantitatively onto mannitol salt agar. Staphylococci were identified to the species level by MALDI-TOF MS. The presence of *mecA* was determined by PCR.

Results

Staphylococci were isolated from BM of all mothers. In mothers of term compared to preterm neonates count of staphylococci was lower, but the prevalence of *S. hominis*, *S. lugdunensis*, *S. aureus* was higher (Table). Higher prevalence of MR-CoNS (35/41 vs 5/20; p<0.001), *mecA*-positive *S. epidermidis (*33/41 vs 3/20; p<0.001), *mecA*-positive *S. haemolyticus* (16/41 vs 1/20; p=0.006), but not *mecA*-positive *S. hominis* (6/41 vs 1/20) was observed in BM from mothers of preterm compared to term neonates.

MR-CoNS appeared in BM later than *mecA*-negative CoNS (median (IQR) 8 (6-12) vs 6 (4-8) days postpartum; p=0.001).

In mothers of preterm neonates, the presence of MR-CoNS in BM was not associated with neonatal GA or delivery mode, maternal use of antibiotics or duration of hospitalization 3 months antepartum or 1 month postpartum.

Table. Species distribution and median count of staphylococci in breast milk of mothers of preterm or term neonates.

	Mothers of	
	preterm neonates (n=41)	**term neonates (n=20)**
Count (cfu/mL); median (IQR)*	4.50 (3.95-4.84)	3.06 (2.40-3.53)
S. epidermidis	41 (100)	20 (100)
*S. hominis**	11 (26.8)	12 (60)
S. haemolyticus	16 (39)	3 (15)
*S. lugdunensis**	5 (12.2)	9 (45)
S. warneri	8 (19.5)	6 (30)
*S. aureus**	4 (9.8)	9 (45)
S. capitis	2 (4.9)	2 (10)
S. pasteuri	3 (7.3)	1 (5)
S. caprae	1 (2.4)	1 (5)
S. saprophyticus	0	1 (5)

cfu - colony forming units

*p-value <0.05

Conclusions

Higher prevalence of MR-CoNS in BM of mothers of preterm compared to term neonates indicates that BM could be source of MR-CoNS. Prevention of colonization of BM with MR-CoNS may have the potential to avoid transmission and subsequent infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0911
E-POSTER DISCUSSION SESSION 24 - CONGENITAL AND PERINATAL INFECTIONS 2 (station 9)

ROLE OF HUMAN BETA DEFENSIN 2 DURING INFECTIOUS PROCESSES IN EXTREME PRETERM NEONATES

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Background

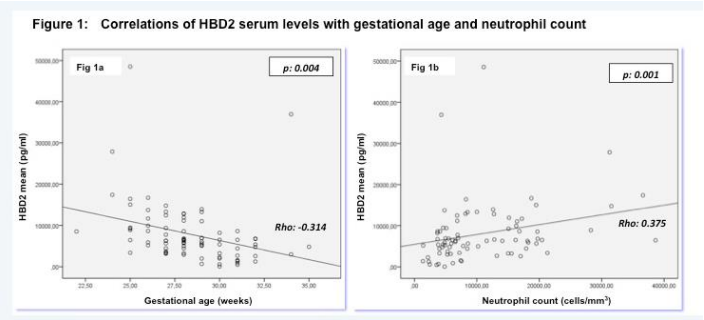
Extreme preterm neonates (GA<32weeks) are prone to suffer from invasive infections and to develop complications due to associated inflammatory responses. Human Beta-Defensin-2 (HBD2) is an antimicrobial peptide and soluble mediator of the innate immune system. Little is known regarding its role in physiologic or pathophysiologic settings in the neonatal period. We describe associations between HBD2 serum levels during suspected infectious processes with selected demographic and clinical variables.

Methods

Extreme preterm neonates with suspected infectious processes were prospectively recruited in a tertiary hospital center during a 4-year-study period. On day 1, 4 and 7 of suspicion of a septic event HBD2 determination in serum samples using *ELISA*-technique and systemic data collection from the clinical charts were performed.

Results

A total of 84 subjects with a median GA of 28.4 weeks (SD± 2.5), presented with a suspected infectious process on day 8 (mean, P25-P75: 7-12 days) of life. 40 blood cultures were positive (coagulase negative *Staphylococcus*, n=30; Gram negative rods, n=9; others, n=1). HBD2 levels did not show significant variations during suspected septic events. The GA and BW were negatively correlated with the HBD2 serum levels (Rho: -0.314, p=0.004 (Figure 1a); Rho: -0.332, p=0.002). HBD2 levels showed a positive correlation with the neutrophil count (Rho: 0.375, p=0.001 (Figure 1b)); but not with the C-reactive protein (p=0.250). Cohort stratification according to blood culture results and the presence or absence of sepsis confirmed these observations.



Conclusions

In this study HBD2 serum levels were highly elevated in the most extreme preterm neonates and correlated positively with neutrophil count but not C-reactive protein. The regulation and interaction between neutrophils and HBD2 requires to be studied further in the future.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0748
E-POSTER DISCUSSION SESSION 24 - CONGENITAL AND PERINATAL INFECTIONS 2 (station 9)

ANTIMICROBIAL POINT PREVALENCE SURVEY (PPS) AND GUIDELINES FOR NEONATAL SEPSIS IN GREEK NEONATAL UNITS AND COMPARISON TO THE UK

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Background

Little is known about antibiotic prescribing in the Neonatal Units (NNUs) in Greece. In the present study we aimed to assess and compare antimicrobial use and policies in Greek and UK NNUs participating in an infection surveillance network (neonIN)

Methods

We performed monthly PPS over three consecutive months using standardised questionnaires. We also collected data on empiric antibiotic policies for early-onset sepsis (EOS) and late-onset sepsis (LOS) as well as antifungal prophylaxis. We compared the Greek data with similar data collected from a subset of UK NNUs.

Results

Eleven Greek and five UK NNUs participated. Overall, 196 of 484 (40%) neonates were on antibiotics in Greek-NNUs compared to 22% in UK-NNUs. Details of the PPS survey are shown in the table. Higher rates and broader spectrum antibiotic use was seen in Greek NNUs compared with UK NNUs. The survey revealed wide variation in guidelines, especially for LOS, among the Greek NNUs

		Greece (11 NNUs)	UK (5 NNUs)
Characteristics of PPS in Greece and UK	Total n of patients on antibiotics	196/484 (40.5%)	51/227 (22.4%)
	Sex (male)	119/196 (60.7%)	33/51 (64.7%)
	Median GA (weeks) (IQR)	35 (32-38)	30 (26-37.5)
	Median Bwt (g) (IQR)	2240 (1557-2990)	1340 (780-2840)
	Median PNA (days) (IQR)	8 (4-18)	8 (4-32.5)
	Respiratory support	79/196 (40.3%)	36/51 (70.6%)
	% of patients on empiric abx regimens	165/196 (84.1%)	45/51 (88.2%)
	Most frequent indication for abx prescribing	Suspected sepsis 103/196 (52.6%)	Suspected sepsis 32/51 (62.7%)
	Most frequently used abx regimen in LOS	meropenem & glycopeptide (62%)	piperacillin/tazobactam & aminoglycoside (58%)
Antibiotic guidelines in EOS, LOS and antifungal prophylaxis by country	EOS	Ampicillin + Gentamicin 73% Benzylpenicillin + Gentamicin 18% Ampicillin + Amikacin 9%	Benzylpenicillin + Gentamicin 89% Benzylpenicillin + Amikacin 11%
	LOS	Piperacillin/tazobactam + Teicoplanin 27% Cefotaxime + Vancomycin 18% Meropenem + Vancomycin 18% Piperacillin/tazobactam + Amikacin 9% Cefipime + Vancomycin 9% Fluclocacillin + Gentamicin 9% Cefotaxime + Teicoplanin 9% (weekly surveillance)	Flucloxacillin + Aminoglycoside 56% if no CVC in-situ Piperacillin-Tazobactam + Aminoglycoside+Vancomycin 56% if CVC in-situ Cefotaxime + Gentamicin 44% Cefotaxime + Gentamicin + Teicoplanin 44% if CVC in-situ
	Antifungal prophylaxis	Fluconazole IV 54% Nystatin PO 18% No prophylaxis 18% No policy 9%	Fluconazole IV (if GA <26 wks and/or Bwt <1000 g.) 33% Nystatin PO (All babies on antibiotics) 55% No policy (Level 1- Special care NNU) 11%

Conclusions

We report on the largest national PPS performed in Greek NNUs with simultaneous data collection on antibiotic guidelines. This survey identifies areas for quality improvement in antibiotic use. Introduction of antimicrobial stewardship programmes based on evidence-based guidelines and local epidemiologic patterns are urgently required.

ESP16-0479
E-POSTER DISCUSSION SESSION 24 - CONGENITAL AND PERINATAL INFECTIONS 2 (station 9)

MATERNAL SCREENING FOR CONGENITAL TOXOPLASMOSIS,30 YEARS OF EXPERIENCE IN A TERCIARY CENTRE

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Background

Nowadays, there is not an universal accepted approaching to themanagement of Congenital Toxoplasmosis (CT). In Spain, until now the screening during pregnancy is universal. Our objectives were: to assess the management of pregnant women with suspicious of CT and to determine the outcomes of theirchildren.

Methods

Retrospective study. One hundred 100 mother-child pairs followed in our centre from 1984 to 2013 were included; all with suspicion of maternal infection or CT. Data from maternal and neonatal reports and follow-up were recorded.

Results

16/100 cases of CT (rate of transmission: 16%) were registered, 11/16 (68%) of them were symptomatic. Maternal serological conversion could be confirmed in 43% of cases, 53% were uncertain and 3% of women were not submitted to maternal screening, being the children studied because of a clinical suspicion of CT due to: strabismus (2) and microcephaly (1). The efficacy of the screening was lower when the seroconversion couldn't be verified (transmission rate 1/53 versus 12/44, OR 0.07 [IC95%0.009 – 0.55] p 0.000), being the first trimester strongly associated with this occurrence (83% versus 17%, OR=16.3 [IC95% 5.9 – 44.5], p<0.000).At birth, high level of protein in CSF determined 4.8 more risk of develop neurological symptoms (if normal, negative predictive value :96%). IgM deteccion in neonatal serum showed low sensitivity(30%). The 56% of CT presented pathological neuroimaging findings at birth but only 12% developed mental retardation and 56% suffered from chorioretinitis.

Conclusions

The lack of specificity of the first trimester serology led to a high rate of overdiagnosis and treatment. Although the neuroimaging alterations were not uncommon in infants with CT, mental retardation was rarely observed. Choriorretinitis was the most common clinical finding. Hyperproteinorachia had great value in neonatal evaluation

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0334
E-POSTER DISCUSSION SESSION 25 - TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS (station 10)

HEPCIDIN CONCENTRATIONS PREDICT HOST RESPONSE AND SUSCEPTIBILITY TO SEVERE FALCIPARUM MALARIA

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Background

The relationship between iron deficiency and malaria is controversial. Hepcidin links iron and inflammation, controlling iron absorption, recycling, and availability to pathogens, and modulating innate immune responses. We assessed hepcidin concentrations in relation to host response, parasite multiplication, and malaria morbidity in Gambian children.

Methods

We measured plasma hepcidin, ferritin, and CRP levels 28 days after treatment for Falciparum malaria in 94 Gambian children without transfusion or iron supplementation. We combined these measurements with individualized estimates of parasite multiplication rate and host immune responsiveness from a recently developed mathematical model of within-host dynamics. We used generalized linear models to determine relationships between variables, and selected the best models to inform simulations of the outcome of malaria infections in children with different ages, levels of acquired immunity, and baseline hepcidin concentrations.

Results

Sixteen children (17%) were iron deficient according to WHO criteria and had low hepcidin concentrations (median 3.5 (IQR 2.4-6.1) vs 10.2 (5.3-15.9) ng/mL in the other subjects, $P<0.001$). Hepcidin showed a weak positive correlation with predicted parasite multiplication rate ($P=0.03$), but a more significant association with host immune responsiveness ($P=0.008$) in multivariate analysis accounting for age ($P = 0.007$) and CRP ($P < 0.001$). Simulations based on these relationships predicted that low hepcidin levels (as seen in iron deficiency) would have negligible effect on the likelihood of developing symptomatic malaria, but would produce up to a 50% reduction in the incidence of severe malaria, primarily by enhancing the host innate response.

Conclusions

Hepcidin may mediate the protective effect of iron deficiency against severe malaria by modulating the host immune response.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0181
E-POSTER DISCUSSION SESSION 25 - TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS (station 10)

TRAVELER'S DIARRHEA IN CHILDREN: USE OF MULTIPLEX PCR IN A PROSPECTIVE STUDY

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Background

Traveler's diarrhea (TD) strikes 30 to 50% of pediatric travelers. In 50% of cases no infectious pathogen is isolated by conventional methods. Multiplex PCR can detect simultaneously several pathogens and thus increase the diagnostic sensitivity. The purpose of this prospective study was to assess the incidence and distribution of pathogens associated with TD in children.

Methods

All the children admitted for TD in the emergency department of Robert Debré hospital, Paris and Jean Verdier hospital, Bondy were included from August 1st to October 15th 2014 and 2015. Stool samples were tested for bacterial and viral pathogens by conventional diagnostic tests (fecal culture and immunoassay for Rotavirus and Adenovirus detection) and multiplex PCR film Array GI panel® (22 pathogens bacteria, virus and parasites detected).

Results

79 samples were collected and tested with conventional methods: 25 samples were positive for bacteria and 10 for viruses with two co-infections. Salmonella was the most frequent bacteria (n=19). 59 of the 79 samples collected were tested with the multiplex PCR. A pathogen was identified in 58 cases. The most frequent pathogens were enteroaggregative E coli (n=32), enteropathogenic E coli (n=26), enterotoxigenic E.coli (n=19), Salmonella, enteroinvasif E.coli (n=16 each), Cryptosporidium, Sapovirus (n=11), Norovirus and

Campylobacter jejuni (n=10 each), Rotavirus (n=9) and Shigatoxine producing E coli (n=4). 52 co-infections were observed including multiple bacteria (n=14), bacteria and viruses (n=21) or bacteria and parasites (n=10).

Conclusions

Multiplex PCR in stools enhances detection of pathogens in TD. Bacteria and particularly enteroaggregative E coli are the leading pathogens associated with TD in this study. However, larger case-control studies are needed to better assess the clinical impact of co-infections and the potential threat of shigatoxine producing bacteria.

ESP16-0246
E-POSTER DISCUSSION SESSION 25 - TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS (station 10)

PREVALENCE OF DENGUE FEVER AND DENGUE CO-INFECTIONS IN INFANTS AND CHILDREN CONSULTING AT THE CHILD AND MOTHER CENTER-YAOUNDE

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Background

Dengue fever, an emerging disease is known as one of the most important arthropod-borne viral diseases affecting humans. Dengue virus can cause a spectrum of diseases ranging from asymptomatic, mild febrile to a life-threatening illness, dengue hemorrhagic fever. The prevalence of dengue virus infection, alone or in association with other endemic infectious diseases in children in Cameroon is not known. Because the main clinical symptoms of dengue is fever, similar to malaria it is important to evaluate its prevalence in children in a country endemic for malaria, thus the aim of this study.

Methods

Children consulting for fever were investigated for dengue, malaria and HIV infection. 249 Children were enrolled. Rapid diagnostic tests (RDT) for dengue NS1 Ag, IgM/IgG Ab combo, for HIV, Dengue IgM/IgG ELISA, microscopy and HIV-1 DNA-PCR were used.

Results

Children presenting DENV-positive test for NS1 Ag, IgM, IgG Abs and IgM/IgG RDT were 0.4% (1/249), 26.9% (67/249), 33.33% (83/249), 24.89% (62/249) respectively. Children with DENV-positive samples on IgM/IgG ELISA were 10.52% (4/38) for IgM (current infection). No IgG was detected by ELISA.

HIV infected children represented 14.46% of the study population (36/249) and those with DENV-HIV Abs were 7.23% (18/249). Malaria infected children were 30.92% (77/249) and Malaria-DEN co-infected children were 10.04% (25/249). Three children had HIV Abs, anti-DENV Abs and Malaria; they represented 1.2% (3/249). The hematological features presented were non specific.

Conclusions

Dengue virus infection is present in children and HIV-DENV or DENV- Malaria co-infections are not uncommon. Hence fever can be due to dengue infection without malaria, vice versa or both. For all children consulting for fever, the diagnosis investigations for DENV and Malaria should be carried out routinely, with extra vigilance for HIV infected children.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0973
E-POSTER DISCUSSION SESSION 25 - TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS (station 10)

CLINICAL PROFILE AND PREDICTORS OF INTENSIVE CARE UNIT ADMISSION IN PAEDIATRIC SCRUB TYPHUS: A STUDY FROM NORTHERN INDIA.

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Background

Scrub typhus, an emerging tropical infection presents with varied clinical manifestations. Understanding clinical profile, complications and outcomes may help formulate management guidelines. Predictors of ICU admission may help plan resource allocation in developing economies.

Methods

Retrospective chart review of all children ≤ 12 years old, admitted with scrub typhus to Paediatric emergency between 2013 and 2015 was performed. Confirmed 120 cases by IgM ELISA were included. Data were presented as mean ± SD or median (IQR). Multivariate logistic regression analysis was done to identify independent predictors of ICU admission.

Results

Mean (SD) age was 6.6 ± 3.3 years. Common presenting symptoms included fever in 120(100%), puffiness - 42(35%), vomiting - 40(33.3%), altered sensorium -29(24%), and seizures in 28(23.3%) cases. On examination, hepatomegaly was seen in 112(93.3%), splenomegaly-70 (58.3%), lymphadenopathy - 61(50.8%), edema - 53(44.2%), respiratory distress - 43(35.8%), rash - 28(23.3%), and eschar in 25(20.8%) cases. Meningoencephalitis was observed in 31(25.8%), raised intracranial pressure - 23(19.2%), shock - 19(15.8%), and pneumonia in 17(14.2%) cases. On initial investigation, thrombocytopenia - 79(65.8%), transaminitis - 79(65.8%), and hyponatremia in 75(62.5%) cases were present. Oral Doxycycline was given in 103(86%) and IV Azithromycin in 10(8%) cases. Median (IQR) time to defervescence was 3[2, 4] days. 46(38.3%) children required ICU admission. Younger age ($p=0.019$; OR=0.98; 95% CI: 0.97-.99), altered sensorium ($p<0.001$; OR=9.8; 95% CI: 2.9-32.7), and rapid breathing ($p<0.001$; OR 37.7; 95% CI: 8.9-160) predicted the need for ICU admission. Majority of children, 112(93%) survived to hospital discharge.

Conclusions

Clinicians should be cognizant of the wide variety of presentations of Paediatric scrub typhus.Neurological and respiratory involvements at admission are common complications associated with need for intensive care. If treated adequately majority recovers and have favorable outcome.

ESP16-0098
E-POSTER DISCUSSION SESSION 25 - TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS (station 10)

SEVERE MIXED INFECTION (PLASMODIUM FALCIPARUM AND PLASMODIUM VIVAX) MALARIA IN CHILDREN: A PROSPECTIVE COHORT STUDY FROM BIKANER, NORTHWESTERN INDIA

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Background

Recent observations from different parts of world have confirmed the existence of severe *P.vivax* malaria, but description of severe mixed infection (*P.falciparum* and *P.vivax*) malaria requires good clinical study. This study evaluated the characteristics of severe mixed infection malaria in children in Bikaner, northwest India.

Methods

This prospective cohort study was conducted on 326 admitted children of malaria from January 2013 to November 2015. The species diagnosis was confirmed with polymerase chain reaction analysis. Severe malaria was defined strictly on WHO criteria (2000). The possibilities of other disease/infections causing similar illness were investigated thoroughly and stringently.

Results

In this cohort study, the proportion of *P.falciparum, P.vivax* and mixed malaria was 156(47.85%), 122(37.42%) and 48(14.72%) respectively. Severe malaria was present in 48.16%(157/326) children, with greatest risk among children of mixed infection [64.58%(31/48)] in comparison to *P.falciparum* monoinfection [49.36%(77/156), RR=1.308{95%CI 0.957-1.673},p=0.065] and *P.vivax* monoinfection [40.16%(49/122), RR=1.608{95%CI 1.139-2.138},*p*=0.006]. Anemia(66.67%) was the commonest pernicious manifestation of mixed infection malaria followed by hepatic dysfunction(54.17%), renal dysfunction(35.42%) and cerebral malaria(22.9%). Although multiorgan dysfunction was present in 57.96%(91/157) children, the risk was greatest in mixed infection [62.5%(30/48)] in comparison to *P.falciparum* monoinfection [24.36%(38/156), RR=2.566{95% CI 1.741-3.571},*p*=0.0001] or *P.vivax* monoinfection [18.85%(23/122), RR=3.315{95% CI 2.109-5.034},*p*=0.0001]. The proportion of all these severe manifestations were highly significantly in <5 years age children (p<0.001). The risk of mortality in severe malaria was 3.68%(12/326) in which mixed infection had greater risk [8.33%(4/48)] in comparison to *P.falciparum* monoinfection [3.20%(5/156); RR=2.600{95%CI 0.600-10.811},*p*=0.219] or *P.vivax* monoinfection [2.45%(3/122); RR=3.389{95% CI 0.658-18.714}, *p*=0.100].

Conclusions

Risk of developing severe malaria, multiorgan dysfunction and mortality was more in children of mixed infection in comparison to *P.falciparum* or *P.vivax* monoinfection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0448
E-POSTER DISCUSSION SESSION 25 - TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS (station 10)

A STUDY OF THE ANTIBIOGRAM OF SALMONELLA TYPHI IN AN INDIAN SETTING WITH THE EFFECTIVENESS OF AZITHROMYCIN IN ENTERIC FEVER

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Background

Background: Typhoid fever has high mortality rate of 30% which is reduced to 0.5% with good treatment. Multidrug resistant (MDR) strains including nalidixic acid resistant strains (NARS) is on the rise in India, limiting treatment options.

AIM:

1. To determine current antimicrobial susceptibility pattern of Salmonella typhi in blood culture in Indian setting

2. To determine MIC values of azithromycin against Salmonella

3. To assess clinical efficacy of azithromycin compared to cephalosporins

Methods

Prospective analytical study from August 2013 to April 2014 in a pediatric tertiary care hospital in Chennai, India.

Clinical details of 40 children one month to 18 years of age with confirmed enteric fever collected. Antibiotic susceptibility testing and azithromycin MIC of Salmonella typhi determined. Children treated with oral Azithromycin (20mg/kg/day) for 7 days or intravenous ceftriaxone (100 mg/kg/day), followed up and monitored for relapse. Out of 40 children, 26 received azithromycin and 14 received ceftriaxone.

Results

Ampicillin sensitivity was 36/40(90%); ciprofloxacin sensitivity was 21/40 (52.5%); ceftriaxone and azithromycin were 100% sensitive. Nalidixic acid was 100% resistant.

65% of the 40 isolates had MIC <4µg/ml, 20% had MIC 6 µg/ml and 12.5% had MIC 8µg/ml. Only one (2.5%) had MIC of 12 µg/ml.

Clinical cure achieved in 96% in Azithromycin group and 100% in Ceftriaxone group with time to defervescence 84 hours and 96 hours respectively. There were no relapses.

Conclusions

Azithromycin is very effective against uncomplicated typhoid fever in children. The once daily oral administration and short duration of therapy makes it score over parenteral ceftriaxone.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0445
E-POSTER DISCUSSION SESSION 25 - TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS (station 10)

IMPLEMENTATION OF RAPID DIAGNOSTIC TESTS FOR DIAGNOSING MALARIA AND OF ARTEMETHER-LUMEFANTRINE AS FIRST-LINE DRUG IN GUINEA-BISSAU

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Background

In 2008 artemether-lumafantrine (AL) was introduced as first line treatment for malaria in Guinea-Bissau, also rapid diagnostic tests (RDT) were introduced to minimize parasitological un-confirmed treatments. To evaluate the adherence to the new guidelines an observational study was performed. However, once a year the staff was retrained and informed on how they complied with the guidelines to evaluate whether this could improve performance.

Methods

Children < 15 years treated for malaria at Bandim Health Centre at the outskirts of Bissau were included January 2010 till October 2012. The children's symptoms during the preceding 12 hours, diagnostic methods, treatment, and prescriptions were recorded following informed consent.

Results

A total of 1323 children with a median age of 7.03 years were included. Of these 585 (44.2%) were prescribed AL, 130 (9.8%) chloroquine, and 608 (46.0%) quinine, of these 498 (81.9%) as intramuscular injections.

During the first 505 days, 338/838 (40.3%) as compared to 317/485 (65.4%) during the second 505-days-period were treated according to guidelines (OR: 1.84 (1.32-2.57), p<0.001).

RDT was performed on 1033/1317 (78.4%) patients with no difference between first and second period. The main reason (239/284, 84.2%) for not performing an RDT was unavailability. A positive RDT increased the likelihood of having correct medication (OR: 13.7 (9.3-30.2)).

Conclusions

Adherence to the new guidelines increased over time, probably due to focusing on the performance. Furthermore, when compared to previous studies the implementation of RDT seems to have reduced the number of children being treated without a parasitological confirmation.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov Identifier: NCT01157689

E-Poster Viewing Abstracts

ESP16-1015
01. S - PATHOPHYSIOLOGY/GENETICS OF HOST RESPONSE TO INFECTION INCLUDING SINGLE GENE AND GENOME WIDE STUDIES

FEDERALISM MASSIVELY IMPAIRS PAEDIATRIC RESEARCH - LESSONS LEARNED FROM AN FP7 FUNDED MULTICENTRE PROJECT

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Background

Euclids is a FP7 funded project that aims to identify genes that determine susceptibility and severity in life-threatening childhood infections. Life-threatening childhood infections are rare and sampling is limited in young age and critical illness. Thus, a multicentre approach can be the key to a large and representative study sample but is also challenging. This study describes one of the challenges in multicentre approaches, namely the process of obtaining ethical and institutional approval.

Methods

The clinical network consists of 164 hospitals in 10 countries (Austria, Gambia, Germany, Lithuania, Italy, Netherlands, Serbia, Spain, Switzerland, United Kingdom). A self-made questionnaire was used to assess differences in obtaining ethical approval and in study details in all participating countries.

Results

For 164 hospitals 111 separate ethical approvals from 59 ethical boards were necessary. Altogether more than 700 ethical board members evaluated Euclids. The biggest administrative burdens were observed in countries with multiple participating hospitals: Whereas Austria, Germany, Switzerland and Spain had to obtain separate ethical approval at each responsible ethical board, the Netherlands and the UK involved only one ethical board each. However, all of them also had to obtain approval from their local institutions, which was especially extensive in the Netherlands and the UK.

Conclusions

The ethical approval process was more time- and work-consuming than expected which resulted in a delayed start of recruitment and had clear impact on recruitment success in the majority of participating countries. We encountered variability and a lack of clarity in recommendations pertaining to feedback to families of diagnostic genetic findings. Federalism evidently impairs paediatric research and thus, a simplification and standardisation process for multicentre studies is urgently needed within the EU.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0978
01. S - PATHOPHYSIOLOGY/GENETICS OF HOST RESPONSE TO INFECTION INCLUDING SINGLE GENE AND GENOME WIDE STUDIES

IFITM3 RS12252 T>C POLYMORPHISM AND RESPIRATORY SYNCYTIAL VIRUS IN IRISH CHILDREN ADMITTED WITH BRONCHIOLITIS

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Background

Host genetics play a role in bronchiolitis disease severity. Interferon inducible transmembrane protein 3 (IFITM3) is a viral restriction factor and the rs12252 T>C single nucleotide polymorphism (SNP) has been associated with more severe influenza. Rs12252 C allele is approximately 4% frequency in Caucasians. The aim of this study is to determine whether severity of bronchiolitis is affected by the rs12252-C allele.

Methods

PCR-RFLP(restriction fragment length polymorphism) and direct DNA sequencing were used to determine the rs12252 SNP in 63 Caucasian patients, admitted with bronchiolitis. Patients were prospectively consented and recruited. Bronchiolitis severity was assessed using the respiratory distress and assessment instrument (RDAI), need for PICU etc. Stata version 11 (College station, Texas) was used for statistical analyses. Comparison between clinical parameters of the heterozygotes TC and the major allele TT was performed. Multivariate regression analysis was done to control for potential confounding by risk factors such as breastfeeding, family history of atopy, presence of siblings, birthweight/ gestation and exposure to household smoke.

Results

Five children were heterozygous (TC) for rs12252 SNP, with no CC homozygotes. There was no association between disease severity in patients with the C allele. There was no difference between TC patients versus TT in RDAI (5 versus 7 p = 0.09), length of stay (3.8 days versus 4.8 p= 0.48) or requirement for PICU (1 TC patient among 17 PICU patients p=1).

Conclusions

No association was seen between patients with one minor allele of the rs12252 SNP *IFITM3* and disease severity in an RSV bronchiolitis cohort.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0643
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

EPIDEMIOLOGY OF BLOOD CULTURE-PROVEN STAPHYLOCOCCUS AUREUS SEPSIS IN CHILDREN IN SWITZERLAND - RESULTS OF THE SWISS PEDIATRIC SEPSIS STUDY

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Background

S. aureus is an important cause of invasive infections in childhood but few prospective studies on *S. aureus* sepsis in children have been performed. Here we describe the characteristics of *S. aureus* sepsis in a large cohort of paediatric patients in Switzerland.

Methods

Prospective observational cohort study of newborns and children <17 years with blood culture-proven sepsis admitted to ten paediatric hospitals in Switzerland between September 2011 and November 2015. For this analysis we considered only children beyond the neonatal age.

Results

In the 4.2 years study period we recorded 738 sepsis episodes. 437 (59%) were due to Gram-positive bacteria. *S. aureus* was isolated in 121 (16%) episodes, for an age-standardised incidence rate of 3.1 per 100'000 children (95CI 2.6-3.6). Sixty-two (51%) *S. aureus* sepsis episodes occurred in previously healthy children (n=359), 59 (49%) in children with comorbidities (n=379). In previously healthy children, median age at *S. aureus* sepsis onset was 127 months (IQR 62-148) versus 27 months (IQR 6-94) in children with comorbidities

(p<0.001). Osteoarticular infection (40, 65%) was the predominant infection type in previously healthy children, but not in children with comorbidities (3, 5%) (p<0.001). Methicillin resistance was rarely detected (3, 2.5%). *S. aureus* sepsis presented as severe sepsis in 25 (21%) episodes, six (10%) in previously healthy children and 19 (32%) in children with comorbidities, p=0.003. One child died following *S. aureus* sepsis.

Conclusions

In previously healthy children *S. aureus* sepsis mainly occurs as a consequence of osteoarticular infection in school age children, while children with comorbidities are younger at sepsis onset and more often suffer from a severe disease course. Case fatality rate in *S. aureus* sepsis was low.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0656
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

EPIDEMIOLOGY OF BLOOD CULTURE-PROVEN ESCHERICHIA COLI SEPSIS IN NEONATES IN SWITZERLAND - RESULTS OF THE SWISS PEDIATRIC SEPSIS STUDY

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Background

E. coli is one of the main causes of early-onset neonatal sepsis (EOS) carrying significant mortality. Here we describe the characteristics of *E. coli* sepsis in a large cohort of neonates in Switzerland.

Methods

Prospective observational cohort study of neonates with blood culture-proven sepsis admitted to ten paediatric hospitals in Switzerland between September 2011 and November 2015. We analysed data on prematurely born neonates <44 weeks gestational age at sepsis onset and term born neonates <28 days of age.

Results

In the 4.2 years study period we recorded 426 neonatal sepsis episodes. The most prevalent organisms were coagulase negative staphylococci (n=118, 28%), *E. coli* (n=88, 21%), and group B streptococci (n=74, 17%). *E. coli* represented 67% (88 of 132) of all Gram-negative isolates. Sixteen (18%) of the *E. coli* sepsis episodes presented as EOS (n=79) and 72 (82%) as late-onset sepsis (LOS, n=347). Median gestational age at birth for *E. coli* EOS was $31^{2}/_{7}$ weeks (IQR $28^{0}/_{7}$-$33^{4}/_{7}$) versus $37^{5}/_{7}$ weeks (IQR $28^{2}/_{7}$-$40^{0}/_{7}$) in LOS (p=0.007). The most prevalent clinical presentation of *E. coli* EOS was primary bloodstream infection (10, 62%) versus urinary tract infection in LOS (30, 42%). Extended-spectrum beta-lactamase

production was detected in three (3.4%) episodes. *E. coli* EOS presented as septic shock in six (38%) episodes, versus nine (12%) in LOS (p=0.020). In ten (62%) *E. coli* EOS episodes mechanical ventilation was required, versus 24 (33%) in LOS (p=0.046). Case fatality rate was 4.5%, with 100% of deaths occurring in preterm neonates born <35 weeks.

Conclusions

In our cohort *E. coli* was the second most common cause of neonatal septicaemia. *E. coli* EOS frequently manifested as primary bloodstream infection and presentation was more severe than *E. coli* LOS.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0744
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

LEUCONOSTOC SPP CATHETER-RELATED BLOODSTREAM INFECTION IN THREE INFANTS: CASE REPORTS

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Title of Case(s)

***LEUCONOSTOC SPP* CATHETER-RELATED BLOODSTREAM INFECTION IN THREE INFANTS: CASE REPORTS**

Background

Introduction: Catheter-related bloodstream infections (CR-BSIs) are an important source of morbidity and mortality. Leuconostoc is a gram-positive cocci. It rarely cause infection. In this case study, we describe three infants with CR-BSI due to *Leuconostoc spp*.

Case Presentation Summary

Case1: A 7 month-old girl had been hospitalized with chronic diarrhea and she required total parenteral nutritional support. On the 71th day of hospitalization, she had a persistent fever and a worsening clinical condition. *L.citreum* was detected in central venous catheter and catheter tip cultures by the Vitek_MS system. Linezolid was then started and given for 10 days.

Case2: A two-year old girl had been hospitalized with receiving chemotherapy because of diagnosing as atypical teratoid rhabdoid tumor at 15-month old. On the 29th day of hospitalization, she had a persistent fever and a worsening clinical condition. Blood cultures were taken from peripherial vein but couldn't be taken from central venous catheter. Klebsiella pneumonia and *L.lactis* were detected in seperate peripherial vein cultures by the Vitek_MS system. Linezolid and meropenem were started and given for 10 days with linezolid and meropenem.

Case3: A five-year-old girl who had been hospitalized since birth due to prematurite. She underwent open surgery; nonviable intestinal bowel was resected on 9th and 47th day of life. On the 150th day of life, she had fever and worsening clinical condition. *L.citreum* was detected in peripherial vein and central venous catheter culture by the Vitek_MS system. Linezolid was then started and given for 10 days with linezolid.

Learning Points/Discussion

As a conclusion *Leuconostoc spp* infections are prone in settings of disrupted bowel mucosa and central venous catheter.

ESP16-0642
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

WATER BIRTH, BE FUN AND SAFE!

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Title of Case(s)

WATER BIRTH, BE FUN AND SAFE!

Background

Neonatal Herpes Simplex Virus (HSV) infections are associated with significant morbidity and mortality. Water birth has received little attention as an influencing factor despite its growing popularity.
Aim: To alert health care providers (HCP) to this potential route of transmission and to highlight the importance of HSV screening prior to water birth.

Case Presentation Summary

A 3742g term baby girl was born by SVD in a water in a Birthing Center, to primigravida with uneventful pregnancy. Parents were immersed in the birthing tub during labour. There was no apparent history of PROM or visible genital or oral herpetic lesions. Baby was discharged home well < 24-hour of age.

By day-2 of life, the baby was febrile (39°C), lethargic with poor feeding. Septic work-up was performed, ampicillin and gentamycin were commenced. Referral to L3 NICU was made by day-6, because of persistent spiking temperature, acyclovir was added on day-6 and herpes screening was performed. The mother was noted to have herpetic whitlow and the father had cold sore. WBC initially was normal, but subsequently the baby developed leucopenia, thrombocytopenia with abnormal LFTs. Her clinical condition deteriorated with severe respiratory failure, hypotension and DIC requiring ventilation, inotropes and blood products transfusion.

Surface swabs, endotracheal aspirate and blood PCR showed positive results for HSV type 1. The baby had severe progressive multiorgan failure. A shared decision was made with the family for comfort care, the baby died on day-8 of life.

Learning Points/Discussion

Conclusion

HSV screening should be carefully pondered prior to a water birth. It is essential to consider neonatal HSV infection in any febrile newborn who is not responding to standard empirical antibiotic management, even in the absence of herpetic lesions.

ESP16-0655
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

RELATIONSHIP BETWEEN ACTIVATED PARTIAL THROMBOPLASTIN TIME, PROTHROMBINE TIME, D-DIMER AND FIBRINOGEN WITH DENGUE SHOCK SYNDROME OUTCOMES OF PEDIATRIC PATIENTS IN DR. SARDJITO GENERAL HOSPITAL, INDONESIA

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Background

High mortality in dengue shock syndrome (DSS) usually ascociated with untreated shock and massive bleeding. Coagulopathy may impaired hemostasis which contrributes to bleeding manifestation in dengue hemorrahgic fever (DHF) and DSS. Parameter of activated partial thromboplastin time (APTT), plasma prothrombin time (PPT), D-dimer and fribrinogen indicate the impact of coagulation system. The aim of this study was to determine the relationship between APTT, PPT, D-dimer and fibrinogen levels with the outcome of DSS patients.

Methods

A retrospective study was applied to patients diagnosed with DSS from January 2010 to March 2014 in Department of Childhood, Dr Sardjito General Hospital, Faculty of Medicine Universitas Gadjah Mada, Indonesia. APTT, PPT, D-dimer and fibrinogen level data during hospitalilzation were collected. Patients were divided into detah and survival groups. Differences between groups were analyzed using unpaired t-test or Mann-Whitney U test. Coagulation parameters as risk factors of mortality were evaluated with bivariate and multivariate analysis.

Results

One hundreds and eight patient were analyzed in this study. There were significant relationship between prolonged APTT, PPT and increasing of D-dimer level with death of DSS patient (p=0.013, p=0.002, p=0.020, respectively). Increasing of D-dimer level was the independent risk factor for death outcome (PR=17.4; p=0.008).

Conclusions

Blood coagulation parameters were correlated with bad outcome of DSS children patient, and especially D-dimer, contributed to the death.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0449
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

ACUTE APPENDICITIS AND LUNG ABSCESS IN A FOUR-YEAR-OLD BOY WITH INFLUENZA A H1N1 INFECTION

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Title of Case(s)

ACUTE APPENDICITIS AND LUNG ABSCESS IN A FOUR-YEAR-OLD BOY WITH INFLUENZA A H1N1 INFECTION

Background

Influenza A virus (H1N1) infection usually causes a mild to moderate illness in children. However, complications, mainly pulmonary, may be seen during the disease. We presented a child with H1N1 infection who had a lung abscess, and acute appendicitis as an extremely uncommon complication.

Case Presentation Summary

A 4-year-old boy was admitted to another hospital with a 2-day history of high fever, headache, cough, vomiting and severe abdominal pain. His past medical history was unremarkable. He was operated with the diagnosis of acute abdomen and had a surgical intervention for imperforated acute appendicitis. He was referred to our hospital since his fever continued after the operation and hypoxia developed. The chest-X-ray demonstrated a parenchymal consolidated opacity and pleural effusion on the left side. A thorax CT showed an abscess in the atelectatic parenchyma of left lung and accompanying pleural effusion. Laboratory tests revealed an increase in acute-phase reactants and a positive PCR for H1N1. Oseltamivir and empiric antibiotic treatment with ampicillin-sulbactam and clarithromycin were administered. No organism was isolated from blood and pleural fluid culture samples. The immunological work-up revealed no pathology. Patient recovered completely with antiviral and antibiotic treatment, and was discharged with no evidence of a medical problem.

Learning Points/Discussion

H1N1 infection may result in complications in children without any risk factors. Lung abscess can be seen as a complication in the absence of any underlying condition. Acute appendicitis can also be encountered as an extremely rare complication of H1N1 infection.

ESP16-0767
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

LOCALIZED TETANUS AND TULAREMIA IN AN ADOLESCENT: CASE REPORT

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Title of Case(s)

LOCALIZED TETANUS AND TULAREMIA IN AN ADOLESCENT: CASE REPORT

Background

Tetanus is still problematic in developing countries due to incomplete immunization coverage. Localized tetanus is very rare form of this forgotten disease presenting with painfull muscle spasms usually localized to muscle groups around the wound. Tularemia is an endemic disease in Turkey, but its diagnosis requires high suspicious index. It must be considered in patients with supurative lymphadenopathy unresponsive to non-spesific antibiotic therapy.

Case Presentation Summary

A 17-years-old boy presented with axillary supurative lymphadenopaty and painfull muscle spasms on his right arm and right leg during last 3 months. In history, he had no immunization due to parental refusal. He had a severe injury to his right hand by a broken glass. Then, he had painfull muscle spasms beginning from right hand and dispersed to right leg lasting spotaneously in 1 or 2 hours. His level of consciousness was not effected during muscle spasms and serum ionized calcium, magnesium and potasium levels were normal. His electroencephalography (EEG) and cranial magnetic resonance imaging (MRI) were normal. Because of the inadequate immunization status against tetanus, he had treated with metronidazol and human tetanus immunoglobulin with wthe presumed diagnosis of localized tetanus. The histopathologic examination of lymph node resulted consistent with supurative granulomatous reaction. Sulbactam-ampicillin therapy was given for supurative lymphadenopaty. The antibiotic therapy was changed to gentamycine when *Francisella tularencis* aglutination test was found as 1/320 positive. His supurative lymphadenopathy and muscle spasm totally recovered.

Learning Points/Discussion

Tularemia must be suspected in patients with supurative lymphadenopathy unresponsive to non-specific antibiotic therapy especially in endemic areas. Tetanus must treated immediately when suspected until the contrary is proved especially in patients with history of lack of adequate immunization against tetanus.

ESP16-0208
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CLINICAL PROFILE AND OUTCOME OF SICK CHILDREN WITH TROPICAL FEVER

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Background

This was a retrospective analysis of patients of tropical fever admiited in our PICU.We wanted to study various factors affecting outcome in such patients so that in future these patients could be managed in a better way to reduce mortality

Methods

This was a retrospective study conducted in a PICU of a tertiary care hospital attached to a medical school.IIn this study the case records of all the consecutive sick children admited to PICU with a provisional diagnosis of tropical fever during the months of august to november 2015 were retrieved and relevant data entered on an excel sheet.The clinical data thus entered was analysed statistically.

Results

During this time period a total of 73 patients of tropical fever were admitted in our PICU.Out of these 28 were females and 45 males.Among these only 7 children(9.7%) were less than 5 years.Majority of patients(58.9%) were above 10 years age.Maximum number of cases were of dengue fever,followed by scrub typhus.Overall 18 out of 73 patients died(24.6%).

Conclusions

In sick children admitted with a provisional diagnosis of tropical fever,judicial fluid management along with early introduction of antibiotics against samonella and scrub typhus along with antimalarials can help in salvaging many lives,till final etiological diagnosis is made.

ESP16-0624
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

LEMIERRE'S DISEASE IN AN INFANT WITH VARICELLA ZOSTER

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Title of Case(s)

Lemierre's Disease in an Infant with Varicella Zoster

Background

An 8 month old boy, recovering from chicken pox, presented with 2 days of rhinorrhoea, cough, fever, lethargy and unilateral green ear discharge. He appeared sleepy, febrile and tachycardic with visible work of breathing. Purulent right-sided otorrhoea was noted without evidence of ear proptosis or mastoid erythema. He had multiple scabbed varicella lesions.

Case Presentation Summary

Bloods revealed the following: CRP 298, platelet count 54, INR 1.4, Bilirubin 67 and an ALT 136. Chest x-ray showed minimal shadowing. Blood gas demonstrated metabolic acidosis. He was treated for group A strep sepsis/ toxic shock syndrome and commenced iv ceftriaxone and clindamycin, receiving 40ml/kg of fluid. In view of fluctuating GCS, acyclovir was added and he underwent urgent CT head. This demonstrated fluid in the external auditory canal, normal CSF spaces, and no meningeal enhancement.

The ear swab grew *fusobacterium* raising the possibility of Lemierre's disease. IV metronidazole was commenced. By day 5 blood cultures grew anaerobes, *Staph. Aureus* and *Strep pneumonia*. Development of a 6th nerve palsy prompted an urgent MRI which showed venous sinus and right internal jugular vein thrombosis, right petrous apicitis, occluded right internal carotid artery and possible septic emboli. He was retrieved to PICU and underwent bilateral mastoidectomy with subsequent heparanisation. He developed left tibial osteomyelitis, requiring 2 surgical washouts (fusobacterium-PCR positive). He completed 12 weeks of iv/oral ceftriaxone and metronidazole/ clindamycin. He requires 6 months of dalteparin and further neuroimaging. He currently has a right convergent squint with otherwise grossly normal development.

Learning Points/Discussion

This case demonstrated complexity of isolating a single diagnosis with apical petritis and nerve palsy suggesting Gradenigo syndrome; however, fusobacterium and venous thromboses suggesting Lemierre's disease.

ESP16-0913
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

NEPHROTIC SYNDROME CAUSED BY EPSTEIN-BARR VIRUS – AN INCIDENTAL DIAGNOSIS

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Title of Case(s)

Nephrotic syndrome caused by Epstein-Barr Virus – an incidental diagnosis

Background

This case is interesting because it is a rare complication of a common virus that would probably elude diagnosis hadn't we requested a routine urinalysis. But should we adopt the same diagnostic approach in every child with suspected mononucleosis in antecipation of such a rare event given its severity when left untreated?

Case Presentation Summary

Epstein-Barr virus (EBV) or human herpesvirus 4 is a member of the herpes virus family. It is a common virus that infects most people at some point in their lives, causing infectious mononucleosis and occasionally other more serious conditions. Symptoms caused by EBV are usually mild and self-limited but the virus can persist all life in a dormant state. Nephrotic syndrome is seldom a complication of viral infections, with rare cases reported of EBV as the responsible pathogen. We present the case of a 3 year-old boy with infectious mononucleosis whose urinalysis showed nephrotic proteinuria, which progressed to nephrotic syndrome. The patient was admitted in the hospital and treated with enalapril 0.2mg/kg/day until nephrotic proteinuria ceased. After discharge the patient was subject to follow-up in an out-patient setting until complete resolution.

Learning Points/Discussion

Although nephrotic syndrome is a rare manifestation of Epstein-Barr virus infection and more so in children, the high frequency of mononucleosis in childhood requires that physicians remain aware of this possible complication. In such cases, the physician should also ask, during clinical interview, if the patient has any urinary complaints or if he has noticed swelling of the face or body.

ESP16-0440
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

OSTEOMYELITIS IN THE BELGIAN SICKLE CELL COHORT: STILL A DIAGNOSTIC AND THERAPEUTIC CHALLENGE

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Background

Sickle Cell Disease (SCD) patients have a high risk of bacterial infections, being osteomyelitis one of the most frequent ones. They remain an important diagnostic and therapeutic challenge.

Methods

Retrospective review of osteomyelitis presented in the Belgian SCD Cohort, until February 2012. Osteomyelitis was concluded if patient presented compatible clinical and radiological signs. Demographical, clinical, biological, microbiological, radiological data and treatment were reviewed.

Results

13 from 402 SCD patients (3.23%) presented 16 episodes of osteomyelitis between 1981 and 2011. The SCD genotype was Hb SS for all the patients with a median age at infection of 7 years (0-16 years). Complete data were available for 10 episodes (8 patients, 2 recurrences). Clinical signs at onset were mainly pain and fever (70%); 30% presented swelling. Biological inflammation was moderate at admission (median WBC 15800/mm³, average CRP 63.6 mg/L, ESR 55 mm/h). In 60% of episodes microbiological isolation was achieved: 4 cases by collection puncture, 1 case by puncture and blood culture and 1 case by blood and stool culture. In 5 cases a Salmonella non-typhi and in one a Staphylococcus aureus were isolated. Radiological management was heterogeneous but, echography (60% of cases) and MRI (40% of cases) were always contributive. Standard X-ray and isotopic bone scan led, in no case, to a definite diagnosis. All the patients received i.v. 3rd generation cephalosporin; oral continuation included mainly fluorquinolones (70% of the cases). Average treatment duration was 7.5 weeks (3-16 weeks).

Conclusions

Combination of clinical, biological and radiological information is needed as diagnosing osteomyelitis is crucial but difficult in SCD patients. Echography can guide periosteal collection puncture for increasing microbiological diagnosis. Optimal antibiotherapy remains unclear.

ESP16-1026
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

RISK FACTORS ASSOCIATED TO A HIGHER MORTALITY IN CHILDREN WITH WHOOPING COUGH HOSPITALIZED IN A PEDIATRIC INTENSIVE CARE UNIT

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Background

To study risk factors associated to a higher mortality in children with whooping cough hospitalized in a pediatric intensive care unit.

Methods

Descriptive retrospective study of patients hospitalized in the pediatric intensive care unit of a tertiary referral hospital that presented a positive PCR in nasopharyngeal swab for *B. pertussis*, between January 2007 and October 2015.

Results

31 children were included in the study with a median age of 31 days [RIQ: 28-66]. 76,7% (n=23) had not received any dosage of pertussis vaccine. 16% presented chronic diseases. 76,7% (n=23) required CPAP, 41,4% (n=12) required mechanical ventilation. Exchangetransfusion was practiced on 26,7% (n=8) and 16,7% (n=5) received ECMO. 6 patients (19,5%) died. 16,1% (n=5) presented pulmonary hypertension and the same number were diagnosticated of radiological pneumonia.

Risk factors associated to a higher mortality were: to present a heart rate over 170bpm at PICU admission, radiological pneumonia and the presence of pulmonary hypertension.

Maximum white blood cell count during hospitalization (p=0,0001), lymphocytes (0,004), neutrophils (0,002) and C-RP (0,012) were higher in patients who died.

White blood cell median to exchangetransfusion was higher in patients that died (81300 cs/ vs 57400 cs/)

Conclusions

In our sample, mortality in children with whooping cough hospitalized in a pediatric intensive care unit is high, and an important percentage required respiratory assistance. Tachycardia (>170bpm), radiological pneumonia and pulmonary hypertension are risk factors associated to a higher mortality. White blood cell count before the first exchange transfusion is lower in children that finally survive.

ESP16-0411
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PNEUMOCOCCAL MENINGITIS

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Title of Case(s)

Pneumococcal meningitis

Background

Actually, in Italy three pneumococcal vaccines are available to prevent invasive disease caused by Streptococcus pneumoniae : one is polysaccharride (PPV23) and two conjugate (PCV10, PCV13).
Aim of the study is both to verify which serotypes cause pneumococcal meningitis and to find out a relationship with complications.

Case Presentation Summary

We reviewed medical records of 313 children admitted to Bambino Gesù Children Hospital, Rome, Italy for meningitis between September 2001 and September 2015. Among them, 44 had a pneumococcal etiology. The serotype was identified in 21 of them. The mean age of patients affected by pneumococcal meningitides was 2.6 years (range 0.2–15.6 years). The highest frequency of cases was observed in children younger than 5 years (89%). Two patients died and twenty-five were discharged with long term sequelae (31.8% auditive, 4.5% ocular and 20.4% neurological). The serotypes of the two dead children were 23B and 19A. Serotypes 1, 7, 9, 15c, 3 and 4 were isolated in the group of patients with auditive sequelae, serotype 3 in those with ocular complications and 7, 14, 23B, 1 and 14 in those with neurological impairment.

Learning Points/Discussion

PCV13 vaccination may have prevent meningitis in most of our patients.
In our case series, serotypes 16, 23B, 10A, 15A and 15 C, not included in the PCV13, caused meningitis in 33,3% of patients. In details, a 2-year-old child died (serotype 23B), a 1.5-year-old child had deafness (serotype 15c) and a 4-month-old baby neurological impairment (serotype 23B).
In conclusion, a strictly surveillance of pediatric pneumococcal meningitis incidence and a correlation between disease severity and serotype are mandatory.Further studies are useful in order to verify if modification in vaccine composition may be suggest.

ESP16-0582
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

LEMIERRE'S SYNDROME IN A TEENAGER PRESENTING AS PULMONARY SEPTIC EMBOLISM

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Title of Case(s)

Lemierre's Syndrome in a teenager presenting as pulmonary septic embolism

Background

Lemierre's syndrome is a rare disease characterized by septic thrombophlebitis of the internal jugular vein, after an acute pharyngeal infection, followed by metastatic infection to the lungs or central nervous system. This disease is easily missed and may be more common than generally appreciated.

Case Presentation Summary

A 17 year-old adolescent girl was diagnosed with acute viral pharyngitis a week before the admission. She had persistent fever in the last 7 days in the day of the hospitalization she presented cough, thoracic pain and dyspnea. She had cervical lymphadenopathies, a painful mass above the left clavicle and severe hypoxemia. The laboratory revealed leukocytosis (24.000/mcL), anemia (Hb 10.6mg/dL), thrombocytopenia (22.000/mcL) and elevated CRP (194.3mg/L). She was admitted in the intensive care unit and received non-invasive ventilation. A diagnosis of Lemierre's syndrome was evoked and she was treated with ceftriaxone and clindamycin. A diagnosis of septic thrombophlebitis of the internal jugular vein was confirmed by Doppler and she was treated with low-molecular weight heparin on D5 because of progressive thrombosis and she improved dramatically. An angio-CT performed on D15 confirmed massive pulmonary thromboembolism and shown a lateral mediastinal mass, later confirmed to be a bronchogenic cyst. The infectious and auto-immune workup was inconclusive. All cultures were negative.

Learning Points/Discussion

A high index of suspicion is required for the diagnosis of Lemierre's syndrome. In young children it is usually a complication of a deep neck abscess but in adolescents and young adults it can complicate a milder disease and have a sudden presentation of short-breathness and hypoxemia. Accurate diagnosis and orientation is mandatory for the treatment of an otherwise potentially life-threatening disease.

ESP16-0912
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

TEN YEARS OF PAEDIATRIC ENTERIC FEVER AT PATAN HOSPITAL, KATHMANDU, NEPAL

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Background

Enteric fever caused by *Salmonella* Typhi and Paratyphi is responsible for significant morbidity and mortality across Nepal. Children are particularly susceptible and contribute significantly to disease burden.

Methods

Demographic, clinical and laboratory data were collected prospectively and daily during 2005-2014 from all children under 14 years admitted to Patan Hospital with suspected invasive bacterial disease. Children with positive blood cultures for *S*.Typhi or *S*.Paratyphi were included in the analysis for this study.

Results

There were 1708 positive blood cultures, of which 177 (10.4%) were *S*.Typhi and 29 (1.7%) were *S*.Paratyphi A. Of the 206 with a confirmed diagnosis of enteric fever, the median age was 4.6 years (range 1-14 years) with 113 (55%) children under the age of 5 years, and 124 (57%) were male. 96 (43.8%) cases occurred between 2005 and 2007 while the last 5 years accounted for 95 (43.3%) cases with only 12 cases in 2014.142 (65%) cases occurred between the months of May and October over the 10 year period. The mean duration of admission was 7.3+3.9 days with no significant association between age and duration of admission. One child died and another was discharged against medical advice; no sequelae were noted among others at discharge. Fever was the most common symptom at presentation seen in 96% of patients.

Conclusions

Enteric fever is the cause of a significant burden of disease among children presenting to hospital services in Nepal, particularly in the hottest and wettest months of the year. There is a declining trend in the number of cases of paediatric enteric fever attending Patan Hospital. This may be due improved water and sanitation, differing health-seeking behaviors, or a local typhoid vaccination campaign in 2014.

ESP16-0408
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

BRONCHOPNEUMONIA AND NEUTROPENIC FEVER DUE TO BOCAVIRUS INFECTION

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Title of Case(s)

Bronchopneumonia and neutropenic fever due to Bocavirus infection

Background

Human bocaviruses(HBoV), members of the Parvoviridae family,were first identified in clinical specimens from children with respiratory tract infections(RTİ) and gastroenteritis.Life-threatening RTİ associated with HBoV are uncommon and usually observed in infants .Also neutropenia secondary to HBoV is not often expected.With this report,we attempted to share our experience with life-threatening RTİ due to HBoV and neutropenie in an infant.

Case Presentation Summary

A-9-month old infant was admitted to the emergency department due to respiratory distress and fever.It was noticed that the patient had lissencephaly,patent ductus arteriosus,congenital dysplasia of the hip,and intrauterine growth retardation from the medical history.On physical examination cachexia, highly arched palate, pectus excavatum, asymmetry in the left hip and bilateral rhonchi were detected.The laboratory investigation reveals a white blood cell count of 3800/µL(absolute neutrophil count:400/ µL),with normal kidney and liver functions and urinalysis results.C-reactive protein was 5.34 mg/dL(0-0.8). Acute bronchopneumonia with hypoxemia,bilateral peribronchial thickening and perihilar reticulonodular opacities and neutropenic fever were diagnosed and ampicillin sulbactam was started.On the second hospitalization day,increased respiratory distress,cutis marmoratus and resistant fever were noted and ampicillin-sulbactam was switched to meropenem,vancomycin,amikacin,and clarithromycin.Blood and urine culture were negative and neutrophil counts returned to normal levels on the follow-up.HBoV was isolated from nasopharyngeal swab.Neutropenia was not recurred for 4 months after discharge.

Learning Points/Discussion

It is known that HBoV is associated with life-threatening acute RTİ with a severe prognosis,especially in infants.We present a case of a 9-month-old female patient with HBoV infection associated with acute bronchopneumonia,complicated by neutropenic fever.No other virus or bacterium was detected in the respiratory and blood samples of our case,which indicates that HBoV is likely to be a true respiratory pathogen that could cause severe and even life-threatening disease.

ESP16-0137
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

LUNG ABSCESS FROM STAPHYLOCOCCUS AUREUS AFTER VARICELLA INFECTION IN A 3 MONTHS OLD INFANT

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Title of Case(s)

Lung Abscess From *Staphylococcus aureus* After Varicella Infection In A 3 Months Old Infant

Background

Varicella is a common, vaccine preventable childhood disease caused by varicella zoster virüs. The virus is present in respiratory secretions and skin vesicles. It is transmitted through airborne route with respiratory secretions and direct contact with the skin lesions. It is an extremely contagious disease, in secondary household contact the rate can be as high as 90%. Although, varicella is generally mild and self-limited illness, it can cause severe complications in infants and immunocompromised patients. Herein, we report lung abscess from *Staphylococcus aureus* after varicella infection in a 3 months old infant.

Case Presentation Summary

A previously healthy 3 months old female infant was admitted with high fever, cough and respiratory distress. Three weeks prior to admission to hospital, she had suffered from varicella infection with her sisters and did not receive any treatment. On examination she had resolving lesions of typical varicella without superinfection of the skin and auscultation of the lungs revealed decreased respiratory sounds in the right upper zone. Laboratory analysis revealed leucocytosis (15400/mm^3), with increased C reactive protein (11.4 mg/dl). Chest x ray showed consolidation with air bronchogram and computed tomography scan of chest demonstrated an abscess of 1.5 centimeters in diameter. The abscess was percutaneously drained. The culture yielded methicillin resistant *Staphylococcus aureus.*

Learning Points/Discussion

This case report highlights a rare complication of varicella and underscores the importance of vaccination against varicella for all age groups because our case developed varicella after her adolescent unvacccinated sisters' primary varicella infection. Vaccination is the most effective strategy in preventing the complications of varicella.

ESP16-0713
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

STAPHYLOCOCCUS AUREUS CAUSING BACTEREMIA AND ILIOPSOAS ABSCESS FOLLOWING TRAUMA IN AN ADOLESCENT BOY

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Title of Case(s)

***Staphylococcus aureus* causing bacteremia and iliopsoas abscess following trauma in an adolescent boy**

Background

Iliopsoas abscess is a relatively uncommon but potentially life-threatening infection of extraperitoneal compartment. Iliopsoas abscess may be classified as primary or secondary. Primary abscess results from hematogenous spread of an infectious process from an occult source in the body. Trauma resulting with intramuscular hematoma formation can predispose to primary iliopsoas abscess formation. The most common bacterial cause of iliopsoa sabscess is *Staphylococcus aureus*. Herein, we describe an adolescent boy with bacteremia and iliopsoas abscess caused by *Staphylococcus aureus* following trauma.

Case Presentation Summary

A previously healthy obese adolesent boy presented with complains of fever, malaise and left-side hip pain. He was unable to walk due to severe pain in his hip. He had the history of falling down while walking two weeks before. On physical examination, he was febrile, had redness, swelling, and increased warmth on the left gluteal region. Laboratory analysis revealed leucocytosis (29.6×10^9/L) and high C-reactive protein level (387 mg/L). Magnetic resonance imaging demonstrated a septated and multiloculated mass at the left iliopsoas muscle extending to left gluteal region indicating iliopsoas abscess and hemotoma. CT-guided percutaneous abscess drainage was performed. Gram staining showed Gram-positive cocci in clusters, *Staphylococcus aureus* was isolated from the abscess and blood. He was treated with cephazolin and clindamycin. Abscess improved gradually and he was able to walk without pain 2 weeks later.

Learning Points/Discussion

In conclusion, iliopsoas abscess is extremely rare and difficult to diagnose because of nonspecific symptoms. Physicians should consider iliopsoas abscess in patients presenting with complaints of lower back or hip pain and fever associated with trauma.

ESP16-0037
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CHRYSEOBACTERIUM INDOLOGENES IN PEDIATRIC PATIENTS: LITERATURE REVIEW

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Background

C. indologenes is a widespread bacteria in the environment, especially hospitals and rarely reported human pathogen. Clinical manifestationsof *C. indologene*s include especially nosocomial pneumoniae, intravasculer catheter related bacteremia, and primary bacteremia. According to the literature, only 16 children with infection caused by *C. indologenes* have been reported until today. There is knowledge gap in the management of *C.indologenes* infections, especially in children because of multiple antibiotic resistance and limited data for effective empirical treatment in the literature. Herein we attempted to share our experience with *C. indologenes* in six children and to evaluate all the pediatric cases in the literature because understanding of the nature of *C. indologenes* infections in pediatric age group is important for the prompt management of the disease.

Methods

This retrospective study was undertaken by the Department of Pediatric Infectious Diseases at the Faculty of Medicine of Hacettepe University. The medical records of patients diagnosed with *C. indologenes* infection between July 2012 and June 2015 were systematically reviewed. Relevant information such as demographics, clinic, laboratory, and treatment findings were recorded on pre-prepared forms.

Results

Early and prompt management of *C. indolegenes* infections, particularly in children with mechanic ventilation, polymicrobial infections, and under two-years old age constitute a major importance because this factors seem to have a negative affect on the prognosis of infections caused by *C. indologenes*. Although it is not clearly known how to manage these infections optimally, combination therapy with TMP-SMX and ciprofloxacin may be more effective than monotherapy-based regimens based on clinical data of the present study.

Conclusions

However, extensive worldwide surveillance programs are vital to understand the appropriate antimicrobial therapies and the clinical context of rarely isolated pathogens including *C. indolegenes*.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0806
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CLINICAL PROFILE OF PEDIATRIC OSTEOARTICULAR INFECTIONS IN A TERTIARY CARE HOSPITAL IN INDIA

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Background

There is paucity of data regarding osteoarticular infections, which have the potential to cause permanent disability, in Indian children . We attempted to study the clinical profile including etiology in a tertiary-care pediatric centre in South India

Methods

The study was conducted at Kanchi Kamakoti CHILDS Trust Hospital, South India from 1st November 2014 – 31st October 2015. Children between 0 – 18 years fulfilling the inclusion criteria of swelling(s), Pain or Limited range of motion of joints were studied

Those in whom an infective cause was ruled out after investigation were excluded. As were those with Transient Synovitis, Hemarthrosis, Reactive arthritis, Connective tissue diseases

For every patient, cultures were sent from blood as well as from joint / soft tissue fluid. Clinical details including history, examination, investigations were entered into the proforma

Chi square test was used for comparison between two groups and unpaired t test was used for continuous variables.

Results

- Out of 36 cases studied, 17 had Septic Arthritis (47.22%), 16 had Osteomyelitis (44.44%) and 3 had both co-existing (8.33%).
- Organisms were identified in 61.11% of cases; most common was *Staphylococcus aureus* (50%)
  · MSSA (63.63%) was more common than MRSA (36.36%) · *Klebsiella pneumonia* and *Pseudomonas aeruginosa* were the most common gram negative organisms isolated. 4 out of 7 were ESBL producing (57.14%) and 3 out of 7 were CRE (42.85%).
  There were 3 *Mycobacterium tuberculosis* osteomyelitis cases· The median duration of hospital stay was 11 days (range: 1 to 37 days).

Conclusions

· *Staphylococcus aureus* is the most common pathogen in pediatric osteoarticular infections; gram negative bacilli are an important etiology among neonates.

· There is an alarming rise in MRSA, ESBL enterobacteriaceae and CRE which emphasises the need for antibiotic stewardship

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1040
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

SOFT TISSUE INFECTION AND NECROTIZING PNEUMONIA CAUSED BY PANTON-VALENTINE LEUKOCIDIN (PVL) CA-MRSA (COMMUNITY-ACQUIRED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS) IN A 8-YEARS-OLD CHILD

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Title of Case(s)

Soft tissue infection and necrotizing pneumonia caused by Panton-Valentine leukocidin (PVL) CA-MRSA (community-acquired methicillin-resistant staphylococcus aureus) in a 8-years-old child

Background

PVL could be secreted by both MRSA and MSSA (methicillin-sensitive staphylococcus aureus) and it is responsible for severe and difficult to treat invasive infections, also in healthy children

Case Presentation Summary

We report the case of a eight-years old healthy child, who was admitted on 28th August 2015 to Pediatric ward of our Hospital for left thigh pain and high fever. At admission she presented poor general condition; her vital signs were as follows: temperature 39.4°C, pulse 100 beats/minute, blood pressure 115/70 mmHg and oxygen saturation 100% in room air. Empiric antibiotic therapy with vancomicin and meropenem was started; she underwent abdominal CT scan, which showed a left obturator internus muscle abscess. The next day blood cultures resulted positive for MRSA. On 30th August the abscess was drained, but after a transient defervescence, fever recurred. Chest X-ray showed left pneumonia and clinical condition got worse; the child was therefore transferred to Pediatric Intensive Care Unit. Antibiotic therapy was modified: daptomicin and ceftobiprole were started on 3rd September. Fever persisted and inflammatory markers increased; in the suspicion of an infection caused by PVL CA-MRSA, linezolid and clindamicin were prescribed on 8th September. In the next few days the child recovered and she was discharged on 13th October on therapy with linezolid. MRSA isolated resulted to be a PVL positive strain

Learning Points/Discussion

PVL production should be considered in severe CA-MRSA infections and the use of antibiotics active against the toxin is mandatory. There are few data about the efficacy of ceftobiprole against PVL production; in our case it didn't seem effective. Further studies are needed

ESP16-0795
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PVL-MSSA INVASIVE DISEASE

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Title of Case(s)

A particularly severe case of septic arthritis

Background

The Panton-Valentine leukocidin (PVL) is a pore-forming toxin associated with community-associated methicillin-sensitive or resistant *Staphylococcus aureus* (CA-MS or MRSA). Positive-PVL strains have higher virulence, inducing suppurative and necrotic lesions, either skin-related or invasive. Searching for PVL imposes when treating deep-seated infections with severe necrotic component.

Case Presentation Summary

11-year old male, previously healthy, presented with septic arthritis of the right hip. An arthrocentesis was performed and intravenous flucloxacillin initiated. On 2nd day evolved to septic shock with ARDS, needing admission in Intensive Care Unit. On D7 of ceftriaxone and vancomycine, clinical status worsened, with persistent fever and MRI evidence of pyomisitis and psoas abscess. Due to hemodynamic instability, medical treatment was decided - clindamycine, linelozid, imipinem. PVL-MSSA was isolated from initial blood culture.
After 30-days, arthritis relapsed, needing drainage; during recovery, a pathologic fracture of the femoral head occurred, needing surgical reintervention. The patient was discharged after 3 months, with oral rifampicine and clindamycine for an additional 3 weeks course.
A second traumatic fracture of the femoral head needed surgical correction.
At 3-years follow-up, evolution was favorable, with stable gait, leg dysmetria of 19mm and no further infections. HIV serology was negative and no immunodeficiency was identified.

Learning Points/Discussion

PVL-CA-MSSA infections were rarely described in Portugal and no pediatric cases were reported so far to our best knowledge. The presence of PVL correlates with infection severity, as in this case, that progressed to shock and ARDS despite of a correct surgical drainage and adequate antimicrobial therapy. PVL suspicion should be treated as PVL-MRSA and later be guided by antimicrobial susceptibilities. Surgical drainage is mandatory and linezolid can be valuable in these severe bone infections.

ESP16-0244
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

SEVERE SEPSIS AND SEVERE PNEUMONIA MAY BE CLINICALLY INDISTINGUISHABLE: ITS IMPLICATIONS

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Background

Background: Chest indrawing is a reliable indicator of hypoxemia which may be caused by severe pneumonia or severe sepsis. The chest X- ray is still considered to be the gold standard for diagnosing pneumonia in the developed world. World Health Organization (WHO) guidelines suggest a diagnosis of severe pneumonia in a child with chest indrawing when X-ray facility is not available (1). We have an increasing number of cases presenting with chest indrawing to have normal chest X-rays. These children commonly present with fever, their peripheral blood counts, taken as proxy for positive blood culture, suggest bacteremia; blood gas study reveals metabolic acidosis and their blood lactate levels are raised. These findings point towards severe sepsis in them.

Methods

Methods: Consecutively admitted thirty-eight children with chest indrawing were studied. Demographic, clinical and investigation details were collected. The two sub-groups, i.e. chest indrawing with or without consolidation, were compared for association of various parameters. Test of significance, Chi-squared or Fischer's test, was applied.

Results

Out of 38 children presenting with chest indrawing 12 (31.6%) presented with consolidation and 26 (68.4%) had no consolidation on X-ray. The two groups differed significantly only in respect to nutritional status, history of diarrhoea and hospital stay.

Conclusions

Hypoxemia associated severe sepsis or severe pneumonia, both, can present with chest indrawing. Treatment guidelines for pneumonia (chest indrawing) in developing countries need to be fine tuned to cover treatment of severe sepsis also. Then only deaths due to “pneumonia” will decline substantially.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0104
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

EFFICACY AND SAFETY OF SACCHAROMYCES BOULARDII IN ACUTE ROTAVIRUS DIARRHEA: AN OPEN LABEL RANDOMIZED TRIAL

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Background

There is paucity of data regarding the beneficial effect of *Saccharomyces boulardii* in acute rotavirus diarrhea. We studied the efficacy and safety of *Saccharomyces boulardii* in acute rotavirus diarrhea in Indian children

Methods

In this randomized open label trial, 115 children (3 months to 5 year) with WHO defined acute watery diarrhea were subjected to stool rotavirus EIA test. Those with severe dehydration, severe malnutrition, chronic illnesses, and documented history of administration of rotavirus vaccines or probiotics were excluded. Sixty rotavirus positive cases were randomized into intervention and control group. The intervention group received *Saccharomyces boulardii* (500mg/day) for five days. Outcomes studied were duration of illness, time to change in stool consistency, duration of vomiting, duration of hospitalization, and adverse effects

Results

The median duration (hours) of diarrhea was significantly shorter in the intervention group (60 vs. 87; p=0.001). The median time for improvement in the stool consistency was faster in the intervention group (40 vs. 52; p=0.04). A significantly shorter duration of hospitalization (74 vs. 98; p=0.001) was also seen in the intervention group, but no significant difference was seen for fever (56 vs. 67; p=0.44), and vomiting (48 vs. 55; p=0.72). There was no report of any adverse events

Conclusions

The present trial showed that *S. boulardii* is effective and safe in acute rotavirus diarrhea

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0112
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

EPIDEMIOLOGY AND OUTCOME OF ACUTE ENCEPHALITIS SYNDROME IN CHILDREN: A DEVELOPING COUNTRY PERSPECTIVE

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Background

Worldwide, acute encephalitis syndrome (AES) is a major pediatric health problem causing high morbidity and mortality. Although viruses are the major pathogens responsible for AES, most cases remain undiagnosed. Our aim was to study the etiology and outcome of viral AES, and compare the outcome with non-viral AES.

Methods

This prospective hospital based observational study was conducted over a period of two-years, and included children (6 months - 15 years) presenting with AES. Demographic and clinical data were recorded in a predesigned format after taking consent from the caregivers. Blood and CSF samples were collected and analyzed for cytology, biochemistry, serological tests (ELISA), and PCR/RT-PCR (for virus isolation). Neuroimaging was done to define the extent of brain injury.

Results

Out of 1010 cases, viral etiology was found in 156 (15.5%). The 5-10 years age group was most commonly affected (Boys:Girls = 1.5:1). No seasonal variation was seen. Compared to non-viral AES, presence of rash, and Glasgow Comma Score (GCS) <8 at admission was significantly higher in viral AES. During hospitalization, development of shock, ventilatory requirement, duration of stay, and mortality was significantly higher in viral AES compared to non-viral AES. The organisms underlying viral AES were: Herpes simplex virus (HSV)-I (78.2%), Herpes simplex virus (HSV)-II (7.3%), Japanese B encephalitis virus (6.4%), Dengue virus (3.2%), Measles virus (2.2%), Varicella virus (2%), and Mumps virus (0.7%).

Conclusions

Viral etiology constitutes a significant proportion of pediatric AES, with Herpes virus being the most common. Viral AES has poor prognosis compared to non-viral AES. Global cerebral injury is common in HSV-II, JE and varicella virus AES.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0114
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

A TWO YEAR PROSPECTIVE STUDY OF VIRUSES CAUSING ACUTE RESPIRATORY INFECTIONS IN CHILDREN UNDER FIVE IN EASTERN PART OF INDIA

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Background

Acute respiratory infections (ARI) are important cause of mortality and morbidity in children under five in a developing country. The present study was designed to study the viral etiology of acute respiratory infections in children under five in the eastern part of India.

Methods

This observational study was conducted over a period of 2 years (October 2011 to 2013) in a tertiary care teaching hospital. Nasal and throat swabs were collected, transported to the laboratory at 2-8°C in viral transport media, and then processed for detection of viruses using mono/multiplex real-time polymerase chain reaction.

Results

A total of 300 children aged 2-60 months with ARIs (Lower respiratory tract infection [LRI]=174; upper respiratory tract infection [URI]=126) were included. The most common age group affected with LRI was 2-12mo (54%), and with URI was >12-60mo (45.2%). Viruses were detected in 248 cases. The virus positivity in ARI was as follows: URI – 61.1% samples were positive for single virus and 10.9% for more than one virus; LRI – 65% samples were positive for single virus and 9.5% for more than one virus. The most common viruses isolated from URI cases were Rhinovirus(RV)[31.1%], Adenovirus(ADV)[18.9%], Respiratory Syncytial virus(RSV)[17%], and Influenza virus(IFV)[17%]. The most common viruses isolated from LRI cases were RSV(30.3%), IFV(17.6%), RV(14.8%), and ADV(13.4%). Most cases occurred in the month of January, December, and August. In LRIs, severe clinical course, severe pneumonia, and cardiac failure were more common in co-infected patients than patients with mono-infection or no infection.

Conclusions

RSV, ADV, RV and IFV are important causes of ARIs among children under five in eastern part of India. These data will be useful for vaccine design, development and implementation purposes.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0239
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

A CLINICAL AUDIT OF DENGUE PRESENTATION, INVESTIGATIONS AND MANAGEMENT IN CHILDREN IN A TERTIARY CENTER IN INDIA

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Background

Dengue is endemic in India. The current WHO guidelines on Dengue provides a clinically useful guide for triage, early diagnosis and management of Dengue. A retrospective audit was conducted on the Dengue cases in a tertiary hospital in Navi Mumbai, India to ascertain the compliance with the revised WHO guidelines.

Methods

The retrospective audit was conducted on the Dengue cases hospitalized in a tertiary centre in India between July-November 2013 using the current WHO guidelines for Dengue. Six criteria chosen for audit included clinical presentation, laboratory parameters, intravenous fluids, antibiotics, vitamin K or blood products and fulfillment of discharge criteria. Areas of improvement in the management of Dengue cases were noted. Educational interventions were carried out to increase the knowledge of the revised WHO guidelines and a re-audit for the deficiencies identified was performed in the subsequent Dengue season in 2014.

Results

87 patients with age ranging from 7 months to 17 years were admitted between July-November 2013. Serum aspartate transaminase levels was found to be statistically significant predictor for severity of Dengue illness. Hypotonic fluids were used in all patients contrary to the recommended isotonic fluids. Antibiotics and Vitamin K were unjustified in 38% and 29.5% respectively. A reaudit of the dengue season in 2014 between July and September showed reduction in antibiotic usage to 26.08%. There was a significant decline in the use of irrational intravenous fluids to 4.3% and Vitamin K to 8.6%.

Conclusions

A regular audit followed by educative interventions is effective in reducing the irrational use of antibiotics in viral infections like dengue and improves the compliance with the standard guidelines.

ESP16-0130
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PYOGENIC VENTRICULITIS DUE TO STREPTOCOCCUS PNEUMONIAE

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Title of Case(s)

PYOGENIC VENTRICULITIS DUE TO STREPTOCOCCUS PNEUMONIAE IN AN 4 YEAR OLD GIRL: CASE REPORT

Background

Introduction: Despite modern intensive care, antibiotic treatment, and the use of dexamethasone, the morbidity and mortality associated with *Streptococcus pneumoniae* meningitis remain high.

We present here a 4 years old girl with *Streptococcus pneumoniae* meningitis, a vaccine preventable disease, whose course was complicated with development of hydrocephalus and ventriculitis.

Case Presentation Summary

Case: A four years old girl, came in pediatric emergency in a moribund state with history of high grade fever, headache, vomiting for past one month and altered sensorium, refrectory seizures, 3 days prior to admission. She was treated with antibiotics, anticonvulsants, ventilator and inotropic support and other supportive care. Neuroimaging showed development of hydrocephalus and ventriculitis in addition to meningeal exudates. CSF and blood culture both came to be positive for streptococcus pneumonia. Hydrocephalus was treated with external ventricular drainage by neurosurgery team. Frank pus was drained. Tracheostomy was required for prolonged ventilator dependence due to poor sensorium. She was shifted to local hospital after PICU stay of 2 weeks, who later survived with major sequalae.

Learning Points/Discussion

Conclusion: Persistence of high grade fever, delirium, seizures in a clinically moribund patient with meningitis should raise suspicion of ventriculitis.

ESP16-0954
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

STAPHYLOCOCCUS AUREUS BACTEREMIA IN EMERGENCY DEPARTMENT PATIENTS

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Background

Most research regarding *S. aureus* bacteremia (SAB) has focused in inpatients, which associate high morbidity. Our objective is to describe features and outcomes of Emergency Department (ED) patients with SAB.

Methods

Retrospective descriptive study including positive blood cultures for *S. aureus*, collected in children <14 years in the ED, in a tertiary Spanish Hospital during eleven years (2004-2014).

Results

We included 57 cases (53 patients), being 35% girls. Median age was 28.7 months (IQR 5.2-89.8). Up to 51% of patients presented at least one risk factor, the most prevalent being invasive medical devices (40%: 19 central venous catheters [CVC], 1 CSF shunt, 1 pacemaker). Fever without source was the most frequent clinical presentation (22 episodes, 38.5%), followed by fever with osteoarticular symptoms (11) and skin and soft tissue involvement (7). Four cases presented septic shock. Ten children were initially managed as outpatients, being 6 admitted after knowing blood culture results. The median length of hospital stay was 8 days (IQR 6-14). Two MRSA (5%) and 8 clindamycin-resistant (15.7%) *S.aureus* were isolated, 1 was resistant to both. CVC-associated bloodstream infection was the most common final diagnosis (17 episodes, 30%), followed by osteoarticular infection (11, 19%). Two patients developed complications: 1 mediastinitis, 1 purulent pericarditis. Nine out of the 27 patients without risk factors (33%) presented with fever without source and normal acute phase reactants. Three never received antibiotic therapy and had a good outcome.

Conclusions

Half of the cases of SAB occurred in previously healthy children, being osteoarticular infections and occult bacteremia the most frequent final diagnoses. The most frequent underlying risk factor was the presence of CVC. Methicillin resistance was low, being cloxacilin the first line treatment.

ESP16-0944
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

WHEN SALMONELLA REACHES BEYOND THE GASTROINTESTINAL TRACT: A RARE CASE OF SALMONELLA SOFT TISSUE ABSCESS IN 5 MONTHS OLD GIRL

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Title of Case(s)

When Salmonella reaches beyond the Gastrointestinal tract: A rare case of Salmonella soft tissue abscess in 5 months old girl

Background

Salmonella is an entero-invasive Gram-negative bacterium and a primarily enteric pathogen. On ingestion, the organisms bypass gastric defenses, multiply, and penetrate the intestinal mucosa. They survive within the macrophages of the reticuloendothelial system and disseminate via systemic circulation, causing infection. The clinical significance of Salmonella extra-intestinal manifestations is not often appreciated. There are very few documented reports regarding such manifestations. Herein, we report a rare case of 5 months old girl diagnosed with Salmonella Gastroenteritis and ended up with Salmonella soft tissue abscess of the left leg

Case Presentation Summary

5 months old female infant , ex preterm was admitted due to febrile enteritis. A stool culture collected on the same day of admission grew Salmonella species. Stool later became bloody suggesting colitis.
24 hours later, she started to spike a high grade fever reaching up to 39C. Meanwhile, the family noticed swelling with overlying erythema at the site of the cannula inserted at the left foot that progressed to an abscess formation. A swab from this site later grew the same Salmonella species that grew in the stools.

Learning Points/Discussion

Infections with Salmonella species can involve any organ or system. Abscess formation by Salmonella species is an uncommon but significant manifestation of salmonellosis. Abscesses may occur as a late complication in almost any Salmonella infection.

Soft tissue infections are rare, accounting for 6%– 12% of all Salmonella infections. Most of the infections are caused by Non-Typhoidal Salmonella (NTS).

ESP16-0977
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

VARICELLA - SOMETIMES, MORE THAN JUST ITCHY RED SPOTS...

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Title of Case(s)

VARICELLA - SOMETIMES, MORE THAN JUST ITCHY RED SPOTS...

Background

Varicella is a common childhood infection, usually benign. Although rare, complications involving various systems may occur – respiratory, dermatologic, neurologic, hematologic and, rarely, musculoskeletal. Cutaneous lesions may function as an entry for some pathogens. The frequency of complications by invasive group-A beta-hemolytic streptococcus is low but appears to be increasing.

Case Presentation Summary

A 3-year-old previously healthy boy, with an 8-day history of varicella, was admitted to our Departement for high fever in the last 3 days and progressive pain and edema of the right knee, with refuse to walk. At admission the knee was slightly swollen, warm and tender, its extension was limited by pain and the child refuse to stand up and walk. Most varicella lesions were scabs. X-ray and ultrasound were unremarkable. Bloodwork revealed 13600 leukocytes/uL (65.3% neutrophyles), CRP of 86.5 mg/L, sedimentation rate of 90 mm/hour and a normocytic normocromic anemia (hemoglobin 10.2 g/dL). Empirical treatement with endovenous flucloxacillin 200 mg/Kg/day was started, along with ibuprofen. Clinical condition improved progressively. Blood culture grew *Streptococcus pyogenes*. MRI was performed at day 10 and osteomyelitis of distal metaphysis and epiphysis of the right femur was confirmed. A total of 21 days of endovenous antibiotherapy was completed. At discharge, bloodwork was normal and blood culture negative. The child still have a slightly limped gait, but was pain free. He completed 21 days of oral flucloxacillin in an out-patient basis and was followed-up by the Orthopedic Departement for the next 8 months. There was complete resolution of symptoms and no further complications occured.

Learning Points/Discussion

Altought varicella is normally harmless, one should be aware of its complications and raise awareness among caregivers.

ESP16-0565
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PNEUMATOCELES IN CHILDREN: RETROSPECTIVE STUDY OF 84 EMPYEMA CASES

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Background

Introduction: Pneumatoceles are thin-walled, air-filled cysts that develop within the lung parenchyma due to alveoli necrosis following pneumonia.

Aim: To study the treatment and prognosis of pneumatoceles.

Methods

Material & methods: Retrospective case record review of 84 pediatric cases of thoracic empyema (2004 – 2015).

Results

Results:Eighteen (21%) of the children studied (age range 5months – 4.3 years) had pneumatoceles. 16 children had unilateral lesions and 2 had pathology in both lungs. S. aureus (5/18) and S. pneumoniae (3/18) were the most common pathogens. In 14 (78%) children the pneumatoceles resolved spontaneously (20days – 2 months). In one child urgent decompression of a tension pneumatocele was required. Three children underwent surgical treatment because of bronchopulmonary fistula formation.

Conclusions

Conclusions: The majority of pneumatoceles resolve spontaneously. Surgical treatment is required in a minority of cases that fail to resolve. Close clinical follow up is sine qua non.

ESP16-1096
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

ACUTE BACTERIAL AND VIRAL MENINGITIS: USEFULNESS OF CLINICAL AND LABORATORY FINDINGS FOR AETIOLOGICAL DIAGNOSIS

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Background

Bacterial meningitis (BM) remains an important cause of morbidity. Early diagnosis and prompt treatment are essential.
Aim: analyse clinical/laboratory findings of BM and viral meningitis (VM) and their utility in the differential diagnosis; evaluate the usefulness of *Bacterial Meninigitis Score* (BMS).

Methods

Retrospective analytic study, including patients with BM and VM and identification of an etiologic agent in the last 10 years. Exclusion criteria were traumatic lumbar puncture (LP), incomplete cerebrospinal fluid (CSF) data, immunodeficiency, ventriculo-peritoneal shunt, immunosuppression and/or antibiotherapy within 2 weeks before the LP. Statistical analysis: *IBM SPSS Statistics* 22 ($p<0,05$). Differences in qualitative and quantitative variables were tested. ROC curve was obtained for parameters with statistically significant differences and their cut-off, sensitivity, specificity and predictive values.

Results

Fourty-seven patients were included, 24 with viral meningitis (51%). The median age was significantly lower ($p<0,001$) in BM (1,8Y vs. 8,2Y). Fever ≥39ºC ($p=0,006$) and seizures /impaired consciousness ($p=0,002$) were more frequent in BM. CSF protein ($p=0,001$), CSF neutrophil count ($p<0,020$) and serum C-reactive protein (CRP) ($p<0,001$) were significantly higher in BM while CSF glucose ($p=0,025$) and CSF/blood glucose ratio ($p=0,006$) were significantly lower. The parameters with greater area under the curve, showing good discriminative power were CSF neutrophil count (ROC c=0,81, cut-off=409cel/m^3, S=86%, E=82%, PPV=67%, PNV=93%) and CRP (ROC c=087, cut-off 5.55mg/dL, S=86%, E=87%, PPV=86% and NVP=87%). BMS identified all patients with BM (sensitivity 100%, specificity 82%).

Conclusions

In this study, high fever, seizures/impaired consciousness, CSF protein, CSF neutrophil count, CSF/blood glucose ratio and serum CRP were found to be useful clinical and laboratory parameters in the distinction of BM. The parameter showing the best discriminative power to distinguish between BM and VM was CRP. BMS identified all patients with MB.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0100
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

HEPATITIS B VIRAL INFECTION IN CHILDREN: A 40-YEAR EXPERIENCE AT A SINGLE CENTER

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Title of Case(s)

Hepatitis B viral infection in children: A 40-year experience at a single center

Background

The recognition of HBV infection from child to adult is important to manage this infection.

Case Presentation Summary

We analyzed retrospectively 222 children with HBV infection. The 222 children were followed from first visit to final visit by our group from 1975 to 2014. The first visit age were from 0-year-old to 20-year-old (median age was 14-year-old), male/female was 119/103. We registered HBV carrier since 1975, and after 1986 registered not only HBV carrier but also the child with transient HBV infection. Results: The age of latest visit age were 6-month-old to 28-year old, median duration of follow was 14 years. The HBV transmission routs were mother to infant 172 (77%), father to child 23 (10%), unknown 17 (7%), the others 10 (5%). There is a 14-year-old girl who was transmitted by STI, and one child born to HBs Ag negative mother, infected from HBV carrier aunt by breast feeding. In any age, chronic hepatitis B were observed. We could not predict the age susceptible to developing chronic hepatitis. The serum conversion to HBe antibody phase (eSC) has gradually increased in proportion to aging. In mother to infant transmission, HBV genotype C (GTC) was significantly higher compared to genotype B (GTB). Fortunately, there was no tendency increasing genotype A (GTA) in children. The proportion of foreigners in HBV infected cases has been gradually increased from around 1986.

Learning Points/Discussion

The reason of large numbers of HBV infection in a single center were due be consulted by our specialty. The significant greater proportion of GTC in vertical transmission was the reasons, until the female becomes childbearing, eSC will be delayed compared to GTB

ESP16-0364
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

BRUCELLOSIS IN CHILDREN: A FIVE YEAR PROSPECTIVE COHORT STUDY FROM BIKANER, NORTHWEST INDIA

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Background

Inspite of high prevalence of brucellosis in animals, human brucellosis has not been reported commonly because of unawareness due to of lack of suspicion and lack of diagnostic facilities. This prospective cohort study describes the occurrence and clinical spectrum of human brucellosis in children in Bikaner, northwestern India.

Methods

During last five years (2011-2015), we came across 98 children with active brucellosis presented with a wide spectrum of clinical manifestations. The diagnosis of active brucellosis was confirmed by demonstration of the raised brucella agglutination titre of ≥1:320 in the serum. Detailed history related to the occupation and exposure to the known predisposing factors and presentation of the disease were noted. The possibilities of other disease/infections causing similar illness were investigated thoroughly and stringently.

Results

The mean age was 8.8±4.3 years (range 2-16 years) and boys were almost twice in number than girls (1.9:1). Fever (82.66%) was the commonest presenting feature (mean duration 17.6±6.6 days). Joint pain was reported in 70.41% children and majority of them were having multiple joint pain. Sacroiliac joint (42.03%) and knee joint (31.88%) were commonly involved. Other modes of presentation were neurobrucellosis (19.38%), manifested as encephalomyelitis polyradiculoneuropathy and myeloradiculopathy; pulmonary involvement (7.14%) presented as pleural effusion; and cardiac involvement presented as infective endocarditis (3.06%). Analysis of risk factors revealed history of raw milk ingestion (91.84%), occupational contact with animals (30.61%) and household contact (16%). All children were treated with standard protocols according to age and respond well.

Conclusions

Brucellosis is an important emerging zoonotic disease presenting with protean manifestations. High degree of suspicion is crucial for diagnosis specifically in vulnerable group of society.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0871
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

INFECTIVE ENDOCARDITIS IN CHILDREN AND YOUNG ADULTS

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Background

Objectives: To determine the features of infective endocarditis (IE), in patients under 25, over 15 years in a Spanish tertiary hospital.

Methods

Descriptive retrospective study of patients aged 0-25 years who met modified Duke criteria for IE, admitted from 2000 to 2015 in our hospital.

Results

34 episodes (31 patients) of IE were identified (76% male). Mean±SD age was 13.8± 6.7years. Fever was the main presenting symptom, with a median duration before admission of 13 days (IQR 4-60). Two presented with septic shock. Three patients (8.8%) were previously healthy, one was a severe burn. Thirty (88.2%) had underlying heart disease, 23/30 (76.6%) had prosthetic heart materials. Causative agents were identified in 25 episodes, 73%(table). Vegetations were documented in all by echocardiography (23.5% required transesophageal echo). Median antibiotic duration was 42 days (IQR 28-126). Acute surgery was necessary in 16 cases (47%). Systemic complications (septic emboli and shock) occurred in 13 cases (38%). There was only one fatal case (candida; 2.9%).

Microorganisms	Number of cases (N: 34)	Prosthetic material (N: 23)	Susceptibilities
Staphylococcus *S. aureus* *CoNS*	**6** 3 3	**5/6** 3/3 2/3	All MSSA All methicillin-susceptible
Streptococcus viridans group *S. viridans spp* *S. sanguis* *S. mutans* *S. anginosus*	**9** 4 3 1 1	**4/9** 2/4 3/3 0 0	All highly-penicillin-susceptible 1 relatively-penicillin-resistant
Enterococcus *E. faecium E. faecalis*	**3**	**1/3** 0 1/2	All ampicillin-susceptible

Microorganisms	Number of cases (N: 34)	Prosthetic material (N: 23)	Susceptibilities
	1 2		
Gemella haemolysans Corynebacterium pseudodiphtericum	**1** **1**	**1/1** **0**	
Haemophilus aphrophilus Haemophilus parainfluenzae	**1** **1**	0 1/1	β-lactamase-negative
Fungal *Candida Aspergillus*	**3** 2 1	**3/3** 2/2 1/1	
Sterile BC Positive serology for *Bartonella*	**4** 1	**3/4** 0	

Conclusions

IE occurs mostly in patients with underlying heart disease, especially in those with prosthetic materials. Most frequently involved microorganism are gram positive (staphylococcus and viridans group streptococci) which are highly susceptible to antibiotics. Mortality in our study was very low.

ESP16-0874
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

GROUP A STREPTOCOCCAL PRIMARY PERITONITIS IN A HEALTHY CHILD

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Title of Case(s)

Group A streptococcal primary peritonitis in a healthy child

Background

Primary peritonitis are rare. Gram negative bacilli, *Streptococcus pneumoniae* and *Staphylococcus aureus* are the main causal pathogens. However, primary peritonitis can complicate Group A *Streptococcus* (GAS) infections.

Case Presentation Summary

A previously healthy 10–year-old girl was hospitalized in a state of septic shock. She had vomited for three days, had abdominal pain, diarrhea, sore throat and fever. Blood pressure was 80/40 mmHg. She had an erythematous rash on the face and trunk, and non-necrotic small petechia on her legs. Abdomen was tense and guarded. Neutrophil count was $8.6 \cdot 10^9$/L, lymphocyte $0.3 \cdot 10^9$/L, CRP 327 mg/L, lactate 2.6 mg/L. Blood capillary gas and coagulation were normal.

She had received fluid bolus, cefazolin and clindamycin in another hospital. Norepinephrine and cefotaxime were added. Abdominal ultrasound reported important peritoneal free liquid. Laparoscopic surgery revealed a large volume of pus, a normal appendice, no bowel perforation nor faeces, hence describing a primary peritonitis. Cefotaxime and cefazolin were changed to piperacillin-tazobactam. She didn't receive immunoglobulins.

Cultures from blood, urine, throat and vaginal secretions were negative. Peritoneal fluid revealed paired Gram-positive *cocci* with no growing. PCR was positive for GAS and for virulence genes *speA, speB* and *smeZ*, while negative for *speC, ssa* and *sic.* It was a M3 serotype, frequently associated with STSS and scarlet fever.

On day 2, abdomen was tender and CRP 128 mg/L. Skin rash lasted 3 days. Clindamycin was given 5 days. Lymphopenia was corrected on day 10, when antibiotics was switched to oral amoxicillin for another 4 days.

Learning Points/Discussion

We report a primary peritonitis due to GAS and highlight the potential benefit of PCR to identify the bacteria in a primary peritonitis when antibiotics have been given prior to surgery.

ESP16-0940
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

SURVIVING SEPSIS CAMPAING: IMPLANTATION IN A PAEDIATRIC HOSPITAL

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Background

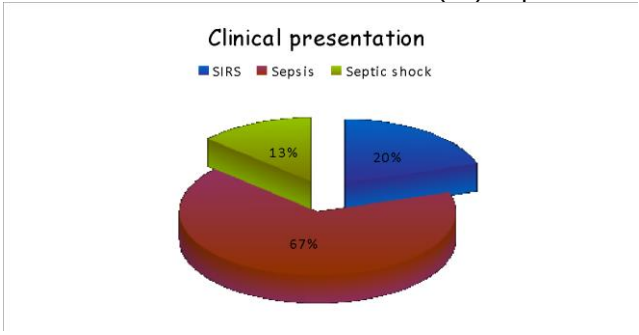
Since 2004 the *Surviving Sepsis Campaign*(SSC).promotes early recognition of sepsis, to reduce the mortality. Sepsis in children is a major cause of mortality in industrialized countries, despite it is lower(2-10%) when compared with adullts. In children it is more complex to recognize sepsis considering appropriate paediatric physiological parameters.

Methods

The Pequeno Principe Hospital (PPH) is a paediatric quaternary hospital and the Epidemiology and Infection Control Service (EICS) with PICU, Pharmacy and Laboratory Services, developed a protocol- campaing to improve the early detection of sepsis and the promptly diagnostic an therapeutic with the aim to reduce mortality. Analyzed diagnosed CID of sepsis and shock (A419,A483,R578,R579) from admission and from mortality notification form(MNF) in 2013 and 2014 years; Developed an educative handout with pediatric physiological and laboratory parameters, Training Teams medical / Training Nursing Team in a pilot units; Creation of *Sepsis KIT*,(plastic boxwith antimicrobials,laboratory materials and intravenous solutions);Antibiotic therapy protocol; Specific form SSC for collect data.

Results

In PPH were 40 and 31 admission cases of sepsis in 2013 and 2014 respectively with determinate CID ,(average 35 cases/ year). The MNF, from sepsis and septic shock ,were 72(Jan-Dez/2013) and 54 (Jan-Ago/2014). Between September 2014 through June2015 the protocol was elaborated and was the trainning period. The protocol initiated July 2015. Data from July until October 2015: 15 forms were filled: 60% (9) female, median age 5.6 years,20%(3) SIRS, 66.66%(10) severe sepsis,13.33%(2) septic shock. Antimicrobials were administered at the first hour in 80 %(12) of patients and no deaths occurred.



Conclusions

The concept improvement of SSC and the early recognition of sepsis in paediatric patients is gradual, continuous and multidisciplinary process .In this short study period we observed a preliminary positive results.

ESP16-0496
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

SCRUB TYPHUS- A MAJOR CAUSE OF MULTIORGAN DYSFUNCTION(MODS)-A SINGLE CENTRE EXPERIENCE FROM INDIA

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Title of Case(s)

SCRUB TYPHUS- A MAJOR CAUSE OF MULTIORGAN DYSFUNCTION(MODS)-A SINGLE CENTRE EXPERIENCE FROM INDIA

Background

Scrub typhus(ST) has been globally recognised as an emerging infectious disease contributing significantly to pyrexia of unknown origin(PUO) and a potential cause of multi-organ dysfunction syndrome(MODS). .Here we studied the incidence of ST as a cause of Pediatric ICU(PICU)admission and MODS in our hospital and its clinical and laboratory characteristics.

Case Presentation Summary

– This study was done in a Paediatric teaching hospital in Kolkata, India. Records of patients admitted with PUO from March-2012 to December-2015 were reviewed. Rathi-Goodman-Aghai(RGA) scoring system was used to identify potential ST patients and confirmed by serological testing. Clinical characteristics, laboratory findings and treatment response were noted of those needing PICU admissions. MODS was defined by simultaneous involvement of more than 2 organ system of the body.
ST was the serologically confirmed final diagnosis in 97 out of 884 children i.e. 11% of PUO admissions. PICU admission was needed in 30 of them(31%). It contributed 8.43% of total PICU admissions and 18.29% of MODS. Septic shock and encephalopathy(60%) followed by ARDS/ALI(43%) was the main cause of PICU admissions. Typical rash, generalised lymphadenopathy, low leucocyte and platelet counts, hypoalbuminemia and hyponatremia are significantly associated with MODS due to ST. Patients were treated with either Doxycycline alone or in combination with Azithromycin. Mean time to complete defervescence was 32 hours after first dose of Doxycycline. Outcome was excellent without a single mortality

Learning Points/Discussion

Scrub typhus is an important cause of PUO as well as MODS in this part of the World, specially in fevers associated with features as identified and not responding to conventional antibiotics.Treatment with Doxycycline is safe in children and life saving.

ESP16-0087
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

HOSPITALIZATIONS CAUSED BY VARICELLA AMONG CHILDREN IN THE DEFINIED POLISH POPULATION.

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Background

This study aimed to analyze the causes of hospitalization in children with varicella, based on a defined Polish population.

Methods

The subject of the analysis was the medical documentation of patients hospitalized for varicella at the Infectious Diseases Ward of the Children's Hospital in Poznan in the period between January 2007 and August 2015. The ward serves almost the entire child population of the Greater Poland region (10% of the Polish population). The analysis was based on hospital records. The case definition consisted of physical evidence of varicella.

Results

359 children were hospitalized for varicella (163 girls and 196 boys) at the Infectious Diseases Ward including 96 children in the first year of life. The mean age was 45 months (median 36 months). The duration of hospitalization ranged from 1 to 25 days (median 6). The children were admitted after different periods in the course of varicella: from 1-13 days (median 3). Rates of hospitalization decreased with age. The highest rates were among children during their first year. Ninety-two percent of children were healthy prior to hospitalization (no chronic diseases). The most common complications were respiratory tract infections, followed by skin infections and neurological symptoms. Almost 10% of patients had more than one complication. The most common coexisting conditions were dehydration and otitis media.

Conclusions

The results presented here serve to remind us that varicella may to lead to severe

complications in unvaccinated children and adolescents. Most children hospitalized with varicella were immunologically healthy. Meningitis was more common in older children (>6 years of age). Streptococcus pyogenes was the most commonly identified bacterial pathogen.

ESP16-0096
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

ECTHYMA GANGRENOSUM IN A PREVIOUSLY HEALTHY CHILD: A SKIN MANIFESTATION OF PSEUDOMONAS AERUGINOSA SEPSIS

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Title of Case(s)

Ecthyma Gangrenosum in a previously healthy child: A skin manifestation of *Pseudomonas Aeruginosa* sepsis

Background

Ecthyma gangrenosum (EG) is described as a typical necrotic lesion, mostly in immunocompromised patients. It reflects a severe sepsis possibly caused by *Pseudomonas aeruginosa* (*PA*).

Case Presentation Summary

We reviewed a case of a 3-year-old healthy girl, admitted in the emergency pediatric department who presented a purpura sepsis with neurological and respiratory distress. A meningococcal disease was strongly suspected, and an empiric antibiotherapy was rapidly prescribed (Ceftriaxone). She had initially painless erythematous and purpuric macules in moist areas, which became nodular, bullous or pustular with an indurated erythematous base and rim after 12 to 24 hours (Figure 1). Then, a gangrenous ulcer had been formed with a gray-black eschar surrounded by an erythematous halo. Forty-eight hours after the admission, blood and wound cultures were positive for *PA*. As a result, the decision was made to change the antibiotic (Ceftazidime). Unfortunately, on day 4, the patient died. Exhaustive immunologic tests are presently being carried out.

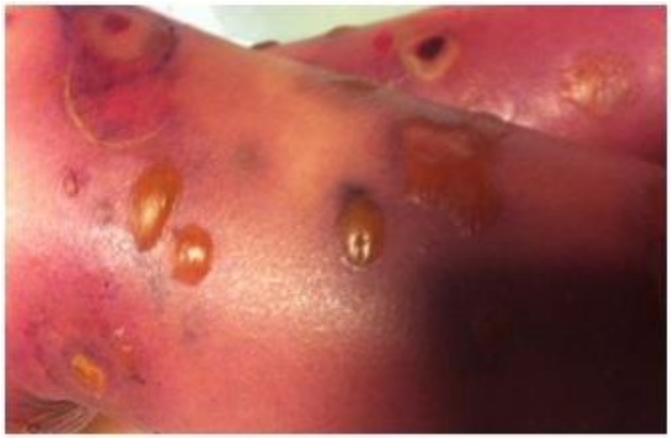

Figure 1: Bulla skin lesions at day 3-4

Learning Points/Discussion

EG caused by *PA* is uncommon in healthy children. A necrotic purpura with sepsis often implies another bacteria: *Neisseria meningitidis*. However, it remains essential to know and recognize EG. A partnership with bacteriology laboratories is crucial in order to get the results rapidly, and optimize the treatment. Moreover, association of aminoglycosides and β-lactams is recommended to avoid emergence of resistance, and shows a decrease in mortality rate.

ESP16-0183
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

BIOCHEMICAL FEATURES IN EARLY STAGES OF SEPSIS AND THE RISK FACTORS OF MORTALITY IN SEPSIS

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Background

Mortality is unacceptably high in sepsis and knowledge of biochemical-derangements during early stages of sepsis may help in the treatment and reducing fatality. This study aimed to describe the features of sepsis, and the risk/associated factors of death in septic-children.

Methods

126 under-5 years old children admitted with diarrhea and sepsis at the Dhaka Hospital of icddr,b in Bangladesh during April-2010 to December-2011 were studied prospectively. Diagnosis of sepsis was made on the presence of systemic-inflammatory-response-syndrome plus any identified/suspected source of infection. Septic-shock was diagnosed if there was additional feature of low volume/absent radial pulse, hypotension and/or delayed capillary refill (>3 seconds) in absence of without dehydration.

Results

Their mean±SD age was 19.1±14.2months; 52% were female; capillary refill time was 4.2±2.0 second; neutrophil and band % were 58±18% and 3.1±5.8%; BUN(mg/dl), PH, Hb(gm/dl) and platelet were 19.4±17.5, 7.3±0.2, 10.1±1.9 and 335,757±232,643; serum TCO_2(mmol/L), potassium(mmol/L), phosphate(mg/dl), calcium(g/dl), CRP(mg/dl), creatinine(µmol/L), creatinine phosphokinase(µ/L) were 15.7±6.7, 3.6±1.1, 4.5±2.1, 8.0.±1.3, 5.9±8.1, 49.3±48.7 and 335±666, respectively. Among these total 126 children 25 (19.8%) died. WHZ (-3.0±2.1 vs. -2.7±1.5), % band cell (5.2±6.4 vs. 2.6±5.5), Na (154±29 vs. 142±21) and BUN (25.7±21.5 vs. 17.8±16.1), septic-shock (92% vs. 9%) were significantly higher, and Hb (9.2±1.6 vs. 10.3±2.0) and albumin (2.9±1.1 vs. 3.4±0.8) were significantly lower among who died compared to alive children respectively. Logistic regression analysis showed that the children who died were 4 times more likely to be severely wasted (SAM) and 3 times more likely to had moderate anemia.

Conclusions

Case fatality rate is significantly high in sepsis particularly in septic-shock and SAM children. These features may help in the better management of septic-children with/without SAM and thus reduce fatality.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0772
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PREVALENCE AND TREATMENT OF DIARRHOEA AND PNEUMONIA IN BANGLADESH: AN EQUITY ANALYSIS

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Background

Pneumonia and diarrhoea are leading killers of the world's children. The poorest regions and countries, especially the disadvantaged children within these societies bear the major burden of diarrhea and pneumonia. Our objective was to assess the inequality in the prevalence and uptake of medical treatment of pneumonia and diarrhoea in Bangladesh from Bangladesh Health and Demographic Survey (BDHS) data.

Methods

We used data from 2007 and 2011 BDHS, a nationally representative sample survey of Bangladesh. We used a concentration index (CI) to examine the socioeconomic inequalities in the prevalence and uptake of medical treatment of pneumonia and diarrhoea using concentration index (CI) separately for children interviewed in 2007 and 2011.

Results

There were 178 and 540 pneumonia cases in 2007 and 2011 respectively. For diarrhea these numbers were 560 and 790 respectively. The CI of "pneumonia prevalence" was -0.139 (95% CI -0.218, -0.060) in 2007 and -0.075(-0.123 , -0.026) in 2011. The CI of "diarrhea prevalence" was -0.029 (-0.082, 0.022) in 2007 and -0.027 (-0.073, 0.019) in 2011. The CI of "medical treatment for pneumonia' was 0.146 (95% CI 0. 0710, 0. 222) in 2007 and 0. 165 (95% CI 0.108, 0.221) in 2011. The CI of "medical treatment for diarrhea' was 0.089 (95% CI 0.037, 0.141) in 2007 and 0.118 (95% CI 0.076, 0.159) in 2011.

Conclusions

The prevalence of pneumonia and diarrhea were both disproportionately concentrated among the poor; the extent of inequality increased from 2007 and 2011. On contrary the uptake of pneumonia and diarrhea treatment were disproportionately concentrated among the rich; the extent of such inequality also increased from 2007 to 2011. The study findings reflects a trend of uneven progress in improving child health in Bangladesh.

ESP16-0961
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

HERPES SIMPLEX INTRATHECAL ANTIBODY SYNTHESIS IN AN ATYPICAL CASE OF MENINGOENCEPHALITIS

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Title of Case(s)

Intrathecal synthesis of anti-herpes simplex IgG antibodies in an atypical case of herpes simplex meningoencephalitis

Background

Herpes simplex virus (HSV) encephalitis typically leads to necrotic and hemorrhagic lesions in the insula, frontal and medial temporal lobe. Nevertheless, atypical presentations appear to be more common in children and this diagnosis should not be excluded on a single negative PCR assay for viral DNA.

Case Presentation Summary

An 8-year old child was admitted after 12 hours of myalgias and headaches, followed by fever, vomiting, visual hallucinations and drowsiness. Neurologic examination revealed myoclonic jerks, an ataxic gait and weakness of the inferior limbs. Lumbar puncture showed a hypertensive cerebrospinal fluid, with a mild increase of the protein concentration (51.6 mg/dl), 37 white blood cells/µL and elevated red blood cells. CSF cultures for bacteria and fungi were negative, as were ELISA IgG and IgM assays for Varicella-zoster virus, Cytomegalovirus, Epstein-Barr virus, influenza, enteroviruses, HIV, Mycoplasma pneumoniae, C. burnetii and B. burgdorferi.

Despite a negative CSF PCR result (Real Time PCR LightCycler©) for HSV type 1 and 2, an Alegria© ELISA IgG assay detected a high intrathecal synthesis of HSV type 1 and 2 IgG (101 UI/ml). Brain MRI revealed necrotic temporo-occipital, left cerebellar, mesencephalic and pontine lesions with a recent hemorrhagic progression of the cerebellar lesion. Routine immunological studies (immunogram, CD4 count, complement levels) were normal. The patient experienced a complete neurological recovery after 21 days of intravenous acyclovir, corticosteroids and polyclonal immunoglobulins. Brain MRI on discharge revealed post-inflammatory sequelae

Learning Points/Discussion

We present a rare atypical case of HSV meningoencephalitis with temporo-occipital, cerebellar, mesencephalic and pontine involvement in a previously healthy child, in which the early detection of a high intrathecal synthesis of HSV antibodies proved diagnostic.

ESP16-0256
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PREVALENCE OF ROTAVIRUS INFECTION AMONG LESS THAN 5 YEARS CHILDREN WITH DIARRHEA IN WAD MADANI PEDIATRIC TEACHING HOSPITAL, GEZIRA STATE, SUDAN

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Background

.In Sudan, rotavirus has been one of the important causative agents of diarrhea among children. The aim of this study was to detect the prevalence of rotavirus infection among children with diarrhea in Wad Madani Pediatric Teaching Hospital during the period from July 2014 to January 2015.

Methods

Stool specimens from 92 children less than 5 years of age suffering from diarrhea were tested for the presence of rotavirus antigen using the solid-phase sandwich Enzyme- linked Immunosorbent Assay

Results

The results obtained were processed and statistically analyzed using chi-square test. Rotavirus antigen was detected in 36 (39.1%) of the patients. Most of the positive cases were in children less than1 year of age (72.2%) and the infection rate decreased with the increasing age. Children infected with rotavirus were more likely to have vomiting (72.2%) and fairly low frequency of fever (61.1%). Out of 36 rotavirus positive cases, 28 were resided Village (77.8%), 8 were from City (22.2%).

Conclusions

Rotavirus prevalence was (39.1%) among children less than 5 years. It is mandatory to have rotavirus vaccine; routine and proper diagnosis of rotavirus infection in children with acute diarrhea helps to determine appropriate treatment, prevents the unnecessary use of antibiotics and minimizes the spread of the disease among susceptible children.

ESP16-0212
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

20-YEARS RETROSPECTIVE STUDY OF INVASIVE MENINGOCOCCAL DISEASE CASES IN CHILDREN FROM ST. PETERSBURG, RUSSIA REGION (1995-2014)

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Background

The incidence of Invasive Meningococcal Diseases (IMD) in St Petersburg is sporadic and decreasing since 1980-s (0.78 per 100 000 in 2014). At the same time it's higher in children (2.94 per 100 000 in 2014). 904 cases of IMD in children (0 – 17 years old) were registered by city centre of disease control in 1995 – 2014 most of them (884) had been hospitalized to our clinic.

Methods

We analysed the epidemiological trends, clinical traits and outcomes of hospitalized cases of paediatric IMDs during the last twenty years. We performed retrospective analysis of medical in-patients cards, archived in our clinic and analysed city epidemiological registry for 1995 – 2014.

Results

Hospitalized cases were registered as Invasive Meningococcal Disease (IMD) based on clinical symptoms in 359 cases and were confirmed by one of the laboratory methods in 525 cases. Diagnostic methods were cultural isolation of *N. meningitis* (liquor or blood), latex agglutination reaction (liquor), meningococcal DNA isolation by PCR (liquor or/and blood). Infants and toddlers were consistently the most vulnerable age groups; they accounted 29% and 32% of all IMD cases, accordingly. Serogroup distribution differed from year to year; B and C were mostly prevalent serogroups. We defined a tendency of meningococcal B cases decrease from 72% to 45%, while IMDs caused by C group increased and caused 42% of IMDs in 2013. Case fatality rate varied from 2.0 to 12.5 %.

Conclusions

Epidemiology of IMD in children is changing within two recent decades. B & C strains stay dominant. The number of IMD fatal cases in children is also varying but stays higher than population average. In the absence of routine meningococcal immunization, IMD introduces a significant risk for young children.

ESP16-0929
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

EVALUATION OF LABORATORY MARKERS AVAILABLE ON EVERYDAY BASIS FOR DIAGNOSIS OF SEVERE BACTERIAL INFECTIONS

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Background

Sepsis and severe bacterial infections are common causes of children mortality. Golden laboratory standard tool for diagnosing sepsis still has not been found. Automatic hematological analyzers are capable of measuring of percentage of immature granulocytes (IG%), the potential sepsis diagnostic marker. The aim of the study was to evaluate the compliance of IG % and other laboratory markers used on everyday basis (total white blood count (WBC), absolute neutrophil count (ANC), C reactive protein (CRP)) with internationally (*Marshal*, 2004) defined criteria for ideal sepsis marker.

Methods

251 children with infection were included in the study. Patients were divided in two groups: infected without SIRS (n=175), patients with sepsis (n=75). For sepsis definition the International Paediatric Sepsis Consensus Conference classification was used.Study parameters were analyzed from the first routine blood analysis sampling. The following criteria were used for the evaluation of laboratory markers: 1)small amount of blood required, 2)method is automatized, 3)low costs, 4)well defined cut-off value, 5)high sensitivity and specificity.

Results

To predict sepsis receiver operating characteristics was performed demonstrating the highest AUC values for CRP 0,87 (0,84–0,91) and WBC 0,77 (0,71–0,82), followed by IG% 0,73 (0,67–0,79), ANC 0,72 (0,66– 0,78). The cut-off values for detecting sepsis patients: 0,45% (57% sensitivity, 83% specificity) for IG%; 56,5mg/ml (0,64% sensitivity, 100% specificity) for CRP, 53 x10^9(0,61% sensitivity, 81% specificity) for WBC and 9,9 x10^9 (0,59% sensitivity, 83% specificity) for ANC.

Conclusions

Inflammatory parameters detectable in the local hospital on 24/7 basis for diagnosis of severe bacterial infections correspond to internationally defined criteria for laboratory markers. Incorporated immature granulocyte percentage serves as an additional useful marker to WBC, CRP and ANC for sepsis prediction without extra costs and additional sampling.

ESP16-0388
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

STREPTOCOCCUS MILLERI PEDIATRIC INFECTIONS IN MONTPELLIER UNIVERSITY HOSPITAL; A RETROSPECTIVE STUDY FROM 2003 TO 2013

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Background

Streptococcus milleri group (*S.m.)*, also known as the *Streptococcus anginosus* groupconsists in facultative anaerobes belonging to the three species *S. constellatus*, *S. intermedius* and *S. anginosus*. Commensal of the oral cavity, the skin, the gastrointestinal tract and the genito-urinary tract, *S.m.* is often associated with pyogenic infections. The significance of this group of micro-organisms in children is not well known.

Our purpose was to conduct an epidemiologic study of the *S.m.* infections in children, to analyse their incidence, clinical manifestations, treatment and prognosis.

Methods

We used the hospital information system to identiy all patients under 18 years who had a microbiologically proven *S.m.* infection, between 2003 and 2013. Patients hospitalized in neurosurgery were not included.

Results

The cohort consisted of 67 children (mean age, 7.7 years). Localization of the infection was: intra-abdominal for 40%, oropharyngeal for 22%, soft tissues for 21%, pulmonary tract for 9%, genitourinary tract for 5%, and bone and joint for 3% of children.Cultures were polymicrobial in 85% of cases including other anaerobic bacteria in 52% of cases. All *S.m* were suceptible to penicillin, and all had a low level of innate resistance to aminosides. The patients were treated by antibiotics in 85% of cases. A surgery was done in 82% of cases. Outcome was favorable in 82% of patients, all patients survived.

Conclusions

S.m. infections in paediatric patients are often polymicrobial, *S.m.* being mostly associated to anaerobic bacteria. They usually require both antibiotic therapy and surgical drainage.The outcome is generally favorable.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0389
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CHLAMYDIA TRACHOMATIS INFECTION IN INFANT UNDER 7 MONTHS

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Background

Chlamydia trachomatis (CT) is a well known agent of sexually transmitted infections, also involved in neonatal infections after mother-to-child transmission. CT is classically involved in conjunctivitis and pneumonia in young infants. Because the systematic screening during pregnancy, and the systematic treatment in newborn have been avoided, the aim of this study was to evaluate the morbidity of CTI.

Methods

We have screened all the children between 0 and 6 months that had positive sample for CT by PCR in our University Hospital between January 2000 and November 2015.

Results

In the study period, 11 cases have been diagnosed: 2 pneumonia, 2 cases of secondary bacterial infection in infants with RSV bronchiolitis, 1 dacryocystitis, 1 blepharitis, and 5 conjunctivitis. The mean age at diagnosis was 22 days. The sex ratio male/female was 0.83, fever was found in 2 patients, 6 patients were hospitalized, the mean duration of hospitalization was 7 days.

Conclusions

CTI in toddlers is rare but not exceptional. If these infections are not treated, ophthalmologic sequelae are possible. In our study, most of the children had ocular involvement. The pediatricians have to consider CTIin these situations, particularly in case of purulent discharge without identification of most common pathogens.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0390
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

DIFFERENTIAL DIAGNOSIS FOR HYPOTONIA WITH RESPIRATORY FAILURE AT ONE MONTH OLD, NOT SO SIMPLE.

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Title of Case(s)

Differential diagnosis for hypotonia with respiratory failure at one month old, not so simple.

Background

We reported the case of a one - month boy who was referred to Paediatric Intensive Care Unit (PICU) for hypotonia with respiratory failure during a seasonal epidemic of bronchiolitis.

Case Presentation Summary

Medical history: He had no past medical history. No abnormalities of behavior, tonus or growth were noticed in the first month. He had an exclusive breastfeeding.

Within 48 hours he developed hypotonia, amimia, thin cry, hypoventilation and diminution of voluntary mouvements, but with normal state of consciousness. He was admitted in (PICU) and treated with non invasive ventilation. He was intubated three days afer for a dysautonomic syndrome with severe bradycardia.

Assessment: Biological (ionogram, blood count, infectious investigation) and radiological cerebral sonography, cerebro-medullar MRI) were normal. Genetic investigations for congenital hypotonia was negative. The electro-neuro-myogram found a presynaptic neuromuscular bloc.

At day 14 a botulinum toxin B was found in the feces.

Treatment and outcome : The treatment was firstly symptomatic with enteral nutrition, and mechanical respiratory support. A specific treatment with anti-toxin equine immunoglobulin was proposed to alleviate the recovery at day 15. At day 16 he was extubated, at day 20 non invasive ventilation was stopped and he was discharged from the hospital at day 42.

Learning Points/Discussion

Botulism has to be considered as a differential diagnosis in neonates or infant's hypotonia. Early diagnosis gives the possibility of a specific treatment to reduce the time to recover from paralysis and to provide reassurance to the family for the prognosis.

ESP16-0163
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

FULMINANT ENDOPHTHALMITIS IN A CHILD CAUSED BY NEISSERIA MENINGITIDIS TYPE C DETECTED BY SPECIFIC DNA

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Title of Case(s)

Fulminant endophthalmitis caused by *Neisseria meningitidis* **type C detected by moleculargenetic techniques**

Background

Neisseria meningitidis infections very rarely cause the sequence of conjunctivitis, uveitis and endophthalmitis without meningitis. Diagnosis of the local ocular infection is difficult, thus performance of moleculargenetic techniques should be routinely performed. The description of a local *Neisseria menigitidis* eye infection with a long protracted course in a previously vaccinated otherwise seemingly healthy child was not been reported so far.

Case Presentation Summary

A healthy 4 ½ vear old girl developed feverish left conjunctivitis treated with ofloxacin. Later, uveitis associated with juvenile idiopathic arthritis was suspected and therapy with steroids initiated.
Due to increased infiltration and increased intraocular pressure (60 mmHg) the child was referred to our institution at the 29th doi. In anterior chamber and vitreous tap aspiration no bacterial growth, no HSV-, VZV- or CMV-DNA and no signs for malignancies was detected. Antiviral and antibiotic therapy was applied locally and systemically. Due to suspected malignancy and complete loss of eye function, enucleation was performed.
Meanwhile, 16s rDNA-sequencing detected *Neisseria meningitides* serotype C, PorA-sequence type 5,2, FetA-sequence type 3-3 sequences. The child was previously vaccinated with a conjugated Neisseria meningitis serogroup C vaccine (Meningitec®). Retrospectively, serum probes revealed highly protective titers of antibody against *Neisseria meningitides*.

Learning Points/Discussion

Rarely, *Neisseria meningitidis* can cause destructive endophthalmitis, which mimics autoimmune uveitis. CD147, also found on eye endothelium, is crucial for *Neisseria* species infection of the CNS. This might explain the tropism to the two organs. Moleculargenetic methods are crucial for the diagnosis of endophthalmitis and should be performed in patients with suspected bacterial endophthalmitis.

Although systemic infection was prevented in the previously vaccinated child, restricted infection to the *immune* privileged eye did occur.

ESP16-0775
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

MENINGOCOCCAL SEPTIC ARTHRITIS

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Title of Case(s)

Meningococcal Septic Arthritis

Background

Bone and joint infections (BJI) have an estimated incidence of 5-12 cases per 100,000 children per year. The development of molecular diagnostics had improved microbiological diagnosis of septic arthritis, but many remain without a diagnosis. *Niesseria Meningitidis* has been described as an infrequent cause of BJI. There has been a recent increase of meningococcal W135 in England, not yet seen in Northern Ireland. We present 3 cases and a short literature review.

Case Presentation Summary

Child A

A previously well 5 month old presented with left ankle septic arthritis. Investigations showed a raised CRP and culture of joint aspirate was negative, but PCR was positive for *N. Meningitidis B*. He was treated with IV cefuroxime, switched to IV ceftriaxone to complete 4 weeks treatment.

Child B

A fully immunised, previously well 5 year old presented with right hip septic arthritis. Investigations revealed a raised CRP and joint effusion. Culture of synovial fluid showed *N. Meningitidis C*. He received 2 weeks of IV ceftriaxone and 1 week oral ciprofloxacin. A booster meningococcal vaccination was given.

Child C

A fully immunised, previously well 3 year old presented with left ankle septic arthritis. Investigations showed a raised CRP and joint effusion. Culture of joint fluid

confirmed a diagnosis of N. *Meningitidis W135.* He was treated with one week IV cefuroxime and switched to orals for total 3 weeks.

All 3 children recovered well from their illness, with no severe complications and had normal complement. CRP levels normalised by day 3-5.

Learning Points/Discussion

Increase the awareness of meningococcal septic arthritis.

Increase awareness of benefit of molecular diagnostics.

Increase awareness of spectrum of meningococcal disease, highlighting that children with meningococcal septic arthritis are clinically stable.

ESP16-0195
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

NOSOCOMIAL ACQUIRED PSEUDOMONAS STUTZERI BACTEREMIA IN A CHILD: CASE REPORT

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Title of Case(s)

Nosocomial Acquired *Pseudomonas stutzeri* Bacteremia in a Child: Case Report

Background

Pseudomonas stutzeri is a non-fermentative, gram-negative aerobic rod that rarely causes infections in immunocompetant humans. This microorganism is a saprophyte found in soil, water and hospital environments. Infections with *P.stutzeri* mostly considered as a contaminant however various infections have been described in literature. In here, we described an infant with bacteremia due to *P.stutzeri* who have been hospitalized with the diagnosis of bronchiolitis.

Case Presentation Summary

Afour-month-girl who admitted to the pediatric emergency room with the compliants of rhinorrhea, cough, tachypnea and fever for two days. Chest radiograph showed hyperinflation. Respiratory syncytial virus (RSV) antigen test was positive in nasopharyngeal aspirate. The patient was diagnosed as RSV bronchiolitis and hospitalized for supportive care. On the 8th day of admission, she had fever and worsening clinical condition. The laboratory results showed a white blood cell (WBC) count of 16200/mm^3, hemoglobin level of 11g/dl, platelet count of 804000/ mm3 and C-reactive protein levels of 3.83 mg/L (0-3 mg/L). Blood and urine cultures were obtained and empirical antibiotic therapy with piperacillin-tazobactam was started. Culture of the blood yielded *P.stutzeri* which was susceptible to piperacillin-tazobactam on antibiogram test. Control blood culture remained sterile and the infant was treated for 14 days after negative culture. The child was discharged without any sequele.

Learning Points/Discussion

Even *P.stutzeri* is mostly considered as saprophyte and a rare cause of infections, it should be kept in mind as a potential pathogen especially in patients with hospitalization history.

ESP16-0267
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

BRAIN ABSCESS DUE TO STREPTOCOCCUS INTERMEDIUS SECONDARY TO TETRALOGY OF FALLOT IN A CHILD: A CASE REPORT

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Title of Case(s)

BRAIN ABSCESS DUE TO *STREPTOCOCCUS INTERMEDIUS* SECONDARY TO TETRALOGY OF FALLOT IN A CHILD: A CASE REPORT

Background

Brain abscess is a focal suppurative collection in brain parenchyma which can ocur in children of any age. It may arise as a complication of congenital heart disease (especially tetralogy of Fallot), meningitis, mastoiditis, sinusitis, orbital cellulitis, dental infections, trauma and surgery. *Streptococcus intermedius* belongs to viridans streptococci that are isolated from human oral and gastrointestinal flora. However, they can cause severe infections such as abscesses.

Case Presentation Summary

In here, we describe a Syrian ten-year-old boy with tetralogy of Fallot who developed brain abscess with *S.intermedius.* He was admitted to emergency room with complaints of headache, vomiting, decreased level of consciousness and imbalance on walking. The symptom of headache was present for ten days. On physical examination, he had subfebrile fever, clubbing of fingers, perioral cyanosis, cyanotic mucous membrane of lips, tongue and gingiva, and on cardiac examination, 3/6 pansystolic murmur at the left mid to upper sternal region. Laboratory tests showed a white blood cell of 35400/mm^3 , C-reactive protein of 187mg/L, erythrocyte sedimentation rate of 23 mm/h and normal biochemistry values. His cranial Magnetic Resonance Imaging (MRI) examination showed 4*2.5 cm abscess formation on the right occipitoparietal region. Abscess culture yielded *S.intermedius.* He was successfully treated with surgical drainage and antibiotic therapy.

Learning Points/Discussion

Normal flora of the mouth and upper airways, such as *S.intermedius* can be pathogenic in underlying facilitator circumstances such as fallot tetralogy.

ESP16-0304
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

BRAIN ABSCESS IN A TWO-MONTH-OLD INFANT: A CASE REPORT

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Title of Case(s)

BRAIN ABSCESS IN A TWO-MONTH-OLD INFANT: A CASE REPORT

Background

Brain abscess is an uncommon but critical life-threatening infection in children. It may ocur as a result of parameningeal infections, congenital hearth disease, trauma and immunocompromised status. However in some circumstances, the origin cannot be identified.

Case Presentation Summary

In here, we describe a two-month-old boy with brain abscess in whom the underlying risk factor was not well-defined. He was admitted to emergency room with fever, irritability and poor feeding for the last two days. He looked discomfort with an axillary temperature of 38℃. On physical examination, his anterior fontanel was pulsatile and excess bulging. The patient was in a normal sinus rhythm at a rate of 130 without murmurs. The patient was hospitalized and quickly diagnostic tests were planned. Laboratory tests showed a white blood cell 18800/mm^3, C-reactive protein of 94mg/L (normal range 0-3), and normal biochemistry values. Blood and urine cultures were obtained. Lumbar puncture was planned, because of excess fontanel bulging cranial ultrasonography was performed and 36*33 mm cystic formulation was seen. The patient was consulted to neurosurgery and magnetic resonance imaging (MRI) was planned. His cranial MRI examination showed 43*32 mm abscess formation on the left frontale lobe. Surgical abscess drainage was applied however abscess cultures remained sterile. Blood cultures yielded two times meticillin resistant coagulase negative staphylococcus. Ecocardiography showed patent foramen ovale. Clinical improvement was observed after surgery and the third day of the antibiotic therapy. He still receives antibiotic therapy.

Learning Points/Discussion

In conclusion, brain abscess can be seen in all age groups in children. Although it is a rare infection, it should be kept in mind in children with unknown source of fever.

ESP16-0866
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CHARACTERISTICS AND FINAL DIAGNOSIS OF PATIENT WITH PROLONGED FEVER IN PEDIATRIC WARD DR SOETOMO HOSPITAL SURABAYA

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Background

The studies examined etiologies and final diagnosis children with prolonged fever have been published. There was no data in Soetomo hospital reviewing the causes and outcome patient with prolonged fever in our pediatric ward. The purpose of this study is to review characteristic, etiologies, laboratory data and final diagnosis children with prolonged fever.

Methods

We conducted cross sectional study of medical review of children with fever persisting longer than10 days between 2011 and 2015. We evaluated clinical presentation, age, sex, nutritional state, the duration of fever, etiologies and laboratory data.

Results

There were 215 children hospitalized caused by prolonged fever during this period and 40 children were included in this study. The boys were 55% more than the gjrls, with median age was 5,9 (range 4 month-18 years) and median length of hospitalization 8.0 (range 2-32 days). Most of patient were good nutrition (65%). Duration of fever was 7-14 days in 72.5% patients, 20% from 15-30 days and 5% patients from 30-60 days. The most of final diagnosis were urinary tract infection (35%) followed by typhoid fever (30%). The comorbidities conditions is cough (20/40) and diarrhea (14/40). Among 31 children who performed culture, blood and urine culture were positive only in 3/31 and 8/31 patient respectively.

Conclusions

The most common cause of prolonged fever in children remain infection. Urinary tract infection and typhoid fever were the most final diagnosis. The comorbidities symptoms were cough and diarrhea

ESP16-0379
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

ISCHAEMIC STROKE COMPLICATING CENTRAL SKULL BASE OSTEOMYELITIS IN A 2 YEAR OLD BOY – CASE REPORT

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Title of Case(s)

ISCHAEMIC STROKE COMPLICATING CENTRAL SKULL BASE OSTEOMYELITIS IN A 2 YEAR OLD BOY

Background

Skull base osteomyelitis (SBO) is rare in children, presenting non-specifically. Central SBO is characterised by sphenoid bone osteomyelitis, often as a result of infection extending through the Haversian canals from paranasal infection. Cerebrovascular complications of central SBO are usually asymptomatic. We describe the first case of symptomatic ischaemic stroke secondary to SBO in a child.

Case Presentation Summary

A 2-year old boy presented with fever, vomiting and sore throat. After 4 days managing presumed bacterial tonsillitis, he developed profound neck stiffness, and features of systemic sepsis - he underwent a full septic screen and ceftriaxone was commenced. CSF WBC count: 267/microlitre; blood and CSF cultures were negative. The following day he developed a left hemiplegia and homonymous hemianopia. MRI showed ischaemic infarction of the right middle cerebral artery (MCA) distribution and clivus osteomyelitis (Figure). Antibiotics were changed to meropenem and clindamycin. Dexamethasone and aspirin were added. He developed focal seizures and a right hemiparesis. Repeat MRI confirmed complicated central SBO from otomastoiditis with MCA infarction, bilateral cavernous sinus thrombophlebitis and suprasellar empyema. Prior to discharge clopidogrel, IVIG and methylprednisolone were commenced to prevent further complications. At 12 months, following 6 months of antibiotics, he had mild left hemiplegia, homonymous hemianopia and hearing loss, was independently mobile with normal developmental milestones otherwise.

Learning Points/Discussion

This case highlights the management of central SBO and illustrates cerebrovascular complications previously undescribed in children. Profound neck stiffness invariably features as a key symptom in this and other published cases and consideration of SBO and need for MRI should be considered. Empirical antibiotic therapy should be broad as a wide range of pathogens have been described causing SBO.

ESP16-0329
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CARRIAGE OF NEISSERIA MENINGITIDIS AMONG HIGH SCHOOL STUDENTS IN KOREA

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Background

Neisseria meningitidis commonly colonizes the oropharyngeal mucosa. Carriage rate is age dependent and very common in adolescents and young adults. To estimate the oropharyngeal carriage rate of meningococcus among Korean healthy adolescents and the relationship of several characteristics of the population to the carrier state, this study was performed.

Methods

A survey of oropharyngeal carriage of *Neisseria meningitidis* was designed as cross-serctional study at nine high schools located in Gyung-gi province, Korea from April 2015 to May 2015. Students in the first grade of high school were recruited. The students answered to a short questionnaire assessing risk factors for carriage and were swabbed at their posterior pharyngeal wall. The oropharyngeal samples were cultured on selective medium for meningococcus. After incubation, colonies resembling meningococci were identified using the technique of matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) by using the Vitek MS system (bioMérieux, France).

Results

A total of 1,460 students was enrolled. *Neisseria meningitidis* was identified from 49 (3.4%) of 1,460 swabs. Active current smokers showed the significantly higher carriage rates (10/122, 8.2%) than those of non-smokers (39/1338, 2.91%). Sex was also significant factor, higher rate (40/902. 4.43%) in male than in female (9/558, 1.61%). Although not significant, subjects who had history of frequent attendance at crowded place within last week showed higher carriage rate. However, passive smoking, dormitory residents and current upper respiratory infection had little or no effects.

Conclusions

Although importance of evaluation of meningococcal carriage in understanding the epidemiology and biology of meningococcal disease, there are only few data in Korea. This study could provide helpful information for meningococcal epidemiology and their changes after vaccine introduction.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0026
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

UNUSUAL CASE OF HERPES ZOSTER OPHTHALMICUS IN A HEALTHY 18-MONTH TODDLER

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Title of Case(s)

UNUSUAL CASE OF HERPES ZOSTER OPHTHALMICUS IN A HEALTHY 18-MONTH TODDLER

Background

Herpes zoster (HZ), caused by reactivation of varicella-zoster virus (VZV), is uncommon in infancy. Even more is rare HZ ophthalmicus, defined as HZ of the ophthalmic branch of the fifth cranial nerve.

We present an unusual case of HZ ophthalmicus in an immunocompetent toddler.

Case Presentation Summary

A previously healthy 18-month old boy was admitted to our department because of a 3-day history of rash on forehead and drowsiness, but afebrile. His mother contracted chickenpox in the late pregnancy.

On presentation the child was afebrile with vesicles on the right side of the forehead and on the nasal tip. The right bulbar conjunctiva was injected with clear discharge. The remainder of examination was without abnormalities.

The consultant ophthalmologist revealed subconjunctival hemorrhages but without corneal scarring. The child was commenced on intravenous acyclovir, acyclovir eye drops and Cetriaxone.

Three days later a vesicular rash appeared on the trunk and limbs, accompanied by a mild temperature. In a week the rash crusted over and the child was discharged greatly improved.

Routine laboratory tests were without abnormalities as was cerebrospinal fluid. Serology was VZV IgG (+) and VZV IgM (-).

No complications were present during the follow-up.

This case was very likely infected with VZV in utero**.** Children with immunosuppression or those with varicella acquired intrauterine have an increased risk of developing HZ.

Learning Points/Discussion

This case has emphasized the importance of early clinical suspicion of this rare disease in infancy resulting in timely acyclovir treatment to prevent any sight-threatening sequelae.

ESP16-0273
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PRIMARY PNEUMOCOCCAL PERITONITIS IN AN OTHERWISE HEALTHY 2-MONTH-OLD CHILD

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Title of Case(s)

Primary pneumococcal peritonitis in an otherwise healthy 2-month-old child

Background

Spontaneous bacterial peritonitis (SBP) is rare in healthy children accounting less than 2% of acute abdomens. Medical conditions resulting in hypogammaglobulinemia such as chronic liver disease and nephrotic syndrome and other immunodeficient states renders a child more vulnerable to SBP.

Case Presentation Summary

A two-month-old boy was admitted with a 2-day history of malaise, crying and fever.

On clinical examination he was circulatory unstable with capillary refilling at four seconds and a pulse of 178 beats per minute. His skin was pale and mottled. The temperature was 39.2°C. He was irritable and had a tender and distended abdomen.

Laboratory results revealed elevated infectious counts C-reactive protein 203 mg/l (normal <8), leukocyte count 13.6 x109/l (6.0-16.3x109/l). Albumin was normal which ruled out nephrotic syndrome. Lumbar puncture and urine culture were negative.

He was fluid resuscitated, and empirically given intravenous antibiotics.

Abdominal X-ray revealed paralytic ileus. Ultrasound scan of the abdomen showed reduced peristalsis and dilated small bowel loops. The following colon enema showed normal passage. Exploratory laparotomy revealed pus and fibrin coating the peritoneum. The appendix was macroscopically normal.

A presumptive diagnosis of primary peritonitis was made, and was confirmed histologically.

Peritoneal culture was negative, but preoperative antibiotic blood culture yielded Streptococcus pneumonia. The patient improved clinically, and he was discharged after ten days. His immunological status and opsonizing capacity was tested and found normal.

Learning Points/Discussion

The exact pathogenesis of SBP still remains to be elucidated.
Primary peritonitis should be considered in all infants presenting with acute abdomens.

Underlying medical conditions should be suspected and ruled out during follow up, particularly in males.

ESP16-1011
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PYOMYOSITIS IN CHILDREN

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Title of Case(s)

Pyomyositis in Children

Background

The limping and febrile child is a common paediatric presentation. Septic arthritis, osteomyelitis and transient synovitis are amongst the differential diagnoses. We present a case series from two paediatric specialist centres where persistent clinical signs, pyrexia and raised inflammatory markers led to MRI imaging of the affected area with unexpected results.

Case Presentation Summary

Case	Age (years)	Presenting features	CRP	MRI findings	Microbiology	Treatment
1	5	Left sided limp and pain	94	Left obturator /quadriceps abscess	**Blood culture:** Staphylococcus Aureus	IV: 9 days flucoxacillin Oral: 4 weeks Augmentin
2	5	Left hip pain, fever	186	Left obturator abscess	No growth	IV: 4 days flucoxacillin Oral: 4 weeks Augmentin
3	1	Pain, swelling right thigh, post chicken pox	77	Quadriceps abscess	**Aspirate:** Group A Strep	IV: 7 days cephalosporin Oral 2 weeks clindamycin
4	13	Right iliac fossa pain , limp, post appendicectomy	350	Psoas abscess	No growth	IV: cephalosporin 7 days Oral 3 weeks Augmentin

Case	Age (years)	Presenting features	CRP	MRI findings	Microbiology	Treatment
5	14	Right sided limp, swollen right hip joint, restricted movement, fever	74	Abscess in quadriceps, iliacus extending to psoas.	**Aspirate:** Clostridium bolteae and clostridium symbiosum	IV: 10 days cefuroxime and oral high dose clindamycin (currently on treatment)

Learning Points/Discussion

Pyomyositis or muscle abscesses are an uncommon problem in paediatrics. These cases illustrate the need to consider the diagnosis when the clinical picture is not typical of septic arthritis or osteomyelitis.

The duration of treatment is not well defined from the literature. Our cases had antibiotic treatment courses similar to osteo-articular infections. Randomised controlled studies are needed to see if an early switch to oral antibiotics and a shorter course is as effective.

ESP16-0620
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

SEPTIC SHOCK BY NECROTIZING FASCIITIS IN A THRRE YEARS OLD CHILD
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Title of Case(s)

Septic Shock by necrotizing Fasciitis in a 3 years old child

Background

The necrotizing fasciitis (NF) is rare in children. The incidence is 0.08/100000 hospitaliceted children.Usually, the NF is monomicrobial in paediatric age, with group A Streptococci as the main pathogenic agent.

We present a shok septic case due to NF

Case Presentation Summary

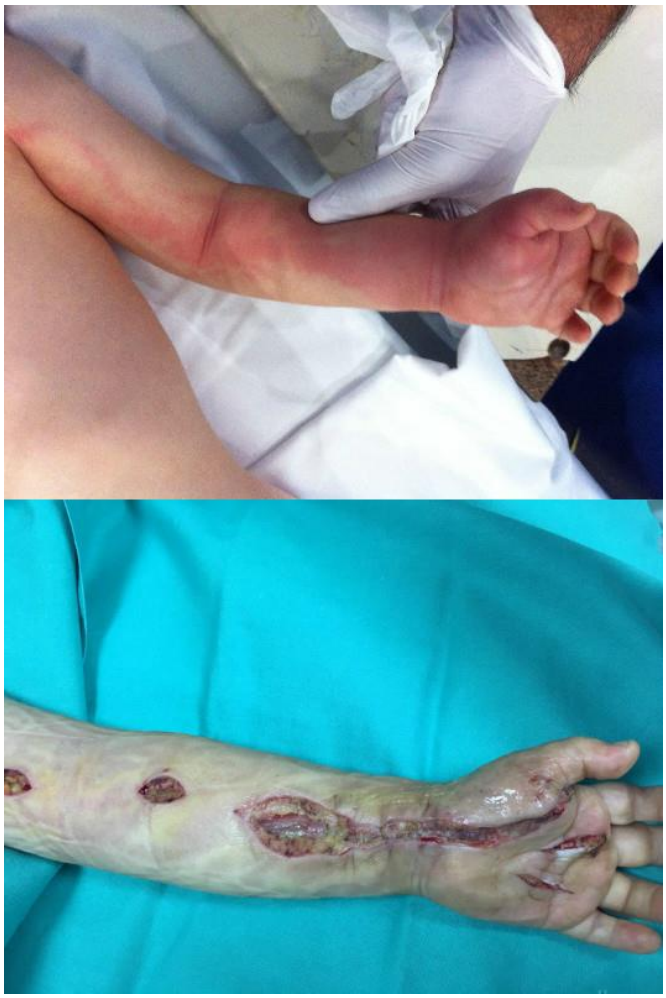
Three years old health child is referred to emergency because he´s fever (40ºC) and swelling on upper left member for two hours. Examination: skin paleness, regular aspect. Tension swelling on left hand until underarm. Warm, flushed and painful soft tissues. Pustule lesion on the base of thumb.

During exploration, the patient shows quick deterioration with affected hemodynamic system and hypoperfusion signs (tachycardia,weak pulse and disturbance of consciousness). We place femoral venous catheter, start expansion with 500ml of saline solution(SS). Antibiotic treatment with ceftriaxone, vancomycin and clindamycin. The traumatology examinates the patient and suggest urgent surgery

Orthopaedic surgeon appreciates pallor muscle and suffering signs on tissues compatible with NF, therefore they made fasciotomy, debridement necrotic tissues and purging with SS and H2O2.

Analyses: 42000 leukocytes, procalcitonin 36ng/ml; CPR 122 mg/L. Blood culture negative. Cutaneous biopsy: S.pyogenes sensitive to penicilin, clindamycin, erythromycin and cefotaxime

Evolution: three days intubated. Hemodynamic: dopamine +adrenaline (60 and 20 hours). Hematological: RBC and plasma transfusion because of coagulophaty. Infection: peniciline and clindamycine. Maximum leukocytes: 50000,CPR 261. Daily, orthopaedic surgeon performing cure and close the incisions progressively. The complete surgical reconstruction is 10 days after.



Learning Points/Discussion

Early debridement is the mainstay of treatment in order to save life. Medical therapy includes antibiotic to cover gram-positive, negative, and anaerobic bacteria until results of cultives are obtained, as penicillin or cephalosporin, aminoglycoside and clindamycin. Our case progressed well thanks to quick surgery and appropriate antibiotic´s choice.

ESP16-0817
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

IT'S NOT OVER UNTIL IT'S OVER': MANAGING PAEDIATRIC POST-EBOLA SEQUELAE - WHAT DO WE KNOW AND WHERE FROM HERE?

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Background and Objective

As the number of acute cases of Ebola Virus Disease has waned during the West African Ebola epidemic, the appearance of post-Ebola sequelae in Ebola survivors has become increasingly apparent. Many of these features cause significant and sometimes permanent disability. Details in children are scarce, but reports of permanent visual loss and dense cataracts are increasing. An urgent guideline for the management of these sequelae was developed by WHO, 'Clinical Care for Survivors of Ebola Virus Disease' – WHO Interim Guidance, to ensure consistent practice as further evidence becomes available.

Methods

A literature review was performed to identify the limited number of papers on post-Ebola sequelae and expert opinion sought from colleagues with experience of managing paediatric post-viral inflammatory complications. Guidelines were developed to encompass disease in multiple organ systems but with a focus on musculoskeletal and ocular sequelae. Development of the paediatric component of the guidelines was complicated by an absence of clinical data indicating the types and incidence of sequelae suffered by child Ebola survivors.

Learning Points Discussion

A consistent approach to Ebola survivors with urgent early intervention at the development of sequelae is essential for the prevention of long term debilitating complications, particularly in relation to ocular sequelae. The underlying pathophysiology of the sequelae remains unclear, with concerns related to viral persistence in survivors the use of immune suppressants for inflammatory processes is recommended with hesitation. With over 16,000 Ebola survivors in West Africa and limited knowledge of post-Ebola sequelae, research is continuing. With 1368 child Ebola survivors it is essential these children access adequate medical services, but psychosocial input is also vital as many are part of the 22,858 children who have lost either one or both parents to Ebola.

ESP16-0511
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

THE KINGELLA KINGAE OF HEARTS

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Title of Case(s)

The Kingella Kingae of Hearts

Background

Kingella kingae is an emerging bone pathogen; will we now also see an increase in the incidence of cardiac associated infections?

Case Presentation Summary

An 18 month old girl presented to A&E with a pyrexia for 10 days. Initial history and examination were unremarkable apart from a persistent tachycardia. There were no murmurs or signs of Kawasaki's disease. Blood analysis showed a CRP of 57 and Neutrophilia of 21.8. Differential diagnoses included sepsis or viral illness. She was admitted and commenced on IV Ceftriaxone. 24 hours post admission review revealed she was hypothermic (<36◦c) but alert, cardiovascularly stable with an unremarkable examination bar a mild tachycardia of ~155. Thirty minutes later she collapsed. Following fluid resuscitation she was noted to have a murmur consistent with aortic regurgitation, hepatomegaly and a wide pulse pressure from an inserted arterial line. She was retrieved to a PICU unit and echocardiography revealed an unknown bicuspid aortic valve that was severely regurgitant secondary to a vegetation on the right coronary cusp. The vegetation was removed in theatre and a peri-valvular abscess cavity was found and repaired. Kingella Kingae was identified by PCR from valvular tissue. From valvuloplasty she recieved 4 weeks of IV ceftriaxone via a PICC line. She remained well and had a Ross procedure 3 months post cessation of antibiotics. She currently has good cardiac function and is developing normally.

Learning Points/Discussion

· Consider SBE in prolonged fever in childhood with minimal clinical signs or no known risk factors.

· Hypothermia is a well-recognised sign of sepsis in neonates but can also be a presenting feature in older children.

· Following acute collapse a widened pulse pressure should raise the possibility of aortic regurgitation.

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ESP16-0579
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CLINICAL CHARACTERISTICS AND MANAGEMENT OF ACUTE HAEMATOGENOUS SEPTIC ARTHRITIS AND OSTEOMYELITIS IN A SINGLE CENTRE OVER 10 YEARS

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Background

Knowledge on optimal management of osteomyelitis (OM) and septic arthritis (SA) has improved over the last decade. The aim of this audit was to review hospital practice for the management of OM/SA in the view of recent evidence.

Methods

Retrospective cohort study (2005-2014). ICD-10 discharge codes for OM and/or SA were searched and verified. Patients with symptoms for >2 weeks, preceding penetrating wound or prior surgical intervention were excluded.

Results

A total of 96 (45 OM, 42 SA and 9 OM+SA) children were included in the final analysis (Table). Median duration of symptoms prior to admission was longer in OM than SA patients 4 (IQR:3-7) and 2 (IQR:1-4) days, respectively, p = 0.003).

In OM-patients bone/periost changes were detected in 30/32 (94%) by MRI, 9/28 (32%) by sonography and 9/31 (29%) by radiography. In SA-patients joint effusion/synovial swelling were detected in 31/34 (91%) by sonography, 7/9 (78%) by MRI and 13/28 (46%) by radiography.

In 56/96 (58%) a pathogen was detected: 35 *S.aureus*, 7 *S.pyogenes*, 5 *S.pneumoniae* and 9 other (including 1 *K.kingae*).In OM- and SA-patients a pathogen was identified by tissue culture/PCR in 16/45 (36%) and 17/42 (41%); blood culture 13/45 (29%) and 4/42 (10%); and by both methods in 2/45 (4%) and 3/42 (7%), respectively.

Median total duration of treatment was 35 (IQR:22-42) for OM and 42 (IQR:34-43) days for SA. Median duration of intravenous treatment was 10 (IQR:7-14) for OM and 13 (IQR:9-14) days for SA.

	OM n = 45	SA n = 42	OM + SA n = 9	Total n = 96	p-value OM vs. SA
Male (%)	26 (58)	24 (57)	5 (56)	55 (57)	ns
Median age (IQR) in years	10 (3.9; 12)	3.7 (1.2; 8.8)	8.7 (2.5; 10.8)	7.5 (2.3; 10.5)	< 0.01
Laboratory values on admission					
Median WBC, (IQR), x 10^9/l	9.4 (6.7; 12.6)	12.3 (10.1; 17.0)	12.9 (7.5; 13.8)	11.0 (8.2; 14.3)	0.01
Median CRP, (IQR), mg/l	24.5 (5.2; 66.4)	60.5 (32.8; 98.3)	69.0 (36.0; 96.5)	46.0 (20.0; 83.0)	< 0.01
Median ESR, (IQR), mm/h	39.0* (23.0; 52.0)	52.0* (23.3; 77.8)	35.0* (26.0; 50.0)	40.0* (24.0; 62.0)	ns
Localisation of infection					
upper limb (%)	6 (13)	4 (10)	1 (11)	11 (11)	ns
lower limb (%)	39 (87)	38 (90)	8 (89)	85 (89)	ns

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IQR, interquartile range; ns, not significant; OM, osteomyelitis; SA, septic arthritis ; WBC, white blood cells;

*n in OM, SA and OM + SA respectively: 34, 34, 7.

Conclusions

Diagnosis was made within 5 days of complaint in 75% of patients. The best imaging modalities in both conditions were MRI and sonography. Improved pathogen detection and shorter treatment duration for patients with SA should be the focus for future patients.

ESP16-0782
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PEDIATRIC INVASIVE PNEUMOCOCCAL DISEASE IN PORTUGAL IS STILL DOMINATED BY ISOLATES EXPRESSING PCV13 SEROTYPES

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Background

While pneumococcalconjugate vaccines (PCVs) have been available in Portugal these were not included in the National Immunization Plan (NIP) until June 2015. We aimed to characterize pneumococci causing invasive disease (IPD) prior to the PCV13 inclusion in the NIP.

Methods

Between July 2012 and June 2015, a total of 183 *Streptococcus pneumoniae* isolates recovered from children (<18 years) diagnosed with IPD in 61 hospital laboratories and pediatric departments located throughout Portugal were characterized by serotyping and antimicrobial susceptibility testing.

Results

Overall, 36 different capsular types, as well as non-typeable isolates were detected. The number of isolates recovered in each epidemiological year was constant and similar to that of 2011/2012. Although the majority of isolates expressed capsular types included in the PCVs, serotypes not included in any PCV formulation accounted for a significant fraction of the isolates (46%, n=85). Among these, serotypes 10A, 12B and 24F were the most frequent, represented by 10 isolates each. Regarding PCV serotypes, isolates expressing serotype 14 (n=22), serotype 1 (n=17), serotype 7F(n=13) and serotypes 3 and 6B (n=11 each) were the most frequently found. Overall, 10% of the isolates were penicillin non-susceptible. Resistance to erythromycin was expressed by 9% of the isolates and simultaneous expression of erythromycin resistance and penicillin non-susceptibility was found in 13.5% of the isolates. The majority of isolates non-susceptible to penicillin or erythromycin expressed serotypes included in the 13-valent PCV.

Conclusions

PCV13 serotypes are still expressed by a significant proportion of isolates responsible for IPD. The data presented here emphasizes the potential role of universal vaccination in diminishing pediatric IPD.

ESP16-0899
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

OTOGENIC SIGMOID SINUS THROMBOSIS AS A COMPLICATION OF ACUTE MASTOIDITIS WITH NO NEUROLOGICAL SIGNS

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Title of Case(s)

Otogenic sigmoid sinus thrombosis with no neurological signs

Background

Two cases of sigmoid sinus thrombosis (SST), a rare but potentially life-threatening complication of acute mastoiditis, are reported.

Case Presentation Summary

Case 1: A 3-year old boy was referred with a two day history of left otalgia; fever and retroauricular erythema developed later. Physical examination showed acute otitis media, protrusion of the pinna, and retroauricular erythema. White blood cell (WBC) count was 29.5 $x10^9$ cells/ml, C-reactive protein (CRP) 220 mg/l. *Streptococcus pneumoniae* was isolated. Treatment with cefotaxime and cloxacillin was started. Forty hours later symptoms persisted; there were no neurologic deficits. A CT scan showed mastoiditis and SST. Antibiotics were continued and anticoagulant therapy was started. No surgery was performed. There was complete recovery without sequelae.

Case 2: A 5-year old girl presented with a 3-day history of fever and otalgia. On day two she was started on oral co-amoxiclav which she vomited. Upon physical examination, her head was deviated to the left and light pressure on the mastoid process elicited severe pain but there was no erythema, warmth or swelling. Otoscopy showed acute otitis media. WBC 14.7 $x10^9$ cells/ml, CRP 138.1 mg/L. Cultures negative. Treatment with IV co-amoxiclav was started. On day 3 she had no fever or neurologic deficits but otalgia and retroauricular pain and tenderness persisted, so a CT scan was performed showing mastoiditis and SST. She was treated with antibiotics and anticoagulant therapy. No surgery was performed. She recovered completely without sequelae.

Learning Points/Discussion

SST is a rare but serious complication of acute mastoiditis. It can occur in the absence of neurologic signs or symptoms so a high index of suspicion is necessary. Medical treatment can be sufficient in selected cases.

ESP16-0189
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PERTUSSIS COMPLICATION IN CHILDREN 0-24 MONTHS OF AGE

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Background

Incidence of pertussis in infants and children still increases around the world. Pertussis complications are caused by respiratory and systemic effects of pertussis toxin, and hypoxemia associated with paroxysmal cough.

Methods

93 unvaccinated children aged 1-24 mon. were under observation. All patients were treated in the Lviv Regional Infectious Diseases Hospital during 2012-2014 yy. Chest radiograph, CBC, sputum culture, cytokines (IL1β, IL2, IL10, INF-γ) levels, sIgA levels were done for all patients.

Results

93 unvaccinated children aged 1-24 mon. were under observation. All patients were treated in the Lviv Regional Infectious Diseases Hospital during 2012-2014 yy. The pertussis complications were observed in 78 patients (83,87%). The most common complications pertussis were apnea (57,69% of patients), pneumonia (34,61%), bronchitis (64,10%) seizures (2,56%), and death (1,28%). A probable correlation has been established between the development of pertussis complications and duration from the onset of the disease to the time of cough occurrence with reprises (r=0,34, p<0,05), the amount of acute respiratory viral infections before diseases (r=0,26 p<0,05), the absolute number of lymphocytes in the peripheral blood (r=0,57 p<0,05), the absolute number of CD3+ T lymphocytes (r=-0,19, p<0,05), the absolute number of CD8+T lymphocytes (r=0,35, p<0,05), and the levels of secretory IgA (r=-0,14, p<0,05). The development of complications of pertussis contributes to incomplete immune response, which is manifested significant (in 1,6-3,4 times) increased levels of proinflammatory cytokines - IL1β, IL2 and decreased levels of γ-interferon (in 5,98-7,90 times) with normal levels of anti-inflammatory cytokines -IL10.

Conclusions

In children aged 1-24 months with complicated pertussis course the mixed Th1/Th2 type immune response developed and the development of pertussis anergy at the end of the third week of the spasmodic cough period has been confirmed.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0025
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

AGE AS A RISK FACTOR FOR ADVERSE OUTCOME OF BACTERIAL MENINGITIS IN CHILDREN

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Background

Since neurologic complications (NC) of bacterial meningitis (BM) in children are encountered frequently, the aim of this study was to analyze the risk for adverse outcome of BM in children depending on group ages.

Methods

This prospective study enrolled 77 children >1 month until 16 years of age, treated for BM during years 2009 – 2010. Children were categorized into specific age groups: <1 year old (n=28), >1-6 years of age (n=29) and >6-16 years of age (n=20). Data were analyzed using Stata 7.1 and the SPSS 13.

Results

Of the 77 children treated for BM, 33 cases manifested acute NC (43%) while two patients died (2.6%). The etiology was proven in 57 cases (74%). The NC observed were: subdural effusion (28.6%), recurrent seizures (7.8%), hemiparesis (6.5%), intracerebral hemorrhage (3.9%), cerebritis (3.9%), facial nerve palsy (3.9%), hydrocephalus (2.6%), and single cases of subdural hematoma, cerebral abscess, subdural empyema, and purulent ventriculitis (1.3%). The highest incidence of NC was observed in children < 12 months of age (20/28; 71%), [RR 2.69 (1.62 - 4.59) (95% CI) ($p < 0.05$)]. Children under 12 months of age had for 4 times higher risk for developing NC [OR=4.09 (1.35<O.R<12.43)] compared to children from >1-6 and for 22.5 times had higher risk for developing NC compared to children >6-16 old [OR=22.5 (4.21<O.R<120.15)]. Children >1-6 years of age had for 5.5 times higher risk for developing NC [OR=5.5 (1.06<O.R<28.42)] compared to children >6-16 old. NC developed more frequently in patients who were infected with *S. pneumoniae* (6/8), *S.aureus* (3/5), Gram-negative bacilli (2/6), *N. meningitidis* (8/32), and *H. influenzae* (1/5).

Conclusions

Age< 12 months was identified as a significant risk factor predicting NC in children suffering from BM.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0603
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF CHILDREN ADMITTED WITH FEVER IN AN EMERGENCY DEPARTMENT WITH OR WITHOUT SEPSIS

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Background

Sepsis definition by Goldstein et al (2005) does not have clinical significance. We aimed to describe and compare the frequency of aetiological agents and topography of initial focus in patients with or without sepsis, to identify risk factors and to assess outcomes.

Methods

All patients aged ≤12 years with report of fever had clinical and demographic data on admission and evolution collected from medical charts, without knowledge of aetiology data, at a Paediatric Emergency Department, in Salvador, Brazil, in a 12-month period. Patients were classified as “with” or “without” sepsis according to Goldstein et al (2005)´s criteria.

Results

Of 254 patients, 120(47%) did and 134(53%) did not have sepsis. Patients with sepsis were older (2.8[1.1-5.3] *vs*. 1.3[0.6-2.9] years;p<0.0001) and had sickle cell disease more frequently (7.6% *vs.* 0.8%;p=0.007). By multiple logistic regression, age (OR[95%CI]:1.0005[1.0002-1.0008) and sickle cell disease (OR[95%CI]:8.8600[1.0938-71.7665) were independently associated with sepsis. The most frequent focuses were pneumonia(46%), diarrhoea(20%) and cellulitis/adenitis(13%). The frequency of these focuses did not differ when patients “with” or “without” sepsis were compared. Aetiology was established in 57(22.4%) patients, 32(26.7%) and 25 (18.7%) with or without sepsis respectively (p=0.1). Overall, *Staphylococcus aureus* infection was detected in 4(3.3%) patients with sepsis whereas none (0%) of the patients without sepsis had this infection (p=0.049). Four(3.4%) patients died in the sepsis subgroup whereas none died in the other subgroup (p=0.048).

Conclusions

Children with sepsis showed differences in age, comorbid (sickle cell disease) and *S. aureus* infection frequency upon admission and were more likely to die.

ESP16-0640
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

LATE-ONSET GROUP B STREPTOCCOCAL (SGB) INFECTIONS: EXPERIENCE IN A THIRD-LEVEL HOSPITAL

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Background

There is limited knowledge of the transmission mechanism involved in the late-onset SGB infections. We describe the epidemiological and clinical features of late-onset SGB infections and analyse the diagnostic and therapeutic measures taken in our Hospital.

Methods

7 to 90-day-old infants admitted to a tertiary-care hospital with positive SGB blood or CSF culture or high suspicion of SGB infection from January 2010 to December 2015.

Results

A total of 22 patients where registered with a median age of 29 days (IQR 22-50). Seventeen of them (77%) were born via vaginal delivery. Prematurity was observed in 7 (32%). In 6 (27%) women, the SGB vaginal-rectal colonisation (VRC) status prior to delivery was positive and in 2 unknown (18%). 60% of them where treated accordingly. Breast-feeding was present in 15 (68%) cases. The main diagnosis was sepsis (n=15, 68%), followed by meningitis (n=3, 14%), cellulitis-adenitis syndrome (n=3, 14%) and occult bacteremia (n=1, 5%). SGB VRC was repeated during admission in 16 (77%) cases, being positive in 10 (46%). Breast milk culture was done in 16 (77%) cases but only 1 was positive. Antibiotic decolonisation was done in all SGB positive mothers. Main empirical antibiotherapy was ampicillin + gentamicin (n=9, 41%), followed by ampicillin + cefotaxim (n=7, 32%). In 91% cases, SGB was grown in blood or CSF. Two patients died of septic shock.

Conclusions

In our series, prematurity was present in a third of the cases. Most patients did not have SGB colonization prior to delivery, but it was present in almost half of the mothers during the episode. It still unclear the role that decolonization of SGB positive mothers have, but it might be helpful to avoid future recurrences

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0645
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

MIMICKING PYELONEPHRITIS IN CHILDREN: NEVER LOSE SIGHT OF NEONATAL APPENDICITIS

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Title of Case(s)

MIMICKING PYELONEPHRITIS IN CHILDREN: NEVER LOSE SIGHT OF NEONATAL APPENDICITIS (NA).

Background

NA is an extremely rare condition often overlooked as a cause of acute abdomen and late identification can lead to higher mortality risk. Prognosis is closely related to urgent surgery and antibiotic treatment of infectious complications. We present a neonate with NA simulating a pyelonephritis.

Case Presentation Summary

A six-day-old girl presented with a 24-hour history of somnolence and refusal to be fed, followed by fever. Upon arrival, poor general condition, fever and tachycardia were noted. General blood count, urine and CSF analysis and subsequent cultures were taken, pointing to a fever without source with bacteremia (CRP 43 mg/L, Procalcitonin 8.21 ng/dL). Empirical antibiotic therapy with ampicillin and gentamicin and support measures were started. General condition improved 24 hours later. On day 3, physical examination showed indirect signs of abdominal pain and right hemi-abdominal guarding. *Escherichia coli* was isolated in blood and urine cultures. Bacteremic pyelonephritis by E. coli was the diagnosis at that moment, so gentamicin alone was continued. On day 4, there was a significant reduction in acute phase reactants. Ultrasounds displayed no signs of pyelonephritis or nephropathy. As fever kept spiking and CRP rose to 145 mg/dL on day 5, ultrasounds were repeated, showing peritonitis signs at abdominal right side. Antibiotics were shifted to piperacillin-tazobactam and urgent laparotomy was performed. Surgery revealed acute perforated appendicitis and purulent peritoneal fluid. After appendix removal, antibiotic was maintained, with improvement both clinically and analytically.

Learning Points/Discussion

NA might be potentially fatal. Early clinical suspicion added to suggestive imaging is essential for a quick diagnosis. Awareness of this medical condition as a differential diagnosis in abdominal sepsis plays a key role in the patient outcome.

ESP16-0617
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

RELAPSING POST-HERPES SIMPLEX VIRUS ENCEPHALITIS: BLAMING AUTOIMMUNITY

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Title of Case(s)

Relapsing post-herpes simplex virus encephalitis: blaming autoimmunity

Background

Herpes simplex virus encephalitis (HSE) is an uncommon potentially lethal disease. Replasing post-HSE is a serious complication with significant morbidity and mortality. It occurs in 13-24% of patients as a result of viral reactivation or secondary immunological mechanisms.

Case Presentation Summary

A previously healthy 8 months-old boy presented with fever and right-sided partial motor seizures. CSF studies showed 6 WBC/uL, proteins of 123 mg/dL, with negative HSV PCR in CSF. Brain MRI depicted insular and fronto-temporal lesions with T2 hypersignal and EEG showed periodic discharges of the right temporal lobe, typical of HSE. He started intravenous acyclovir and antiepileptic drugs with initial clinical improvement. Nine days after the onset of HSE the patient became progressively encephalopathic, developed severe choreoathetosis, orofacial dyskinesias and sleep dysfunction. This neurologic relapse was reminiscent of N-methyl-D-aspartate receptor (NMDAR) encephalitis and NMDAR antibody testing was positive in serum and CSF. High dose metilprednisolone and human intravenous immunoglobulin was started with no clinical improvement and the patient was subsequently treated with rituximab showing significant clinical improvement. At 1-year follow-up, he has residual deficits with a quadriplegic asymmetric cerebral palsy and well-controlled epilepsy. Levels of NMDAR antibodies in serum are slowly reducing.

Learning Points/Discussion

HSE is increasingly recognized as a trigger of cell-surface/synaptic autoimmunity and about 11% of patients with HSE develop NMDAR autoantibodies. Movement disorders are major manifestations of this condition. This case highlights the importance of testing for anti-NMDAR encephalitis in the presence of relapsing, worsening or prolonged symptoms post-HSE. Establishing the correct diagnosis is essential because anti-NMDAR encephalitis related symptoms are potentially responsive to immunotherapy.

ESP16-0393
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

SEVERE STAPHYLOCOCCUS AUREUS OSTEOMYELITIS COMPLICATED WITH PERICARDIC EFFUSION: ABOUT TWO CASES

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Title of Case(s)

Severe *Staphylococcus aureus* osteomyelitis complicated with pericardic effusion : about two cases

Background

The 2 most commonly found pathogens for bone and joints infections are *Kingella kingae* and *Staphylococcus aureus.*

Severe pericardial complications are not frequently reported for this type of infections.

We report here the clinical evolution of 2 cases of severe *Staphylococcus aureus* osteomyelitis in our hospital located in French Guiana. French Guiana is the only French overseas territory located in South America.

Case Presentation Summary

The first case is about a 4 year old girl, admitted in our hospital for an acute haematogenous osteomyelitis located on her right proximal tibial metaphysis. The second case, is about a 13 year old girl with an acute haematogenous osteomyelitis located on her left distal tibial metaphysis.

Blood cultures came back positive for a Panton Valentine leukocidin secreting strain of *Staphylococcus aureus* for both patients. An adequate antibiotic therapy with an anti toxin antibiotic (clindamycin) was administered, along with surgical management (drainage).

For both patients, a pericardial effusion was diagnosed by echocardiography and required surgical intervention.

The 4-year-old girl eventually died of cardiac tamponade in the operating room whereas the outcome for the second child was favourable after a surgical intervention.

Learning Points/Discussion

Panton Valentin leukocidin secreting strains Staphylococcous aureus pericardial effusion is a serious life threatening complication. A close monitoring of children admitted for severe

Staphylococcus aureus infections with echocardiography, looking for pericardial effusion is essential for an accurate and early management of these threatening complications. These 2 cases, occurring in a six month interval remind us that pericardial complications in severe Staphylococcus infections can be fatal if not diagnosed accurately.

ESP16-0535
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

BILATERAL TUBO-OVARIAN ABSCESS IN A NON-SEXUALLY ACTIVE ADOLESCENT GIRL

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Title of Case(s)

Tubo-ovarian abscess in a non-sexually active adolescent

Background

Tubo-ovarian abscesses usually occur as a complication of pelvic inflammatory disease in sexually active female patients; many studies reported Tubo-ovarian abscesses in non-sexually active young girls. Usually the presenting symptom is abdominal pain, fever and an incidentally found abdominal mass. In some cases reported in the literature the organism was isolated, while in some other reported cases the etiology remained unknown. Diagnosing and treating tubo-ovarian abscess is a challenge to pediatricians, pediatrics surgeons and ER physicians as there is no clear guideline that addresses imagining modalities and treatment options.

Case Presentation Summary

We report a case of a 14 years old, previously healthy, non-sexually active Emarati girl, who presented with abdominal pain, fever and an incidentally found abdominal mass. Upon examination she was found to have a large abdominal mass extending into the pelvic area. Child was admitted, started on IV piperacillin- tazobactam empirically. CT pelvis was done and showed a huge cystic mass originating from the right ovary. child was taken for exploratory laparotomy after few days, bilateral tubo-ovarian abscesses were drained. Child continued IV piperacillin-tazobactam for a total of 14 days, and was discharged home on a 7 days course of cefotaxime. US pelvis after treatment showed complete resolution of intra-abdominal condition and child was followed in the clinic, she is doing well since then.

Learning Points/Discussion

We are reporting this case to alert paediatricians about the possibility of tubo-ovarian abscess on the differential list of young girls with abdominal pain and to promote for further research about the possible etiology and the methods of treatment.

ESP16-0503
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

BLOODSTREAM INFECTIONS IN CHILDREN CAUSED BY CARBAPENEM-RESISTANT VERSUS CARBAPENEM-SUSCEPTIBLE GRAM-NEGATIVE MICROORGANISMS: RISK FACTORS AND OUTCOME

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Background

Carbapenems are often considered the last resort agents reserved for treatment of infections due to highly antimicrobial resistant organisms such as *A.baumannii* and *P.aeruginosa.* However, the prevalence of carbapenem-resistant Gram-negative (CRGN) pathogens has become much more prevalent in the last decade. The objective of this study was to determine risk factors for and outcome of bacteremia caused by Gram-negative microorganisms in a pediatric tertiary-care hospital.

Methods

Among 97 patients with hospital-acquired Gram-negative bacteremia, 66 patients with carbapenem-susceptible Gram-negative pathogens (CSGN) were compared with the remaining 31 with CRGN isolates.

Results

The overall clinical response and microbiological response rates were 83.3% and 43.9% in CSGN group, and 54.8% and 32.3% in CRGN group, respectively (p=0.002 and p=0.004, respectively). The treatment failure and relapse rates were 18.2% and 6.1% in CSGN group, and 38.7% and 6.5% in CRGN group, respectively (p=0.03 in each). The infection-related mortality rates were 10.8% in the CSGN group and 32.3% in the CRGN group (p=0.01). The total length of stay in hospital before infection was longer in patients with CRGN bacteremia than that of the CSGN bacteremia (p=0.002). The extended spectrum antibiotic usage prior to infection was significantly different between the groups (p=0.008).

Conclusions

Infections due to CRGN are generally associated with poorer patient outcomes. Longer hospital stay and extended spectrum antibiotic usage prior to infection are the most important risk factors for CRGN bacteremia in our cohort.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0307
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

ACUTE MENINGITIS IN PATIENTS WITH FIRST COMPLEX FEBRILE SEIZURES: A HOSPITAL BASED PROSPECTIVE CROSS SECTIONAL STUDY

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Background

Febrile seizure is the most common cause of seizures in children in age group of 6 months to 6 years and 25-30 % of febrile seizures are of complex variety. There are no guidelines for children presenting with first complex febrile seizures. This study aims to find incidence and predictors of acute meningitis in patients with first complex febrile seizures.

Methods

Children (n=70) in age of 6 months to 6 years with first episode of complex febrile seizures were included in the study. Complex febrile seizure included patients with fever and seizures for more than 15 minutes and/or focal seizures and/or seizure recurrence within 24 hours and/or post-ictal neurological deficit.

Results

8.5% of the study patients were diagnosed as acute meningitis on the basis of cerebrospinal fluid cytology and biochemistry. The odds of having acute meningitis in first complex febrile seizures who had > 3 seizures was 14 times (CI= 2.2, 89.2) than in patients with < 2 seizures at presentation. The incidence of meningitis was significantly high (*P*=0.004) in patients with seizure recurrence after admission.

Conclusions

Incidence of meningitis in patients with first complex febrile seizure was 8.5%. More than 2 seizures at presentation and seizure recurrence after admission are predictors of meningitis in complex febrile seizures.

Clinical Trial Registration (Please input N/A if not registered)

Clinical Trial Registry of India No 2014/12/008158

ESP16-0557
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

KINGELLA KINGAE IS THE PRIMARY CAUSE OF SEPTIC ARTHRITIS IN A UK ORTHOPAEDIC REFERRAL CENTRE

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Background

Septic arthritis affects 12 individuals per 100 000 per year and children are amongst the most commonly affected. The most common causative organism in septic arthritis has classically been *Staphylococcus aureus.* However several recent paediatric series have suggested that *Kingella kingae* is a now common aetiology in septic arthritis. This audit analysed a 3 year cohort of patients with septic arthritis seen in a large UK orthopaedic surgery centre.

Methods

Retrospective review of all children admitted with septic arthritis at Alder Hey from November 2012 to May 2015. Patients were routinely reviewed by the infectious diseases team with joint washout performed by the orthopaedic team. In most case where specimens were negative by traditional bacterial cultures, a targeted multiplex PCR assay which included *Kingella kingae* was performed.

Results

Fifty-five patients (29 males and 26 females) were admitted with a diagnosis of primary septic arthritis. Mean age was 37 months. The most common organism isolated in joint fluid was *Kingella kingae* (14, 25%), followed by *Staphylococcus aureus* (7, 13%), *Streptococcus pyogenes* (5, 9%) and *Streptococcus pneumoniae* (4, 7%). Patients with *Kingella kingae* infection were all less than 5 years old. There were no statistically significance difference in ESR, CRP and white blood cell counts between *Kingella kingae* and other pathogens. However children with *Kingella kingae* had significantly less IV antibiotic days, repeat surgeries and shorter hospital stays compared with other aetiologies.

Conclusions

Kingella kingae is the most common cause of septic arthritis in the UK setting. Infections occur in patients less than 5 years and tend to displays a more benign clinical course than other bacterial aetiologies.

ESP16-0847
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

SALMONELLA TYPHIMURIUM BACTERAEMIA COMPLICATED WITH MENINGITIS AND CEREBRAL ABSCESS IN A 3-MONTH-OLD BOY

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Title of Case(s)

***SALMONELLA* TYPHIMURIUM BACTERAEMIA COMPLICATED WITH MENINGITIS AND CEREBRAL ABSCESS IN A 3-MONTH-OLD BOY**

Background

We report an atypical case of non-typhoidal *Salmonella* bacteraemia complicated with meningitis and cerebral abscess.

Case Presentation Summary

A 3-month-old boy with no underlying condition or travel history, previously hospitalized for bronchiolitis with acute otitis media and treated with oral amoxicillin-clavulanic acid for 5 days, was readmitted six days later for persistent fever, bulging anterior fontanel, vomiting without diarrhoea. Cerebrospinal fluid (CSF) analysis showed 280 WBC/mm3, 380 RBC/mm3. Glycorrachia was 2.1 mmol/L (glycaemia was 5 mmol/L); protein 0.58 g/L. Gram staining was negative. C-reactive protein was 217 mg/L and procalcitonin 0.62 ng/mL.

Cefotaxime (200 mg/kg/day) and gentamicin (5 mg/kg/day) were started. The same day, he presented left hemicorporeal seizures, followed by homolateral hemiparesis. CSF culture was sterile and universal 16S rRNA PCR was negative. *Salmonella* Typhimurium grew on initial blood culture. Brain magnetic resonance imaging with gadolinium revealed a right frontal lesion with peripheral enhancement, a frontal subdural collection and a right fronto-parietal meningeal enhancement (Figure). Subdural and frontal cerebral lesions were consistent with empyema and cerebral abscess, respectively. Intravenous cefotaxime and ciprofloxacin (30 mg/kg/day) were administered for 6 weeks, followed by oral ciprofloxacin for 6 weeks. Immunoglobulin levels, lymphocyte immunophenotyping, complement fractions and neutrophil oxidative burst were normal. The child was HIV negative. Fever and left hemiparesis resolved

within two days.

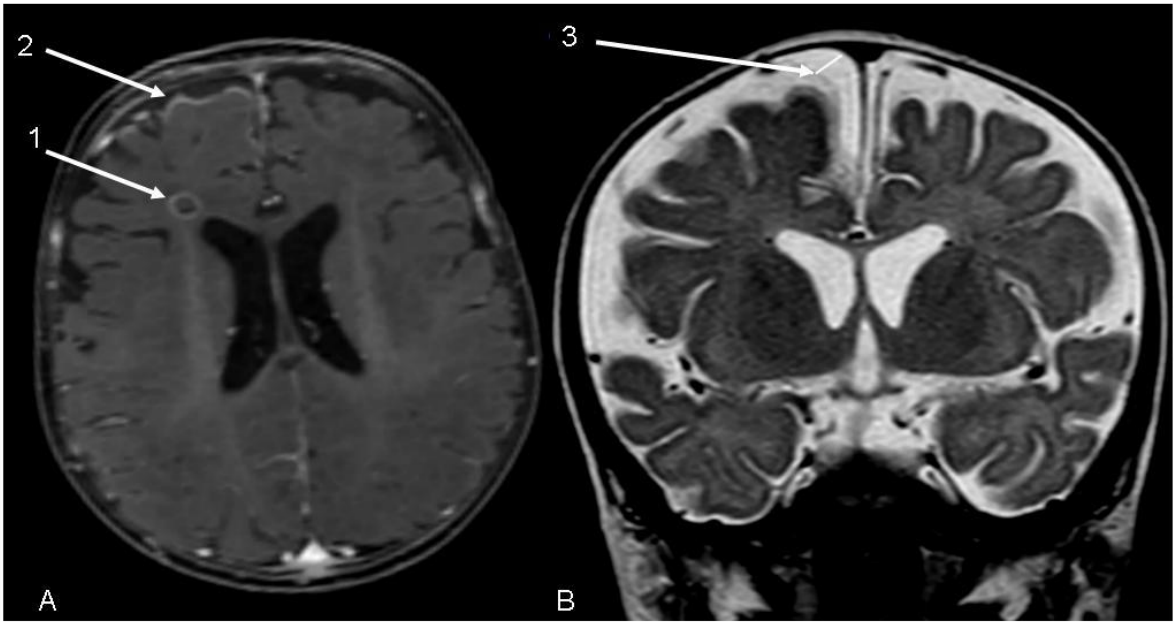

Figure 1. A, T1-weighted with gadolinium brain MRI shows an 8x6 mm frontal cerebral abscess (1) and meningeal enhancement (2); B, T2-weighted imaging shows a 6 mm subdural empyema (3)

Learning Points/Discussion

Central nervous system involvement of non-typhoidal *Salmonella* is rarely described except in immunocompromised patients. In this observation, young age might be the main factor leading to this complication. Clinicians should be aware of the risk of central nervous system involvement associated with minor *Salmonella* bacteraemia in young infants.

ESP16-0870
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

ACUTE HEMATOGENOUS OSTEOARTICULAR INFECTIONS IN CHILDREN IN SIRIRAJ HOSPITAL, THAILAND

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Title of Case(s)

Acute hematogenous osteoarticular infections in children in Siriraj hospital, Thailand.

Background

Acute hematogenous osteomyelitis (AHO) and septic arthritis (SA) in children may lead to a significant morbidity and sequelae. There is very few data in Thai children.

Case Presentation Summary

Methods: Children under 15 years of age with AHO and/or SA treated between January 1, 2002 and December 31, 2012, at Siriraj Hospital were retrospectively studied. Acute osteoarticular infections secondary to penetrating trauma, surgery, or infection at the contiguous site were excluded.

Results: Sixty-eight patients were included in the analysis including 11 AHO, 43 SA, and 14 combined AHO and SA. The median age was 44 [interquartile range (IQR) 9-94] months,41 (60%) were under 5 years of age, and 66% were male. The most common sites for AHO were femur (31%) and tibia (24%); and for SA were hip (32%) and knee (30%). The pathogens were identified in 39 of 65 (60%) patients with specimen submission. The most common organisms were *Staphylococcus aureus* (33.8%) and *Salmonella* (7.7%); the latter was responsible for 20% in 20 infants. The median duration of antibiotic treatment was 34, 37, and 73 days for SA, AHO, and combined, respectively. The one-year sequelae of AHO was chronic osteomyelitis (33%); and of SA and combined were mostly limb length discrepancy (12% and 14%) and joint contracture (5% and 7%). Multivariate analysis revealed that recovery without sequelae (68%) was significantly associated with onset less than a week (p = 0.02) and being immunocompetent (p = 0.04).

Learning Points/Discussion

S. aureus and *Salmonella* were the most common pathogens among children with acute osteoarticular infections. Empirical antibiotics should be against both organisms. Children with short onset and were immunocompetent had better outcome.

ESP16-0094
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

GROUP B NEISSERIA MENGITIDIS AS CAUSE OF MENINGITIS IN AN IMMUNOCOMPETENT CHILD VACCINATED AGAINST GROUP C

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Title of Case(s)

Group B Neisseria Meningitidis meningitis in an immunocompetent child.

Background

Neisseria Menigitidis (NM) is the leading cause of acute bacterial meningitis worldwide. It is also known as cause of epidemic meningitis with particular burden in children and adolescents. In Italy, group B and C are actually the most frequent; group C, more common in the past, dramatically decreased its impact due to the introduction of the specific vaccination on 2006.

Case Presentation Summary

Male, 8 years old with no particular problems in the past medical history. He referred to the A&E of our hospital due to the sudden onset of high temperature, headache, deficit of walking and speaking, rigor nucalis and opistotone. Immediately admitted in our paediatric ward the patient did a brain CT scan (normal), blood tests (increase of C-reactive protein and white cells count, in particular neutrophils) and full-septic screen: urine and blood cultures were negative, and lumbar puncture that revealed high level of proteins (3.57 grams/L), low glucose (20 mg/dL with blood sugar level 135 mg/dL) and a very high leukocytes count (5300 cells/µL, 100% neutrophils). Intravenous antibiotic treatment was promptly started with ceftriaxone (initially 100 mg/Kg/dose every 12 hours, then once a day after the third day of treatment) with graduate recovery and no neurologic sequelae.

Learning Points/Discussion

NM and Streptococcus pneumoniae are the main causes of meningitis worldwide. An immediate recognition of signs and symptoms with an appropriate empiric antibiotic treatment are fundamental for the prognosis of patients. The only way try to decrease this pathology is the promotion of specific vaccinations, in particular in risk groups.

ESP16-0798
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

A SERVICE EVALUATION OF THE MANAGEMENT OF OSTEOARTICULAR INFECTION (OAI) OVER 10 YEARS IN A SINGLE CENTRE

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Background

Practice in treatment of OAI varies widely in the United Kingdom and little data is available about recurrence and complication rates.

Aim: To evaluate patient demographics and practice, specifically duration of antibiotic course and route, use of peripherally inserted central catheter (PICC) lines and complications.

Methods

A previous service evaluation was extended. Cases were identified by hospital coding, clinician and microbiology records. OAI in children aged 0-18 years presenting to a regional Childrens Hospital from 01/09/2005 - 01/09/2015 were included.

Results

149 cases were identified, 46 were excluded for incorrect coding or availability of notes leaving 103 for analysis. Male to female ratio was 58:42% with mean age at presentation 6.1 years. 64 had osteomyelitis (OM), 35 septic arthritis (SA), and 4 had both. 3 presented <3 months old; 39 had complex disease. Co-morbidities included Trisomy 21 (1), Type 1 Diabetes (2), sickle cell disease (1) and hypogammaglobinaemia (1). The tibia was the most commonly affected in OM, and the knee in SA. Organisms were isolated in <50%; staphylococcus aureus was most common. There were 2 cases of PVL associated MSSA infection and 1 of MRSA. Median antibiotic duration was 45 days (range 7-358) of which median intravenous course was 2 weeks. 40 had PICC lines, of which 6 had complications (line sepsis (2), mechanical problems (4)). Complication of OAI included hyperesthesia, prolonged chronic OM and pain.

Conclusions

Management of OAI varied due to diversity in presentation and organism. Randomised trials to reduce the length and intravenous component of antibiotic administration are required in the UK.

ESP16-0541
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

SUBDURAL EMPYEMA CAUSED BY NEISSERIA MENINGITIDIS: A CASE REPORT AND REVIEW OF THE LITERATURE

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Title of Case(s)

SUBDURAL EMPYEMA CAUSED BY NEISSERIA MENINGITIDIS: A CASE REPORT AND REVIEW OF THE LITERATURE

Background

Neisseria meningitidis is one of the commonest causes of bacterial meningitis in children worldwide, but subdural empyema complicating the clinical course is rare. We report an infant with *N. meningitidis* subdural empyema and also review the clinical features, investigations, treatments and outcome of fourteen previously reported cases.

Case Presentation Summary

Methods

We defined cases of subdural empyema due to *N.meningitidis* when cases had microbiological evidence of *N.meningitidis* consisting of at least one of: a positive culture of blood and/or cerebrospinal fluid (CSF) and/or surgically evacuated material; Plus radiological evidence of subdural empyema or physical evidence of frank purulent material.

Results

Median age was 13 weeks. Subdural empyema was a complication of meningitis in all cases; 12 (80%) had seizures. A persistently abnormal inflammatory profile (raised white cell count (WCC) and C-reactive protein (CRP)) and cerebrospinal fluid (CSF) profile (raised CSF WCC, raised protein, low CSF glucose) was identified and abnormal neuroimaging was seen in all 14 (93%) cases where undertaken. Ten (67%) children had neurosurgical intervention. Clinical outcome was available in 14 (93%) cases; a full recovery was reported in 10 (71%) and one child (7%) died.

Learning Points/Discussion

Subdural empyema due to *N meningitidis* appears to be rare but should be considered in young children with meningococcal meningits when the temperature fails to settle despite appropriate antibiotics, if seizures or focal neurological signs develop or if blood and CSF parameters remain grossly abnormal or worsen. Cranial imaging should be ordered for such children and if a subdural empyema is identified neurosurgical treatment should be considered. Despite a high likelihood of focal neurology acutely there appears to be a good outcome in most cases.

ESP16-0665
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

ACUTE EXTENSIVE MYELITIS SECONDARY TO ADENOVIRUS INFECTION: A RARE PRESENTATION

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Title of Case(s)

ACUTE EXTENSIVE MYELITIS SECONDARY TO ADENOVIRUS INFECTION: A RARE PRESENTATION

Background

Introdution Adenoviruses cause a wide spectrum of illnesses in children, most commonly respiratory infections and acute gastroenteritis. Neurologic manifestations are uncommon.

Case Presentation Summary

Clinical case Previously healthy 17-month-old male, presenting periods of irritability followed by prostration, inability to stay seated and imbalance when standing. Four days prior, he had had a viral upper respiratory infection. The neurologic examinaton revealed torticollis to the left, reached objects preferably with left arm, and had a right sided brachial and facial hemiparesis. Trauma, accidental intoxication were excluded. Initial blood test showed leukocytosis (18700 cells/mm3), c-reactive protein of 18.3 mg/dL and normal cerebrospinal fluid (CSF). Brain and spinal magnetic resonance imaging (MRI) unveiled a T2-hyperintense intramedullary lesion, extending from C2-C3 until D9, involving preferably the posterior collumns, compatible with acute longitudinally extensive transverse myelitis (TM). Acute disseminated encephalomyelitis (ADEM) was considered unlikely regarding the continuity of the lesion and absence of brain lesions. The etiologic research revealed an acute adenovirus infection and other etiologies, namely auto-immune and metabolic were excluded. Polimerase Chain Reaction (PCR) for adenovirus was positive in respiratory secretions and other specimens (stool, CSF) were negative. High-dose methylprednisolone during 5 days was given with favourable response and was revaluated after 3 months maintaining excellent evolution.

Learning Points/Discussion

Commentaries Acute TM, rare in childhood, can be caused by various disorders including trauma, space occupying lesions, vascular malformations, infarction, autoimmunity and infections. In parainfectious TM, 20 to 40% of patients have preceding or concurrent viral infection. The association of adenovirus infection and transverse myelitis is extremely rare.

ESP16-0200
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

MANAGEMENT OF VENTRICULAR SHUNT INFECTIONS IN CHILDREN: A SINGLE CENTRE AUDIT

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Background

Ventricular shunt infections are a serious complication of ventricular shunts that can result in significant morbidity and mortality. Treatment consists of surgical and antimicrobial therapy, but there is a lack of evidence regarding the details of optimal management. We audited current management practice in our institution against local standards, in the absence of national guidance, to identify areas for improvement.

Methods

We identified all cases of ventricular shunt infection from January 2000 until April 2015 in our institution in North-East England. All included patients were <18 years at the time of infection with permanent shunts. Information was collected from digital and clinical notes with use of a standardised proforma. Non-parametric tests were used for statistical analysis.

Results

There were 92 episodes of infection in 65 patients. The most common microorganisms from cerebrospinal fluid (CSF) were coagulase-negative staphylococci (47%) and *Staphylococcus aureus* (16%). Surgical management: 15% underwent shunt externalisation and 67% complete removal, of which 80% received an external ventricular drain (EVD). Medical management: 97% received antibiotics; most frequently vancomycin, linezolid, cefotaxime, meropenem and rifampicin. The median duration of antibiotic treatment was 18 days (IQR 14-25 days). Two patients died from consequences of an infection and seven had a recurrence, despite appropriate antibiotic duration.

Conclusions

Complete shunt removal and placement of EVD is the safest evidence-based surgical treatment. Our newly implemented guideline will include empirical antibiotic treatment with linezolid and meropenem, commenced immediately after taking CSF cultures. Antibiotics can be rationalised with CSF culture results. Prophylactic antibiotics should be changed from cefuroxime to single-dose teicoplanin during shunt insertion to cover most frequently identified microorganisms, in particular coagulase-negative staphylococci. Re-audit will close the cycle following three years of guideline implementation.

ESP16-0201
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

RECOGNITION OF VENTRICULAR SHUNT INFECTIONS IN CHILDREN: A SINGLE CENTRE AUDIT

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Background

Ventricular shunts are required to treat life-threatening causes of hydrocephalus. Shunt infections are a common and serious complication of ventricular shunts requiring prompt diagnosis and treatment to prevent significant morbidity and mortality. However, recognition of shunt infections can be difficult, since clinical manifestations in children can be highly variable. We therefore surveyed a regional neurosurgical referral centre in North-East England to analyse the risk factors and presentation of shunt infections.

Methods

We identified cases of ventricular shunt infection from January 2000 until April 2015 in our institution in North-East England. All patients were <18 years at the time of infection. Clinical, radiological and microbiological information was collected from digital and clinical notes with use of a standardised proforma. Non-parametric tests were used for statistical analysis.

Results

There were 92 episodes of infection in 65 patients. 46% of patients were born prematurely and 41% were <1 year old at first infection. There was positive correlation between number of infections and shunt insertions (Spearman's Rho 0.247, p=0.05), with risk highest in the 2 weeks following any shunt surgery. Presenting symptoms including; fever (67%), irritability (30%), vomiting (29%), cutaneous manifestation (23%) and abdominal pain (19%). Infections with *Staphylococcus aureus* seem to present relatively more often with cutaneous manifestations, headache and diarrhoea, while Coagulase-negative Staphylococci present more often with irritability.

Conclusions

Clinical recognition of patients with shunt infection is difficult, due to non-specific symptoms that overlap with other paediatric conditions. In the context of a child with a shunt, fever, irritability, vomiting, cutaneous manifestations and/or abdominal pain should lead to investigations for shunt infection. Suspicion of an infection should be higher in young children, prematurely born children and especially in children who have had recent shunt surgery.

ESP16-1064
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

STREPTOCOCCUS INTERMEDIUS CAUSING SUPPORATIVE INTRACRANIAL AND INTRAORBITAL COMPLICATIONS IN THREE ADOLESCENTS WITH SINUSITIS

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Title of Case(s)

Streptococcus intermedius causing suppurative intracranial and intraorbital complications in three adolescents with sinusitis

Background

Sinusitis is a common disorder that can result in rare but serious complications caused by bacteria, fungi and parasites. Among the bacteria, the *Streptococcus milleri* group is frequently involved (50-70%), including *S.constellatus*, *S.intermedius*, and *S.anginosus*. Staphylococci (10-30%) and enteric bacteria -*Escherichia coli, Klebsiella, Proteus* spp.- (10-25%) have also been isolated.

Case Presentation Summary

We report a series of three male adolescents treated by our Emergency Unit from October to December 2015 with rhinosinusitis, fever, persistent worsening headache, and, in one case, focal epilepsy. Head CT and contrast-enhanced brain MRI scans with venous MR angiography revealed three different complications of pansinusitis. Patient 1: Pott's puffy tumor with frontal subdural empyema and brain abscess; Patient 2: intraorbital abscess with signs of dural inflammation; Patient 3: frontal epidural empyema. Indirect spread of infection between the sinus and the epidural or subdural space through the mucosal veins of the sinus to the emissary veins was detected in all cases.

All patients were initially treated with broad spectrum intravenous antibiotics (Table 1), analgesics, anticoagulants, and underwent ENT sinuses drainage shortly after. *S.intermedius* was isolated from the drained pus in all cases. The antibiotic was continued for six weeks and

the patients recovered gradually without any sequelae

Clinical, biochemical and radiologic features of the patients

	Patient 1	Patient 2	Patient 3
Sex	M	M	M
Age	13 y	12 y	12 y
Biochemical findings at the presentation	Neutrophilic leukocytosis PCR 6,33 mg/dl (nv <0,46)	Neutrophilic leukocytosis PCR 7,56 mg/dl (nv <0,46)	Neutrophilic leukocytosis PCR 16,61 mg/dl (nv <0,46)
Clinical findings			
Initial presentation	Headache, fever, severe stupor Frontal swelling, seizures	Eye pain, fever Palpebral edema, ptosis, frontal swelling	Headache, fever, palpebral edema, ptosis Worsening of palpebral edema, ptosis
Time between clinical presentation and diagnosis	4 days	3 days	3 days
Radiologic findings (CT scan and MRI)	Pott's puffy tumor with frontal subdural empyema and brain abscess	Intraorbital abscess with signs of dural inflammation	Frontal epidural empyema
Microbiologic findings	*Streptococcus intermedius OxaS Staphylococcus epidermidis OxaR*	*Streptococcus intermedius OxaS*	*Streptococcus intermedius OxaS*
Therapy			
Antibiotic iv	Ceftriaxone Metronidazole Vancomycin replaced by Ampicillin - sulbactam Cotrimoxazole Rifampin	Ceftriaxone Metronidazole Rifampin	Ceftriaxone Metronidazole Rifampin
Other	Dexamethasone Hypertonic sol. 3% Levetiracetam Phenylhydantoin Anticoagulant ENT sinuses drainage	Dexamethasone Hypertonic sol. 3% Anticoagulant ENT sinuses drainage	Dexamethasone Hypertonic sol. 3% Anticoagulant ENT sinuses drainage
Duration th parenteral + oral	6 w	4 w (2 iv + 2 po)	4 w

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Learning Points/Discussion

Intracranial abscesses are uncommon complications of frontal and ethmoidal sinusitis. Rapid spread of the infection with a short period of time between the symptoms of sinusitis and the signs of CNS involvement has been described in adolescents. In these patients, an early contrast-enhanced head CT and/or brain MRI with venous angiography are useful to detect possible intracranial suppurative complications, thus tailoring the antibiotic treatment and surgical ENT procedures.

ESP16-0514
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH) 2ND TO TYPHOID FEVER - REPORT OF A CHILD AND LITERATURE REVIEW

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Background and Objective

Case presentation and systematic review of the literature of HLH 2nd to typhoid fever.

Methods

Database: Medline, using the terms "*Salmonella typhi, Salmonella paratyphi*, typhoid fever AND hemophagocytic lymphohistiocytosis, hemophagocytic syndrome, hemophagocytosis". All published articles (English or Spanish) reporting patients aged<18 years old were included

Learning Points Discussion

Results:

All cases (n=11) reported in 9 publications were from endemic areas (median age of 12,9 years). Clinical presentation included fever (100%), gastrointestinal (50%) or neurologic (50%) symptoms. Splenomegalia (75%), hepatosplenomegalia (62%) and jaundice (25%) were the most common found. Cytopaenias (72%), elevated transaminases and bilirubin (62%), hyperferritinemia (50%) and hypertriglyceridemia (50%) were detected. Haemophagocitosis was present in all bone marrow aspirates (BMA). Microbiologic diagnosis was made by serology (n=3), blood (n=4) and BM culture (n=3). All patients received antibiotic therapy (ceftriaxone n=6); one received additional corticoid therapy becoming afebrile within 48h. Overall fever persisted 4-31 days. Outcome was favourable in all but one patient who relapsed and was subsequently successfully treated with co-trimoxazol.

We present a previously well 7 years-old boy, born to non-consanguineous parents, who was admitted with fever, diarrhoea, abdominal pain, ascitis, lethargy and hepatosplenomegaly associated with jaundice.

Complementary tests were suggestive of HLH including pancytopenia, hyperferritinemia, hypertriglyceridemia, hipofibrinogenemia, whilst blood and stool cultures grew *S.typhi*. BMA was not performed. He was managed with iv ceftriaxone (14 days) plus iv Methyl-prednisolone (2mg/kg/day for 7 days, subsequently tapered over 14 days) as he fulfilled 5/8 HLH criteria, resulting in excellent clinical response within 48h.

Conclusion:

In Europe, HLH 2nd to typhoid fever is uncommon. Antimicrobial plus additional immunomodulatory therapy, as used in our case, should be considered in the management of

this patient group to ensure good clinical outcome.

Author	No. of cases	Age/ Sex	Symtomps	Physical Examination	Analitycal	Microbiology	Bone Narrow: Hemophagocytosis	Treatment	Outcome
Fame TH et al. 1986	Case report	13Y/M	Fever. NL: Letargy.	Hepatosplenomegaly. Letargy.	Cytopaenias. ↑ transaminases. Blood coagulation disorders.	BC: *S typhi.* SC: *S typhi*	+	Ampiciline iv (10d) ↓ Amoxicline po (14d)	Recurrence ↓ Cotrimoxazol (10 iv —> 14d po)
Chien YH et al. 1990	Case report	13Y/M	Fever. NL: Pshycosis.	-	Pancytopaenia	BMC: *S typhi*	+	Ceftriaxone	Favorable
Caksen H et al. 2003	Case report	6Y/M	Fever (10d). NL: Abdominal pain. DG: Headache.	Hepatosplenomegaly. Jaundice.	Pancytopaenia. ↑ transaminases and bilirrubin.	Widal test +	+	Cloranfenicol (14d)	Favorable
Karthik R et al. 2007	Case report	17Y/M	Fever (14d) DG: Bloody diarrhea	-	Pancytopaenia. ↑ transaminases. ↑ ferritenemia. ↑ triglyceridemia.	BC: *S typhi.*	+	Ceftriaxone (14 d)	Favorable
Pramanik S et al. 2009	Case report	6Y/M	Fever (31d)	Hepatosplenomegaly. Cervical lymphadenophaty.	Pancytopaenia	Widal test +	+	Antibiotherapy	Favorable
Shah P et al. 2011	Case report	18Y/F	Fever Chills and rigors DG: Abdominal pain	Splenomegaly	Pancytopaenia. ↑ transaminases. ↑ ferritinemia. ↑ triglyceridemia.	BMC: *S typhi*	+	Ceftriaxone (10d)	Favorable
Pandey M et al. 2012	Case report	10Y/M	Fever (5d) NL: Letargy	Hepatosplenomegaly. Pallor. Petechie.	Pancytopaenia. ↑ ferritinemia. ↑ triglyceridemia.	Widal test +	+	Ceftriaxone (14 d)	Favorable
Rajapola S et al. 2012	Review	18Y/F	-	-	-	BC: *S typhi.*	+	Antibiotherapy	Favorable
		17Y/M	-	-	-	-	-	Ceftriaxone (14 d)	Favorable
		6Y/M	-	-	-	-	-	Antibiotherapy	Favorable
Nath UK, et al. 2013	Case report	18Y/M	Fever (4d). NL: Headache. Letargy. DG: Abdominal pain and vomiting. Bloody diarrhea	Hepatosplenomegaly. Jaundice. Ecchymosis. Cervical lymphadenophaty.	Pancytopaenia. Blood coagulation disorders. ↑ transaminases and bilirrubin. ↑ferritinemia. ↑tryglyceridemia. ↓fibrinogen.	BC: *S paratyphi.* BMC: *S paratyphi*	+	CeftriaxonE + Vacomycin (10d). Dexamethasone (10mg/m2, 14d)	Favorable

Y= Years. F= Female. M= Male. NL: neurologic manifestations. DG: digestive manifestations. BC = Blood culture. SC = Stool culture. BMC = Bone marrow culture.

ESP16-0286
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CLINICAL SPECTRUM OF DENGUE FEVER IN PEDIATRIC AGE GROUP IN A TERTIARY CARE HOSPITAL IN LAHORE.PAKISTAN

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Background

BACKGROUND. Dengue fever (DF) is an acute infectious disease of antiquity. It is probably the most important arthropod-borne viral disease in terms of human morbidity and mortality, with 100 million infections occurring annually for which no effective therapy exists. Up till now study done locally, that shows the clinical spectrum of dengue fever in infants and children, is scarce. Dengue fever presents differently in different countries and during last epidemic Lahore was the main city to be affected.

AIMS: To assess frequency of various clinical presentations of dengue fever in pediatric age group in a tertiary care hospital

Methods

METHODS: Study completed in Nine month from Dec 2012 to Sep 2013 in pediatrics department Jinnah hospital Lahore. Cross sectional survey

Results

RESULTS: Out of 150 patients enrolled mean age of 8.4 years and standard deviation (SD) of ± 2.8 years. Age ranges from 1 year to 14 years. Amongst all 150 subjects 86 (57.3%) were males and 64 (42.7%) females. Male to female was 1.3: 1Fever was present in all 150 patients (100%).Diarrhea present in 21(14 %) patients. Petechia was present in 25 (16.3%).Epistaxis was present in 20 (13.3%).Hematemesis present in 8 (5.3%) Hepatomegaly was observed in 33(22%) patients .Splenomegaly was noted in 15 (10%) subjects.

Conclusions

Most of dengue fever cases were from 5 to 10 years of age group. Fever was the most common clinical manifestation of dengue fever followed by hepatomegaly, petechiae and diarrhea, epistaxis, splenomegaly and then hematemesis. . Dengue fever was more common in males as compared to females

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0052
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

AN UNUSUAL CASE OF NEONATAL MENINGITIS

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Title of Case(s)

An Unusual case of Neonatal Meningitis

Background

M.hominis is relatively common species to colonise the female urogenital tract. Although it is uncommon cause of Neonatal bacterial meningitis. Neonates are usually infected by vertical transmission of the organism from mother.

Case Presentation Summary

We present the case of an eight-day-old neonate who was admitted with pyrexia and poor feeding.The CSF was purulent with a white cell count of 3500/cmm (90% polymorphs), protein 2.95 gm/L and glucose 0.6 mmol/L. The CSF failed to grow any organism on conventional media. However 16s PCR was positive for *M. hominis*.

The baby was initially commenced on empirical intravenous Cefotaxime and Amoxicillin. After four days, due to poor clinical response, Gentamicin and Acyclovir were added with no benefit. On day seven, once the organism was identified, Ciprofloxacin was commenced and continued for three weeks. Clinical response was noted two days after starting Ciprofloxacin. Brain MRI on day five was normal. A repeat Brain MRI day twenty-two revealed small haemorrhage in the posterior aspect of the lateral ventricle .The baby made a complete recovery .

Learning Points/Discussion

This case gives a message that when we face a baby with clinical features of bacterial meningitis + cultures remains negative and baby fails to respond to empiric antibiotics - We should always consider *Mycoplasma hominis* and provide appropriate antibiotic cover.

ESP16-0024
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

NEWBORN CARE PRACTICES AT HOME AMONG MOTHERS OF NEONATES ADMITTED WITH LATE ONSET NEONATAL SEPSIS IN PEDIATRIC UNIT OF B.P. KOIRALA INSTITUTE OF HEALTH SCIENCE

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Background

Child rearing practices and family environment determine the health of the newborn**.** Harmful newborn care practices are the risk factors for LONS. Objective of study was to identify newborn practices related to breast feeding, cord care, hygiene of newborn and thermal care of admitted neonates with diagnosis LONS in pediatric unit of BPKIHS.

Methods

A descriptive cross sectional study was carried out from 21st December to 17th January using consecutive sampling. Semi structured, pretested questionnaire was used to interview 40 mothers. Data were analyzed using SPSS 20, descriptive (mean, standard deviation, median, percentage andfrequency were calculated) and inferential statistics (Chi-square test) were used.

Results

More than half **(**60%) of the mother had not practiced breastfeeding within one hour of delivery. Among neonates, 65% were given colostrum, 25% were given pre lacteal feed, and 45% were given milk other than breast milk. Majority (72.5%) of mother used mustard oil to care umbilical cord. Mustard oil was used by 40% of the mother to care cord stump. More than half (62.5%) of the mother used to wash hand before touching the baby.Kajal was applied for 52.5% of the newborn, 95% newborns were massaged in house by mustard oil. Majority (75%) of the mother had practiced of burning charcoal to keep newborn warm. None of the socio-demographic variables (age, sex, education, income, parity of mother, type of family**)** were associated with breast feeding, cord care, newborn hygiene and thermal care of newborn. But, the study revealed association between newborn care and mother education, per capita income of family and family type (p =0.012, p= 0.012, p=0.039) respectively.

Conclusions

In this study among the components of newborn care practices cord care was found to be poor.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-1021
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

BACTEROIDES FRAGILIS: A CASE STUDY OF SEPTICEMIA

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Title of Case(s)

BACTEROIDES FRAGILIS: A CASE STUDY OF SEPTICEMIA

Background

Bacteroides fragilis group strains are the most frequently isolated anaerobic bacteria from patients with intra-abdominal or deep tissue infections and bacteremia. The recent increased recovery of these organisms in children has led to greater appreciation of the roles they play in bacteremias. The early recognition and administration of appropriate therapy contributes to the prevention of mortality and morbidity, otherwise presenting with high mortality rates. In recent years increasing resistance to antimicrobial agents has been reported for this group, being with the broadest spectrum of recognised resistances.

Case Presentation Summary

The aim is to present a case of B. fragilis septicemia in a 15 years old female adolescent transferred to our department from a local hospital, where she was admitted for 3 days, complaining of fever, diffuse abdominal pain, nausea and vomiting. She was started on empiric therapy with Gentamicin for the suspicion of urinary tract infection, but she continued to present high fever, deteriorated clinical state and marked inflammatory response. At arrival in our Emergency Department the patient presented signs of sepsis; after blood cultures were sent, antimicrobial therapy was initiated with Meropenem and Metronidazol, with a successful clinical outcome. Blood culture came back positive for B. fragilis. Further investigations did not reveal the source of bacteremia.

Learning Points/Discussion

This report summarises the case of an anaerobic septicaemia and highlights the need for awareness of early recognition of anaerobic bacteremia, emphasising the importance of obtaining repeated blood cultures. B. fragile group infections require early treatment, usually before susceptibility results are available, and so it would be of great importance to survey antimicrobial susceptibility and report any emerging resistance in our region also.

ESP16-0892
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

FATAL CASE OF STREPTOCOCCAL TOXIC SHOCK SYNDROME IN A 16-MONTH-OLD GIRL

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Title of Case(s)

Fatal case of streptococcal toxic shock syndrome in a 16-month-old girl

Background

Over the past decades, a resurgence of invasive group A streptococcal infection has been observed in developed countries causing significant morbidity and mortality. Invasive group A streptococcus infection is defined as the isolation of group A streptococcus from a normally sterile site. Streptococcal toxic shock syndrome is a toxin-mediated illness which can rapidly progress to severe and intractable hypotension and multisystem dysfunction. Given the rapid clinical progression of streptococcal toxic shock syndrome, immediate and aggressive management of hypovolemic shock and appropriate antimicrobial therapy is essential.

Case Presentation Summary

A 16-month-old previously healthy female presented to our hospital with a 3-day history of fever and sporadic episodes of vomiting and diarrhea. Her condition worsened a few hours before admission demonstrating lethargy. On arrival in our department, the child appeared seriously ill, pale and mentally confused with fever and hypotension. She was noted to have cool peripheries and necrotic finger desquamation. She immediately received fluid resuscitation and intravenous ceftriaxone. As soon as her condition did not improve she was transferred to Pediatric Intensive Care Unit. Initial investigations revealed kidney and liver failure, thrombocytopenia and elevated inflammatory markers. Despite prompt initiation of supportive care and antibacterial management she died 6 hours after her arrival to our hospital. Blood culture revealed group A streptococcus pyogenes.

Learning Points/Discussion

Streptococcal toxic shock syndrome is a rare but potentially life-threatening condition secondary to invasive group A streptococcal infection. Pediatricians and emergency physicians must be aware of this possibility and immediately initiate aggressive treatment when suspected. This case illustrates the fulminant clinical course of streptococcal toxic shock syndrome despite aggressive hemodynamic resuscitation and antimicrobial therapy in a 16-month-old female patient.

ESP16-0106
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

COMPARISON BETWEEN QUELLUNG AND MICROARRAY SEROTYPING TECHNIQUES TO ASSESS PNEUMOCOCCAL NASOPHARYNGEAL CARRIAGE IN NEPALESE CHILDREN

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Background

Conventionally pneumococci are serotyped using the WHO recommended Quellung reaction method. A recent study employed a microarray-based molecular serotyping method to identify the prevalence and serotype distribution of multiple pneumococcal serotype carriage by Nepalese children aged between 6 weeks and 24 months, prior to the introduction of a pneumococcal conjugate vaccine. This study aims to compare the serotypes detected by microarray with those identified by Quellung reaction.

Methods

Nasopharyngeal swabs were collected between May and October 2012, and pneumococci detected using a microarray (BµG@S SP-CPS microarray) performed on bacterial DNA extracted from blood agar culture plate sweeps. Using a random subset of 81 swabs which had previously been shown by the microarray to contain pneumococci, Quellung serotyping using reference sera (SSI, Denmark) was conducted after processing the swabs according to WHO guidelines.

Results

71/81 (87.65%) samples analysed using Quellung identified the same primary serotype as the microarray analysis, whilst 75/81 (92.59%) of samples identified the same primary serogroup. More than one serotype was found in 28.4% of samples using microarray analysis compared to none using conventional microbiology and Quellung. One primary serotype identified by Quellung was detected as a secondary serotype on microarray. 6 non-typeable pneumococci were found using Quellung compared to 7 primary non-typeables using microarray.

Conclusions

Concordance between Quellung and the serotype of highest abundance detected by microarray is good. Although Quellung remains the WHO recommended method for serotyping, application of a molecular serotyping approach using microarray allows identification of multiple additional serotypes of lower abundance, demonstrating prevalence of co-colonisation.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0327
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

BRAIN ABSCESS DUE TO AGGREGATIBACTER APHROPHILUS AND STREPTOCOCCUS INTERMEDIUS

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Title of Case(s)

BRAIN ABSCESS DUE TO *AGGREGATIBACTER APHROPHILUS* AND *STREPTOCOCCUS INTERMEDIUS*

Background

Brainabscess is serious infection of brain parenchyma, has high fatality rate. The most common pathogens responsible are *streptoccocus* and *staphylococcus* species. Here we report brain abscess due to *Aggregatibacter aphrophilus* and *Streptococcus intermedius* in a healthy child. Because *Aggregatibacter aphrophilus* is rare pathogen, we aim to discuss clinical characteristics, management and outcome of brain abscess due to combination of these microorganisms.

Case Presentation Summary

Six year old girl was admitted to the Department of Neurosurgery because of minor trauma, her cranial computed tomography revealed 2 cm mass lesion in the right parietal lob, magnetic resonance imaging showed the same lesion with ring enhancement in diameter of 27x31 mm. Before this trauma she did not have any complaint. But four months ago, she had undergone dental filling for four teethes. Stereotactic biopsy was done for differential diagnosis, during the procedure purulent material came out. Cefotaxime and metronidazole treatment was initiated for this incidentally found brain abscess. In pus culture *Aggregatibacter aphrophilus* and *Streptococcus intermedius* grown, both were susceptible to ceftriaxone, so treatment was not changed. Previous dental fillings was assumed as predisposing factor, other probable factors were investigated; she did not have cyanotic or acquired heart disease, echocardiography was normal, otolarygeal examination was normal, there were no sinusitis, mastoiditis, otitis. This brain abscesses regressed without any complication, and treatment was discontinued at 12th weeks.

Learning Points/Discussion

This is the first reported case of brain abscesses due to combination of *Aggregatibacter aphrophilus* and *Streptococcus intermedius*, and this case also remind us critical role of appropriate treatment in management of brain abscesses to achieve a favorable clinical outcome.

ESP16-0337
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

EMERGENCY IN HEMATOLOGIC MALIGNANCY: ACUTE RETINAL NECROSIS DUE TO CYTOMEGALOVIRUS INFECTION

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Title of Case(s)

Emergency In Hematologic Malignancy: Acute Retinal Necrosis Due To Cytomegalovirus Infection

Background

Recently studies conducted that Cytomegalovirus (CMV) retinitis also seen in patients with acute lymphoblastic leukemia. Here in we presented 5 years old boy admitted to ED with conjunctival hyperemia and blurred vision in left eye.

Case Presentation Summary

Five years old boy admitted to ED with conjuctival hyperemia and blurred vision in left eye. In his medical history he was diagnosed acute lymphoblastic leukemia three years ago. He was in maintenance phase of chemotherapy. The ophthalmological examination revealed best corrected visual acuity (BCVA) of 20/400 in the right eye (RE) and light perception (LP) in the left eye (LE). Slit lamp examination of the anterior chamber and retina of the RE were normal, whereas, 4+ anterior chamber cellular reaction, mild keratic precipitation, approximately 2 milimeters hypopiyon were observed in the LE. The patient was undergone pars plana vitrectomy and silicon oil injection. During the surgery we observed that, retina and choroid had atrophic and haemorrhagic areas, ghost vessels, optic atrophy and widespread preretinal membranes. Cytomegalovirus DNA was 131 copies/ml in the blood sample and 4412782 copies/ml in intravitreal fluid detected by the polymerase chain reaction (PCR) analysis. Intravenous Ganciclovir therapy was started immediately. On the third day, in the retinal examination, there were exudated and heamorrhagic lesions on the papullomacular bundle therefore, intravitreal ganciclovir was injected to both eyes. On his final retinal examination, the resolution of the active retinal lesions were observed and pigment deposition was localized around all lesions. Before discharge, oral valganciclovir prophylaxis was initiated.

Learning Points/Discussion

Control of CMV retinitis necessitates both awareness in immunodeficiency settings and commencing treatment at an early stage of the disease.

ESP16-0476
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

VENTRICULOPERITONEAL SHUNT INFECTION CAUSED BY COLISTIN RESISTANT ACINETOBACTER BAUMANIIIN A CHILD

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Title of Case(s)

VENTRICULOPERITONEAL SHUNT INFECTION CAUSED BY COLISTIN RESISTANT *ACINETOBACTER BAUMANII* IN A CHILD

Background

Multi-drug resistant (MDR) gram negative bacteria is usually responsible for health care associated infections. Herein we report a case of ventriculoperitoneal shunt infectioncaused bycolistin resistant*Acinetobacterbaumanii*.

Case Presentation Summary

A thirteen-year-old girl was admitted to hospital with complaints of vomiting, decreased level of consciousness, imbalance on walking. On neurological examination, she was ataxic.Her cranial Magnetic Resonance Imaging examination showed mass formationon the right cerebellar hemisphere. The patient underwentsurgery to excision of cerebellar mass and ventriculoperitoneal (VP) shunt placement for hydrocephalus. On the thirth day of operation, she had fever and worsening clinical condition. Aspiration of serebrospinal fluid (CSF) from the VP shunt reservoir was performed, CSF analysis showed white blood cell count of 640 cells/mm^3, protein level of 148mg/ml and glucose of 19 mg/ml. CSF cultureyielded multidrug resistant *Acinetobacterbaumanii complex* which was resistant to colistin.Minimal inhibitory concentration for colistin was 16 mcg/ml by E-test.The patient underwent VP shunt removal and placement of an external ventricular device. Ampicillin-sulbactam, rifampicin, intraventricularand intravenous colistin were started and continued for 21 days. Control CSF culture became sterileand new VP shunt was placed.

Learning Points/Discussion

Health care associated infections caused by MDR microorganisms are increasingly detected and may carry a high mortality because of limited options of antimicrobial treatment. Clinicians need to consider appropriate early empirical antibiotic coverage. Antibiotic combinations can be used as an alternative treatment to include MDR gram negative bacteria.

ESP16-1090
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

DIPHTHERIA: PRESENTATION AND COMPLICATIONS

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Title of Case(s)

Diphtheria: Presentation and complications

Background

Universal vaccination has practically eradicated many serious childhood infections. However, in resource-limited settings with low levels of immunization and limited access to passive immunization, they continue to contribute to morbidity and mortality. In Haiti a resurgence of Diphtheria was seen in 2010 and since then sporadic cases have been reported.

Case Presentation Summary

A six year-old boy presented to the paediatric emergency department in Hôpital St Thérèse, Haiti with a three-day history of sore throat, hoarseness, difficulty swallowing, malaise and persistent fever. On examination, he had drooling, significant cervical lymphadenopathy, and inspiratory stridor. A limited examination of his oropharynx revealed white-grey membranes covering his tonsils and uvula. He received erythromycin for empiric therapy for diphtheria. He was subsequently transferred to a tertiary care center for airway management, isolation and further treatment. One week later, an eight year-old girl living in the same neighborhood as the previously described patient, presented with similar symptoms; she received similar emergent management. Upon transfer, she received emergent tracheostomy.

No diphtheria antitoxin was available in Haiti for either case presentation. Both patients initially recovered within two weeks. Both cases, however, suffered inpatient sudden cardiac arrest and died despite attempted cardiopulmonary resuscitation.

We suspect the cause of death in both cases was likely due to arrhythmia in the setting of myocarditis secondary to diphtheria toxin. Local epidemiologic authorities were informed, but thankfully, no other cases have been recorded since.

Learning Points/Discussion

These two cases underline the importance of vaccination, especially in settings where appropriate treatment and isolation are not readily available. Both of our patients only reported receiving TB vaccination.

ESP16-0302
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

ROTAVIRUS ASSOCIATED ACUTE MYOCARDITIS

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Title of Case(s)

ROTAVIRUS ASSOCIATED ACUTE MYOCARDITIS

Background

Rotavirus infection is a common cause of acute gastroenteritis in children, which can cause severe dehydration and even death. There are many publications on extraintestinal manifestations that have been associated with rotavirus infection. It has been associated with neurological manifestations as afebrile seizures, convulsive status, cerebellitis, encephalitis or encephalopathy, digestive manifestations as pancreatitis and even increased risk of type 1 diabetes mellitus. There are also publications relating to cardiopulmonary manifestations with Rotavirus as myocarditis and pneumonitis and even sudden death.

Case Presentation Summary

We report 2 cases of acute myocarditis following rotavirus gastroenteritis in ten years period. Both of children at age 1 were previously healthy without any significant medical history. The illness started as severe gastroenteritis requiring hospital admission. During the hospital stay we noticed progressive worsening of cardiovascular functions with tachycardia, systolic murmur appearance and cyanosis beside adequate fluid and electrolyte resuscitation which ultimately led to cardiovascular collapse(heart failure). The diagnosis of acute myocarditis was suspected by abnormal values of cardiac biomarkers and characteristic ECG and echocardiographic changes. Both of children were transferred to pediatric ICU where diagnosis was confirmed and therapy for heart failure and corticosteroids was initiated. After the stabilization of cardiovascular functions they were discharged from hospital, but the treatment and regular follow ups continued one year afterwards with complete recovery.

Learning Points/Discussion

Acute myocarditis is only one of many potentially fatal extraintestinal manifestations of rotavirus infection emphasizing the need for active prevention in countries where vaccination against rotavirus is not implemented.

ESP16-0330
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CLINICO-EPIDEMIOLOGICAL PROFILE OF CHILDREN HOSPITALISED WITH DENGUE ILLNESS: A PROSPECTIVE OBSERVATIONAL STUDY FROM BIKANER, NORTHWESTERN INDIA

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Background

Dengue illness ranks highly among the newly emerging infectious diseases in Indian subcontinent with significant mortality and morbidity. Disease is more severe in children than adults. The present study describes the clinical and epidemiological profile of children hospitalized with dengue illness at Children Hospital of Sardar Patel Medical College, Bikaner since January 2015 to December 2015.

Methods

Total of 1138 ELISA confirmed dengue seropositive cases (titre≥1:400) satisfying WHO criteria were analysed after ruling out other possible evident causes of fever thoroughly. Data were appropriately analysed by SPSS 22.0.0 software.

Results

The mean age was 10.38+3.83 years. Male to female ratio was 1.17:1. Children of 6–12 years were most commonly affected (52.55%). Dengue fever was diagnosed in 63.18% children while 36.82% had dengue hemorrhagic fever (DHF) [DHF1 9.75%, DHF2 18.10%, DHF3 7.12% and DHF4 1.84%]. Common symptoms were fever (100%), abdominal pain (60.45%), vomiting (51.14%), myalgias (42.36%) and itchy rash (21.31%). Bleeding manifestations were seen in 33.67% children with petechiae (75.19%) being the most common, followed by epistaxis (31.59%), gum bleeds (8.09%), hematemesis (4.96%), melena (2.35%) and haematuria (1.82%). Thrombocytopenia was documented in 87.43% children and bleeding occurred more often with severe thrombocytopenia. Mean platelet count in DHF children was 34576+17210/mm^3. Tourniquet test was positive in 38.75% children. Most common atypical manifestation was hepatitis found in 31.28% children followed by febrile diarrhea (19.24%), coagulopathy (8.17%), encephalopathy (1.85%), ARDS (1.14%), acalculous cholecystitis (1.05%) and myocarditis (0.97%). Seven children expired due to refractory shock and coagulopathy.

Conclusions

This study focused common and atypical manifestation of dengue illness in children. Clinicians should have a high index of suspicion for varied and multi-systemic manifestations which can go unrecognized.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0352
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

EVIDENCE BASED ASSOCIATION OF ACUTE MYCOPLASMA INFECTION WITH KAWASAKI DISEASE: A CASE REPORT

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Title of Case(s)

Association of Kawasaki disease with acute *Mycoplasma pneumoniae* infection in a child

Background

Kawasaki disease (KD) is an acute systemic vasculitis. Its precise etiology is still unknown, considering various viruses and bacteria. Association with *Mycoplasma* species has limited evidence for being a trigger pathogen. This study emphasizes the linking of KD with acute *Mycoplasma* infection, an occurrence not frequently described in literature previously.

Case Presentation Summary

A 4-year-old girl presented with a five-day history of high grade fever (upto 39.5°C), sore throat, cough, vomiting and weakness. Physical examination revealed non-pruritic generalized macular erythematous desquamating rash, strawberry tongue, pharyngeal erythema, edematous palms with periungual desquamation, bilateral nonpurulent conjunctival hyperemia, palpable cervical lymph nodes (the largest was 3.5 cm) and hepatosplenomegaly in evolution with time. Laboratory workup showed leucocytosis (18,000/mm^3), thrombocytosis (6,54,000/mm^3), elevated CRP (188 mg/dL), high ESR (90 mm/hour), hypoalbuminemia (2.2 g/dl) and sterile pyuria. Chest X-ray showed bilateral interstitial markings with pleural effusion. *Mycoplasma pneumoniae* IgM serology was positive. Cultures taken from the throat, urine and blood were negative. A diagnosis of acute *Mycoplasma pneumoniae* infection was suspected and treatment given but fever not subsided. Echocardiogram on day 3 of hospitalization showed mild dilatation of right coronary artery. Subsequently considering the diagnosis of KD, intravenous immunoglobulin was started. Fever and erythematous skin lesions subsided in 2 hours. Follow-up at 6 weeks, all examinations and laboratory findings were normal.

Learning Points/Discussion

Normal 0 false false false EN-US X-NONE HI

· •Although diagnosing *Mycoplasma* is a difficult task, it should always be considered in differential diagnosis of KD.
•*Mycoplasma* species acting as superantigens may trigger an immunological cascade causing the vasculitis seen in KD.
•Acute *Mycoplasma* infection in KD may ultimately affect the severity of disease, prognosis and treatment.

ESP16-0359
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

DENGUE MYOCARDITIS: ATYPICAL MANIFESTATION OF DENGUE ILLNESS IN CHILDREN IN BIKANER NORTHWESTERN INDIA

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Background

Majority of dengue illness follow a benign self limiting course but recently rare atypical manifestations like cardiac involvement are increasingly seen due to rising burden of disease and increased awareness. The present hospital based observational study describes dengue myocarditis in tertiary care hospital from January 2014 to December 2015.

Methods

Diagnosis of dengue illness was made on WHO criteria and ELISA based analysis of IgM and IgG (titre≥1:400) and confirmation of dengue infection was done by RT-PCR. Malaria PCR, leptospira IgM, typhoid serology and blood culture were negative.

Results

Total 11 children were diagnosed as dengue myocarditis. Median age was 9 years (range 3-11 years). Median duration of fever was 6 days (range 3-13 days). Common cardio-respiratory symptoms at time of admission were shock (54.55%), heart failure (27.27%) and chest pain (18.18%). Chest X ray showed cardiomegaly (63.64%), pleural effusion (54.55%) and pulmonary edema (18.18%). Cardiac biomarkers cretinine kinase MB isoenzyme (mean±SD=141±55.91 U/l) and Troponin I (mean±SD=7±2.92 µg/l) were elevated in all these children. Electrocardiogram showed either widespread ST segment elevation (63.64%) or T wave inversion (27.27%) or both (27.27%). Transthoracic echocardiography revealed depressed left ventricular ejection fraction (100%), abnormal left ventricular wall motion (54.55%) and pericardial perfusion (18.18%). Cardiac involvement was confirmed in 7 children by cardiac MRI. All these children were treated according to standard cardiac protocols and all recovered well.

Conclusions

Although dengue myocarditis was self-limiting in our patients under supportive treatment, it may be clinically fatal. Possibility of dengue myocarditis should always be considered in dengue fever patient having refractory shock and congestive heart failure because avoidance of aggressive IV fluids therapy are crucial life saving measure and can improve the survival.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0534
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

MORE THAN A HEADACHE

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Title of Case(s)

MORE THAN A HEADACHE...

Background

Introduction: Intracranial hypertension is a rare entity in prepubertal children, and its differential diagnosis includes a number of systemic diseases, drugs, vitamin deficiencies and excesses, and hereditary conditions.

Case Presentation Summary

Case report: A previously healthy 9-year-old-boy, whose past medical history is irrelevant except for cows' milk and flucloxacilin allergy. He was admited with daily pulsatile fronto-temporal headache, pallor, photophobia and phonophobia, without night awakening, vomiting nor visual changes. He had been to the Pyrenees and in rural areas in Portugal. He was in a good general condition and his neurological exam revealed papilledema but was otherwise normal. Head CT scan was normal. A lumbar puncture was performed with clear CSF, cell count: 30 (predominantly mononuclear), proteins: 29 mg/dL, glucose: 55 mg/dL and an increased opening pressure (50 cmH_20). Blood tests were normal except of an ESR of 36 mm/h. He started acetazolamide and was admitted for investigation. The serology for *Borrelia burgdorferi* in the CSF was positive (IgM 28,38 U/mL, IgG 12,19 U/mL), and serum IgG was also positive (>240 Au/mL). Head MRI with angio-MRI was normal. The diagnosis of neuroborreliosis was assumed and intravenous ceftriaxone was started and completed a 21-day-course with full recovery.

Learning Points/Discussion

Conclusions: Lyme disease can present with central nervous system involvement in 2% of the cases, and rarely can present with a pseudotumor cerebri-like picture with inflammatory CSF profile. In Portugal, neuroborreliosis is a rare entity, so, a careful history, considering the exposure to rural areas together with the cranial hypertension and inflammatory CSF, were important clues to the diagnosis allowing the institution of appropriate treatment.

ESP16-0410
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

CLINICAL CHARACTERISTICS OF CHILDREN WITH VIRAL SINGLE- AND CO-INFECTIONS AND AN INFECTION ASSOCIATED SEIZURE

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Background

Specific viral infections have been associated with seizures in young children. Nonetheless, a systematic analysis of a wide range of viral infections with modern available techniques as quantitative real-time polymerase chain reaction in the context of infection associated seizures is lacking.

Methods

We conducted a prospective study in children (0 to 18 years) presenting with a seizure and signs or symptoms of infection at the emergency department between January 2014 and January 2016. In nasopharyngeal aspirates the following viruses were analyzed by quantitative real-time polymerase chain reaction: influenza A and B (INF), parainfluenza viruses (PIV), human respiratory syncytial virus A and B (RSV), human metapneumovirus (HMPV), rhinovirus (RV), enterovirus (EV), adenovirus (ADV), human coronavirus OC43, 229E, NL63 (HCoV), human bocavirus (HBV), and human-herpes virus 6 (HHV6). Furthermore, clinical characteristics and course were determined.

Results

The mean age of children was 23 months, 94/ 148 (63,5%) were male, 129/148 (87,2%) had fever and the mean temperature of these was 39.1°C (+0.89). A broad range of infections were observed with upper respiratory tract infections being the most frequent. The majority of patients had a generalized convulsion (143/148; 96,6%). A viral pathogen was identified in 72,9 % cases. Viral single infections were observed in 53,7% of cases and co-infections in 46,3%. In virus positive samples the frequency of the cases with the observed pathogens were for HHV6 46 (42,5%), INF 27 (25,0%), ADV 22 (20,4%), RV 18 (16,7%), RSV 14 (12,9%), HCoV 9 (8,3%), EV 9 (8,3%), PIV 7 (6,5%), and HMPV 3 (2,7%).

Conclusions

Infection associated seizures are equally associated with viral single- and coinfections. HHV6, INF, ADV, RV and RSV are the predominant pathogens.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0938
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

POLYMICROBICAL BRAIN ABSCESS IN A HEALTHY CHILD

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Title of Case(s)

POLYMICROBICAL BRAIN ABSCESS IN A HEALTHY CHILD

Background

Brain abscess is a rare disorder (4/1000000 cases) with high rate of mortality. We describe the clinical and diagnostic features and outcome of a rare case of a healthy child with brain abscess.

Case Presentation Summary

A 5 year old Greek female presented with a 2 days history of mild fever, nausea and vomiting. On admission physical and neurological examination revealed no abnormalities. However a performed retinoscopy revealed Roth's spots and an urgent CT scan demonstrated two lesions in the left parietal lobe, indicative of an abscess or malignancy. An MRI clearly demonstrated that the lesions referred to a brain abscess. She immediately underwent surgical drainage of the abscess and was treated with intravenous antimicrobial therapy covering aerobes and anaerobes. An extensive laboratory work out, including full dental examination, to exclude predisposition factors due to autoimmune, cardiovascular, traumatic, anatomical or infectious diseases was normal. The results of the abscess cultures revealed multiple pathogens (cambylobacter gracilis, clostridium perfingens, clostridium aquaticum, actinomyces odontolyticus, streptococcus mitis, staphylococcus epidermidis). 7 days after the treatment's induction (surgical drainage and antimicrobial therapy) our patient presented recurrence of the treated lesion and underwent a second drainage procedure with modification of the antimicrobial therapy. She was dismissed from the hospital after 8 weeks of IV antimicrobial therapy. In 6 months follow up she remains in perfect condition with normal MRI findings.

Learning Points/Discussion

Our case is rare due to the acute onset and short duration of symptoms, the lack of predisposition factors or previous history of infection, the multiple pathogens isolated to the culture and the perfect clinical outcome. Although all organisms isolated were those of the normal nasopharygeal flora, none anatomical abnormality was found.

ESP16-1034
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

MASKED MASTOIDITIS: UNCOVERED BY ITS COMPLICATIONS

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Title of Case(s)

MASKED MASTOIDITIS: UNCOVERED BY ITS COMPLICATIONS

Background

Mastoiditis has a large clinical spectrum, ranging from absence of symptoms to life-threatening disease due to complications. Epidural empyema is a rare supurative intracranial complication of mastoiditis. Symptoms may be mild, unspecific and mimic the symptoms of the underlying infection. Therefore we must have a high degree of suspicion for an early diagnosis.

Case Presentation Summary

We report a case of a 5-year-old boy with epilepsy and global development delay secondary to neonatal stroke with lateral and longitudinal sinus thrombosis who had a previous negative study for the existence of prothrombotic factors. He presented a 2-day history of altered consciousness, fever, cervical pain and anorexia. No cervical trauma history or ear pain reported. He had an ill appearance and meningismus. Blood analyses had leucocytosis and CRP 25mg/dL. No cytochemical abnormalities in CSF. ENT observation revealed no signs of acute disease. Cranial-TC and MRI showed left otomastoiditis complicated with empyema and thrombosis of left sigmoid sinus and internal jugular vein. Cultures (blood and CSF) were negative.

Left miringotomy and antroatticotomy were performed. Ceftriaxone and vancomycin were administered for three weeks with clinical and laboratory improvement, followed by one week of ceftriaxone. Anticoagulation with enoxaparin was maintained for 4 months with partial sinus thrombosis resolution.

Learning Points/Discussion

Clinical presentation of mastoiditis is variable. A delay in the recognition of intracranial complications in children and in the institution of appropriate therapy may result in high morbidity and mortality.

Imaging studies are essential tools for diagnosis and to delineate its extension, which determines prognosis. Antibiotherapy and surgical drainage are the mainstays of treatment for intracranial complications of acute mastoiditis.

ESP16-0754
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

PARAPHARYNGEAL ABSCESS DUE TO A NON-VACCINE PNEUMOCOCCUS SEROTYPE: AN UNUSUAL PRESENTATION

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Title of Case(s)

Parapharyngeal abscess due to a non-vaccine pneumococcus serotype

Background

The introduction of pneumococcal vaccines has been successful in reducing morbidity and mortality of invasive pneumococcal disease (IPD) in children, however non-vaccine serotypes are still circulating. Deep neck infections (DNIs) are typically polymicrobial from resident flora of the contiguous mucosa, while pneumococcus is not a frequently reported pathogen in the literature.

Case Presentation Summary

We present the case of pneumococcal parapharyngeal abscess in a four-month-old girl who presented in early winter. She had a two day history of increased work of breathing, poor feeding and isolated fever (39.4oC). She was previously well and up-to-date with her vaccinations, including two doses of thirteen-valent pneumococcal vaccine (PCV13). Her birth history was unremarkable. She was initially managed as presumed bronchiolitis. However, she continued spiking high temperatures and four days later developed stridor and worsening respiratory distress. She was further investigated with microlaryngoscopy bronchoscopy and CT neck and chest, which revealed a 3cm left parapharyngeal abscess and bilateral pulmonary consolidation. She required intubation and ventilation for the diagnostic procedures and drainage of 30 ml of pus from the abscess; remaining in intensive care for four days. A fully sensitive S. pneumoniae grew from both abscess and blood cultures. She was successfully treated with a seven day course of intravenous benzylpenicllin and completed a further fourteen day course of phenoxymethylpenicillin, but with significant morbidity. Serotyping confirmed non-vaccine pneumococcal serotype 27. Her immunology investigations were normal.

Learning Points/Discussion

Pneumococcus has become a rare cause of invasive infections where PCV13 is available and DNIs are a rare occurrence in paediatrics, however vigilance and early recognition of severe bacterial infections is essential where the clinical course of a common illness is atypical.

ESP16-0891
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

A NEONATE WITH SEVERE MENINGOENCEFALITIS NOT RESPONDING TO EMPIRIC ANTIBIOTIC THERAPY

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Title of Case(s)

A NEONATE WITH SEVERE MENINGOENCEPHALITIS NOT RESPONDING TO EMPIRIC ANTIBIOTIC THERAPY

Background

Mycoplasma hominis commonly colonizes the adult genitourinary tract. After vertical transmission during vaginal delivery it can cause life-threatening CNS infections in neonates. Because routine bacterial cultures are often negative, the diagnosis of *M. hominis* meningoencephalitis is difficult and optimal antimicrobial therapy in neonates is not known. We describe a neonate with severe *M. hominis* meningoencephalitis who was successfully treated with moxifloxacin.

Case Presentation Summary

An 11-day-old girl was referred to the hospital because of fever. CSF examination revealed an elevated WBC count ($1892x10^6$ cells/l) and empirical treatment was initiated with amoxicillin, cefotaxime and acyclovir. In the following days the patient developed seizures and an hydrocephalus. Repeated lumbar punctures showed a persistent elevated WBC count, while bacterial cultures and PCR in blood and CSF remained negative. Cerebral MRI showed bitemporal empyema, tri-ventricular hydrocephalus, vasculitis and cerebritis with ischemia of the left hemisphere, suggestive of severe meningoencephalitis.

Mycoplasma hominis was identified by 16S ribosomal primer PCR and moxifloxacin (9 mg/kg/day) once daily was started. Moxifloxacin levels were determined (in steady-state) showing therapeutic serum concentrations. The patient showed no adverse events or toxicity. She recovered in the following weeks with only a mild right-sided hemiparesis at the age of 6 months.

Learning Points/Discussion

M. hominis can cause severe CNS infection in neonates with risk of permanent neurologic sequelae. Culturing *M. hominis* is difficult, therefore 16S rDNA PCR should be considered in neonates with persistent CNS infection of unknown aetiology. *M. hominis* is resistant against empiric antibiotic therapy for meningitis. In this patient with complicated *M. hominis* meningoencephalitis monotherapy with moxifloxacin was effective and safe. More research is needed to determine adequate dosing regimens for moxifloxacin in neonates.

ESP16-0416
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

SEVERE ANEMIA AND CONGECTIVE CARDIAC FAILURE IN A CHILD WITH RENAL MICROABSCESSES

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Title of Case(s)

SEVERE ANEMIA AND CONGECTIVE CARDIAC FAILURE IN A CHILD WITH RENAL MICROABSCESSES

Background

Pyelonephritis causing microabscesses in the kidney is an uncommon presentation. We describe a 2 and a half year old boy who presented with cardiac failure secondary to anemia in sepsis due to Ecoli pyelonephritis

Case Presentation Summary

A two years boy was admitted with high fever for two weeks and abdominal distension since 5 days. There was history of consumption of unpasteurised milk, but no other significant history. On examination,the child was febrile with tachycardia and tachypneoa with distress. There was tender hepatomegaly of 6 cm below right costal margin and spleen was palpable 2 cm below left subcostal margin. Investigations revealed severe anemia with hemoglobin was 6.2g%, TLC 31870 L/cmm with 71% polymorph ,platelets 2.97 L/cmm and no malarial parasites. Hemoglobin was 13 gm% four days prior . Urine routine showed 15-20 pus cells and a urine culture later revealed a significant colony count of E.coli sensitive to Ceftriaxone. Blood culture as well as Brucella IgM was negative. An ultrasound scan of the abdomen showed hepatosplenomegaly with normal kidneys. The child received a blood transfusion and intravenous ceftriaxone. As the fever persisted despite 5 days of ceftriaxone, CT scan of abdomen was done which revealed bilateral interstitial nephritis with microabscesses. Patient became afebrile on 9th day of antibiotic and hepatosplenomegaly regressed and was given cefixime for total 14 days. Repeat USG again showed normal sized kidneys with no dilatation. The child clinically remains well on follow-up.

Learning Points/Discussion

Renal microabscesses secondary to pyelonephritis have been described uncommonly. This child developed severe anemia secondary to sepsis due to pyelonephritis that resulted in congestive cardiac failure. This is an unusual presentation

ESP16-0368
02. S - SEVERE/INVASIVE BACTERIAL AND VIRAL INFECTIONS

A CASE REPORT OF ACUTE HUMAN BOCAVIRUS 1 INFECTION IN CHILD WITH SEVERE RIGHT-SIDE PNEUMONIA

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Title of Case(s)

A CASE REPORT OF ACUTE HUMAN BOCAVIRUS 1 INFECTION IN CHILD WITH SEVERE RIGHT-SIDE PNEUMONIA

Background

Human bocavirus 1 (HBoV1) has been associated with mild to severe acute respiratory infections and symptoms ranging from the common cold to life-threatening pneumonia. However, limited information about pathogenesis is available. Thus, clinical cases are the important source of novel information about the course of infection and the related pathophysiology.

Case Presentation Summary

A 17-months-old boy was admitted to the Children's Clinical University Hospital of Riga on the 7th day of illness in January 2015. He had have cough presented for 7 days and fever (axillar T^0 39 ^{0}C) for last 2 days. He experienced severe respiratory distress and was transferred to the intensive care unit. The child had a respiratory rate of 44 breaths/min, a heart rate of 146 beats/min, chest wall in drawing and both-side crepitation on auscultation. Tracheal intubation was performed. His leukocyte count was 30.6x 10^3/μL and serum C-reactive protein level was 5.09 mg/L. A chest radiograph showed right-side infiltrations.

NPA and faeces collected from the patient were positive for HBoV1 DNA by PCR. Also a whole blood and corresponding cell-free blood plasma sample were HBoV1 DNA positive. Serologic studies showed positive both HBoV1-IgM and IgG class antibodies by in-house ELISA. Nasopharyngeal swab for respiratory syncytial virus (RSV), adenovirus, parainfluenza 1-3, influenza A and B was negative.

The patient was treated with intravenous ceftriaxone and methylprednisolone.

Learning Points/Discussion

The patient has life-threatening pneumonia associated with acute HBoV1 infection. Acute HBoV1 infection is proved by the presence of HBoV1 DNA in a whole blood, in cell-free blood plasma as well as in NPA and faeces, and by the presence of HBoV1-IgM class antibodies.

ESP16-0980
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

HUMAN BOCAVIRUS INFECTION IN ISTANBUL

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Background

Human bocavirus (HBoV) is a recently discovered virus which is a member of Parvoviridae family. It is mostly detected in pediatric patients in respiratory tract and stool specimens with the diagnosis of acute respiratory tract infections and gastroenteritis, respectively.

Methods

Hospitalized children aged 1-56 months with the diagnosis of lower respiratory tract infection (LRTI) at whom HBoV DNA was investigated by PCR method between 01 February 2009- 21 May 2009 were included in this prospective study. A questionarrie form were applied for all of the patients. Written informed consent of a parent or legal guardian was required.

Results

Among the total of 120 hospitalized children whom were investigated for HBoV DNA PCR, 43 (35.8%) were female and 77 (64.2%) were male and the male/female ratio was 1.8. The mean age of the group was 9.9 months (1-56 months). HBoV DNA PCR in nasopharyngeal swabs was positive in 8 (6.7%) of 120 patients. In HBoV (+) LRTI group, to have an ill subling with similar symptoms (p=0.044, OR:4.091; %95 CI: 0.948-17.654) and number of sublings (≥3 or more) (p=0.038, OR:4.355; %95 CI:0.981-19.323) were found to be risk factors. In HBoV (+) group serum level of CRP was significantly lower than HBoV (-) group (p=0.011).There was no difference in age, gender, maternal age, socioeconomic status, duration of breastfeeding, cigarette smoke exposure and family history of asthma between HBoV (+) and HBoV (-) groups.

Conclusions

The clinical spectrum of HBoV infection ranges from no symptoms or mild respiratory symptoms to severe acute respiratory disease. Since there is lack of data investigating the frequency of HBoV respiratory tract infections in our region, our study has importance for providing new datas.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0900
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

ACUTE EXUDATIVE TONSILLOPHARYNGITIS; EPSTEIN-BARR VIRUS, HERPESVIRUS AND ADENOVIRUS

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Background

Exudative tonsillopharyngitis(ExTP) is a common illness that requires a careful clinical assessment in order to identify underlying etiology and to avoid morbidity and mortality.Tonsillar exudate culture confirmed group A streptococcal(GAS) tonsillitis. Differential diagnosis includes Epstein-Barr virüs(EBV), adenovirus, Fusobacteria, *Arcanobacterium hemolyticum*, *Corynebacterium diphtheriae, C. ulcerans, Francisella tularensis, Yersinia entercolitica*, and *Neisseria gonorrhoea*. Epstein-Barr virus, the most common cause of pseudomembranous tonsillitis, causes tonsillitis with or without infectious mononucleosis. The tonsils can be severely enlarged which are covered with an extensive necrotic, greyish-white membranous exudate. In this study, we aimed to analyses the presence of EBV, Adenovirus and Herpesvirus typ- 1(HSV-1) in ExTP

Methods

Molecular diagnosis was performed for EBV, Adeno and HSV 1 detection with swab samples from tonsillar membranous exudate of 51 paediatric patients with Exudative tonsillopharyngitis after GAS ruled out(21 men and 30 women, ages between 2 and 16 years). At the same time, also monospot test was performed. DNA extraction from swap samples was carried out from tonsillar membranous exudate, using the Magnesia® Extraction Kit by using the Nucleic Acid Extraction robot (Magnesia® 2448)(Anatolia Geneworks). Bosphore® EBV DNA, ADENO and HSV type 1 Quantification Kits were used for EBV DNA, ADENO and HSV type 1 PCR by Montania® 4896 RT PCR platform (Anatolia).

Results

The frequency of positive EBV DNA cases in the tonsillar membranous exudate in swap samples were 21.5 % (11/51). Monospot test was only one of the positive cases in EBV DNA positive. On the side a case of adenovirus, the HSV-1 was detected in two cases

Conclusions

A meticulous clinical examination would differentiate between the 2 most common causes; Streptococcus and EBV. Adeno and HSV were determined as less causative agents.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0952
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

NEONATAL HERPETIC KERATOCONJUNCTIVITIS – VERTICAL OR HORIZONTAL TRANSMISSION?

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Title of Case(s)

NEONATAL HERPETIC KERATOCONJUNCTIVITIS – VERTICAL OR HORIZONTAL TRANSMISSION?

Background

Herpes Simplex Virus (HSV) disease of the newborn can be acquired in intrauterine period, peripartum or postpartum, being this last, the most common form. The disease results with infection of the central nervous system, disseminated disease or mucocutaneous infection, but two or more entities can coexist.

Case Presentation Summary

A 47 days-old infant with lacrimation and ocular discharge of the right eye, followed by mattering, since the 2nd week of life, was admitted. On the 7th day of life, vesicular lesions were noticed in the upper right eyelid. A diagnosis of unilateral keratoconjunctivitis with extensive corneal ulcer was made and empirically treated with topical tobramycin and acyclovir. The patient was a full-term, delivered via an uncomplicated eutocic birth. In further observation, we found worsening of corneal lesions, extensive ulceration and stroma infiltration, and intravenous cefotaxime and acyclovir was started. HSV-1 polymerase chain reaction (PCR) was positive in corneal scrapings, but negative in blood and cerebrospinal fluid, excluding other forms of herpetic disease. She was discharged after 14 days of intravenous acyclovir and kept on prophylactic acyclovir. Her mother has no history of genital herpes, but was being treated with immunosuppressives for rheumatoid arthritis and has recurrent muco-cutaneous herpes, with lesions reported one week after giving birth.

Learning Points/Discussion

A maternal immunosuppression cannot exclude the possibility of vertical transmission. However, the mother's history, the infant's age and the HSV1 suggest a horizontal transmission. Prophylactic acyclovir in mucocutaneous disease with keratoconjunctivitis is not consensual.

ESP16-0279
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

INFANTS WITH SUSPECTED PERTUSSIS: IS IT A BACTERIA OR A VIRUS?

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Background

Despite high vaccination coverage, pertussis remains prevalent in young infants. Still, its clinical presentation is non-specific therefore warranting laboratory testing. Accordingly, we examined the prevalence of Bordetella pertussis (Bp) and other respiratory pathogens in a sample of nasopharyngeal (NP) specimens submitted by hospital and clinics to a pertussis laboratory of infants suspected of having pertussis

Methods

One hundred and forty seven NP samples were collected in this retrospective cross-sectional study, 2/2015-12/2015. Bp Real-time PCR targeting pertussis IS 481, parapertussis IS 1001, ptxS1g, holmesii BHIS 1001 and culture were performed as well as PCR of sixteen respiratory viruses (RV-16).

Results

RV-16 positivity was more common than Bp, 61.22 %(95% CI: 53.2-68.7%) vs. 32.65% (95% CI: 25.6-40.6%) chi square=24.01, p<0.001 in infants <1 year suspected of having pertussis. Among the RV-16 positive samples,Human rhinovirus was the most prevalent virus (51.0%); followed by Adenovirus (24.5%), parainfluenza (16.2%) and metapneumovirus (10.1%). The incidence of respiratory viruses in infants with Bp was significantly lower than the incidence of respiratory viruses in infants without pertussis (OR: 3.87, 95% CI: 1.86-8.04; p<0.001). There were no significant differences in the frequency of pertussis by age, 0-2, 2-4, 4-6, and 6-12 months. Notably, 50% of Bp PCR positive samples were also Bp culture-positive.

Conclusions

In young infants suspected of having pertussis, respiratory viruses frequently mimic Bp's clinical presentation and are more likely to be the causative agent. Laboratory confirmation of Bp should be pursued to assure the judicious use of antibiotic treatment and chemoprophylaxis

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1056
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

PAEDIATRIC ADMISSION WITH INFLUENZA IN THE ERA OF WIDESPREAD IMMUNISATION

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Background

For Flu season 2014-2015 UK recommendations for influenza vaccine included well recognised clinical risk groups and preschool children age 2-4 years, most of whom received live nasal vaccine. While efficacy of antiviral agents remains controversial, guidance at that time recommended antivirals be given to children at risk of severe disease. Live nasal Flu vaccine may result in false positive virological results. An audit was undertaken of paediatric influenza cases during 2014-2015 to assess this.

Methods

92 children had confirmed influenza in our hospital between October 2014 and June 2015. 87 care episodes were reviewed and information collected on duration of stay, antibiotic and antiviral use, complications, including intensive care admission and evidence of having received Flu vaccine that season.

Results

The average length of stay was 7 days, with 11.5% of patients requiring intensive care. 45 children received antibiotics. 37 received antiviral treatment; 29 of who had chronic health problems. Complications included lower respiratory tract infection (20%) respiratory failure (7%) bacterial meningitis (2.2%) and myositis (1%). 60 children met criteria for immunisation; 55 children from high risk groups and 5 well pre-school children. A flu vaccination history was documented in 2 cases at admission, and in 5 cases during the admission. 14 routinely vaccinated haematology/oncology children developed influenza. Communication from secondary care to primary care recommending immunisation of children in risk groups and their families was poor.

Conclusions

Influenza may still cause serious disease despite immunisation and in otherwise healthy children. A flu vaccine history should be taken in all children admitted with influenza to allow interpretation of clinical results and improve vaccine uptake if opportunities have been missed. Strategies to improve the management and documentation with electronic reminders have been implemented.

ESP16-0802
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

PEDIATRIC PERIOBITAL AND ORBITAL CELLULITIS: A SINGLE-CENTER 10-YEAR EXPERIENCE

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Background

Although, periorbital cellulitis (PC) and orbital cellulitis (OC) may be confused with one another, they are two distinct childhood diseases with very different clinical, therapeutic and prognostic implications.

Aim:
To study the predisposing factors, clinical presentation, laboratory and CT findings, management and outcome of these two clinical entities.

Methods

Children with PC or OC hospitalized in a tertiary care pediatric hospital between 1/2006-6/2015 were retrospectively reviewed

Results

Twenty-one children (male: 13) aged 7m-13yrs (median age: 4yrs) were identified. Based on CT/MRI findings, 5 children had OC (diffuse orbital fat infiltration: 2, subperiosteal abscess:2, orbital phlegmon:1), all associated with pan-sinusitis. Sixteen children had PC related to pan-sinusitis in 6, maxillary and/or frontal sinusitis in 5, insect bites in 3, dental abscess in 1 and conjunctivitis in 1. All patients with OC or post-sinusitis PC were systemically ill and febrile. There were no differences in mean blood cell count, ESR, and CRP between children with OC and post-sinusitis PC. Blood cultures obtained from 10/21 patients were negative. One conjunctivae culture was positive for *S. pneumoniae*. All children were successfully treated with parenteral antibiotics and no surgical intervention was required. The range of duration of hospitalization was 14-25days in children with OC and 4-14days in those with post-sinusitis PC. Repeat CT scan performed after discharge from the hospital revealed improvement and near complete resolution of the orbital complications and/or sinus congestion.

Conclusions

Clinical examination and laboratory test are not always helpful to differentiate OC from post-sinusitis PC. CT/MRI scans are necessary both to identify/stage orbital complications and to exclude the presence of sinusitis. In our study, pan-sinusitis was the most common cause, a finding with important clinical implications in terms of choice of treatment.

ESP16-0948
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

HERPETIC ESOPHAGITIS, A DIAGNOSIS TO TAKE INTO ACCOUNT IN PATIENTS WITH ACUTE DYSPHAGIA AND FEVER

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Background

Herpetic esophagitis (HE) is a disease commonly associated with immunosuppression, although it also has been described in immunocompetent patients. Herpes Simplex Virus can affect almost any mucocutaneous part in the body, due to primary infection or reactivation. Our aim is to describe the clinical, epidemiological and laboratory findings in pediatric patients with HE presented in a secondary level hospital.

Methods

Retrospective descriptive study reviewing electronic clinical records. We identify children with HE based on endoscopic, anatomopathological and microbiological findings, during 8 years (2007-2015). We describe demographic, clinical, management and evolution data of these patients.

Results

During the period of study, 1040 endoscopic procedures were performed: ten of those patients had a suspicion of HE, but only 7 had laboratory confirmation (70%). The mean age was 8 years (SD3.56), with a predominance of boys (80%). The more frequent symptoms were fever, and odynophagia or dysphagia, presented at emergency department in 90% of the patients. One patient was receiving oral treatment with fluticasone (because of eosinophilic esophagitis) when the symptoms began, but no alteration in immune system was detected at any patient.

Nine children were admitted and managed with intravenous acyclovir. They all improved to complete resolution of symptoms. A follow-up endoscopy was performed, and an underlying condition at gastrointestinal tract was detected in all the children. An eosinophilic esophagitis, previously unknown, was diagnosed in 7 of them.

Conclusions

HE should be suspected in patients with fever and acute dysphagia. It is necessary an endoscopy at acute phase to confirm diagnosis. A follow-up endoscopy after resolution will help us to rule out an underlying esophageal disease.

ESP16-0433
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

MILD ENCEPHALITIS/ENCEPHALOPATHY WITH A REVERSIBLE SPLENIAL LESION ASSOCIATED WITH RHINOVIRUS INFECTION

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Title of Case(s)

MILD ENCEPHALITIS/ENCEPHALOPATHY WITH A REVERSIBLE SPLENIAL LESION ASSOCIATED WITH RHINOVIRUS INFECTION

Background

Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is a clinoco-radiological entity. The clinical manifestations consist of relatively mild neurologic symptoms, most commonly delirious behavior, impermanent consciousness disturbance and seizures. Magnetic resonance imaging (MRI) typically shows reversible lesions with reduced diffusion in the splenium of the corpus callosum, sometimes associated with symmetrical white matter lesions. MERS has been mostly associated with influenza virus, mumps virus, rotavirus and adenovirus infections.

Case Presentation Summary

We report a 7-year-old patient with MERS presenting with recurrent delirious behavior, hallucinations and seizures following common cold. Cranial MRI showed a high intensity signal in the splenium of the corpus callosum on T2- weighted and diffusion weighted images. A low apparent diffusion coefficient (ADC) was noted in the same area. Cerebrospinal fluid (CSF) examinations were normal, CSF cultures and PCR assays of CSF were negative. Serologic testing were also negative. Rhinovirus was detected in the nasopharyngeal swab specimen by multiplex PCR. This is the first reported case of MERS associated with rhinovirus infection. After pulse methylprednisolone therapy, the patient improved rapidly and her cranial MRI findings completely disappeared within 15 days.

Learning Points/Discussion

We have described a case of a previously healthy child who developed MERS secondary to rhinovirus infection. Nonrespiratory symptoms, however, are very rare. The association of MERS with rhinovirus infection has not been previously reported in the literatüre. However, since many patients with MERS have recovered without the administration of corticosteroid therapy, it is difficult to conclude the necessity of steroid pulse therapy for MERS.

ESP16-0953
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

KAWASAKI DISEASE AND EPSTEIN-BARR VIRUS – A COINCIDENCE?

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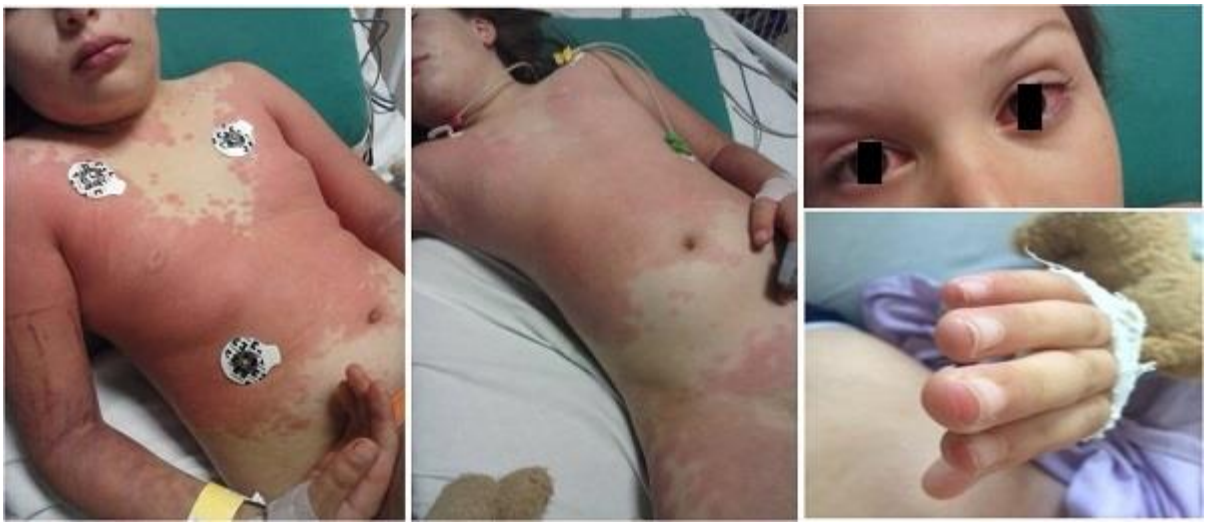
Title of Case(s)

KAWASAKI DISEASE AND EPSTEIN-BARR VIRUS – A COINCIDENCE?

Background

Kawasaki disease (KD) is a systemic vasculitis of unknown etiology. More common in males and between 6 months and 5 years of age (85%), rarely after 7-8 years. Some authors propose an infectious etiology.
With preference for the coronary arterial system, this is the leading cause of acquired heart disease in children, contributing to cardiovascular morbidity and mortality in adults.

Case Presentation Summary



We report a 8-year-old female, previously healthy, with fever and signs of mucocutaneous inflammation. The child presented with progressive and sequential, exuberant and polymorphic exanthema, cervical lymphadenopathy, fever (fourth day), bilateral nonexsudative conjunctivitis and erytema of lips, edema in hands/feet, chest and periungueal desquamation. Persistent sinus tachycardia was identified since third day. No coronary aneurisms were identified.
Blood analyses: elevation of CRP (65-238mg/L) and ESR (29-89mm/h); thrombocytosis (at a later stage); doubtful EBV serology and positive EBV-DNA; other serologies, cultures and immunological investigation were negative.

At day 5 of illness, due to clinical and analytical worsening, antibiotics (ceftriaxone and clindamycin) were prescribed. At fifth day of fever, (KD completed criteria), she started intravenous non-specific immunoglobulin (IVIG-2g/kg - single dose) and aspirin (90mg/kg/day). Fever resolved 48 hours after IVIG, with progressive clinical improvement, and aspirin was reduced to 5mg/kg/day. At two months follow-up, due to persistent supraventricular extrasystoles (SVE) atenolol was started.
Currently (17 months follow-up), she maintains aspirin, atenolol and no clinical signs.

Learning Points/Discussion

KD is a clinical diagnosis requiring a high index of suspicion and expectant attitude, especially in atypical cases.
In this case, although no structural cardiac pathology was found, due to persistent SVE, a long term follow up is mandatory.
What is the EBV role in etiology of KD and cardiac involvement?

ESP16-0992
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

DISSEMINATED HUMAN PAPILLOMA VIRUS (HPV) INFECTION IN 13-MONTH OLD CHILD

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Title of Case(s)

Disseminated Human Papilloma Virus (HPV) infection in 13-month old child

Background

The human papillomaviruses (HPV) cause the formation of verrucous papules and plaques, called anogenital warts or condylomata acuminata. They can occur in children due to heteroinoculation from an infected person or by intrauterine or perinatal infection from the mother who had cervical/vulvar warts during pregnancy. We present a case of a 13-month old girl with disseminated anogenital warts on the skin and mucous membranes, and the progress and effectiveness of treatment with 5% imiquimod cream. So far, there have been few cases described about using this medication in children.

Case Presentation Summary

The 13-month old girl was admitted to our hospital due to anogenital warts that appeared in 9th month of life. Infection occurred from her mother, who had the warts during pregnancy and they resolved spontaneously after childbirth (the cesarean section was performed). There were extensive flesh-colored warts, demonstrating a “cauliflower appearance” in the area of external genitalia and surrounding diaper area. A big, flattened “cockscomb-like” lesion was present in the perianal area. Hyperkeratotic plaques have been observed in the skin folds of the neck and the knee as well. The child had low immunoglobulins IgG and IgA concentration in the serum. Due to extensiveness and localization of skin lesions, the surgical treatment was impossible, therefore we decided to start the “off-label” treatment with 5% imiquimod cream, the mother signed the consent. The treatment resulted in local irritation and progressive reduction of the warts.

Learning Points/Discussion

HPV infection in pregnant women pose a risk of fetal, perinatal and postnatal infant infection. Imiquimod treatment may be an alternative to surgical treatment. Disorders of humoral immunity may predispose to massive infection and its insufficient control.

ESP16-0202
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

VIRAL CROUP COMPLICATIONS IN CHILDREN IN LVIV, UKRAINE

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Background

Viral croup is the most common form of airway obstruction in children 6 months to 6 years of age. Current treatment have reduced the mortality and morbidity associated with croup, but approximately 15% of patients experience a complication of the illness.

Methods

391 immunocompetent children hospitalized in Lviv Infectious Diseases Hospital with with viral croup from January 2013 through November 2013 were enrolled in the study. Their ages ranged between 1 mon. and 60 mon. old. Chest radiograph, CBC, C reactive protein and sputum culture were done for all patients. The Chan croup severity score were used.

Results

3 groups of patients according to the croup severity due to Chan score were formed. The average age of patients at the group 1 was 27,57±1,44 mo, group II - 27,0±0,91 mo, group III - 37,7±5,91 mo. The complications rate were proportional to the croup severity: in children group 1 complication developed in 3.85% patients, group 2 - 13,65%, group 3 - 47,06% patients. The common complications in group 1 & group 2 were acute or obstructive bronchitis, in group 3 - pneumonia. Positive culture upper respiratory tract swabs children with complicated croup was found less frequent (in 63,81% patients) than it in a similar group of patients with uncomplicated disease (78,41% patients, p<0,05). The most common bacterial were *St. viridians, St. pneumonia, St. epidermidis, St. aureus.*

Conclusions

Age of children with severe croup was higher (p<0, 05) than the age of patients hospitalized with croup I - II degree severity. Severe croup developed significantly more often in older children. We don't found any relationship between complications and the rage of identified microorganisms in upper respiratory tract.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-1003
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

BOUTONNEUSE FEVER IN CHILDREN: STUDY OF AN ENDEMIC REGION

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Background

Boutonneuse fever (BF), or Mediterranean spotted fever, is more prevalent in Mediterranean countries. Children are a particularly vulnerable group due to close contact with household animals and playing in gardens or fields. **Aims**: Characterization of clinical features and treatment choices in a level A hospital.

Methods

Prospective study of BF cases admitted to the emergency department, between January 2013-December 2015. After the diagnosis, clinical data was registered by the attending pediatrician and parents were later contacted by telephone for follow-up clinical data. Demographics, clinical presentation, orientation and follow-up were analyzed.

Results

We registered 32 cases of BF (59% males; average 5,2 years old). Most (93,9%) were reported during July to October. First clinical observation was on D3 of disease in 44%. The most frequent related clinical issues were myalgia (37.5%), abdominal pain and headache (25%). Exanthema was present by the 3rd day of fever in 84.4%: maculopapulonodular (53.1%); papular (37.5%) and macular (9.4%). Eschars were found in 59% and regional lymphadenopathy in 46.9%. Most children (75%) owned a domestic animal. Azithromycin (84.4%) or doxycycline (15.5%) was the treatment; with an average of 2 days length of fever after antibiotic beginning. No complications were reported.

Conclusions

Doxycycline is the antibiotic of choice for all patients, however, it is a difficult drug to prescribe to children due to the need of an expensive galenic preparation. Although some studies show better efficacy and safety when compared to macrolides, azithromycin seems to be an efficient alternative and safer in younger children, as showed by this study. It also has a pediatric formulation, is cheaper and only requires a single daily administration.

ESP16-1058
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

ATYPICAL BINOCULAR VESICULAR ERUPTION IN A 5-YEAR-OLD BOY

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Title of Case(s)

Atypical binocular vesicular eruption in a 5-year-old boy

Background

This is the case of a toddler presenting an acute binocular vesicular eruption, associated with high fever, not commonly described as a presentation of HSV-1 infection.

Case Presentation Summary

A 5-year old boy presented in the emergency room with an itching binocular vesicular eruption going on for 5 days, associated with high fever and blurry vision. He just came back from a trip to Florida and he had not met anyone presenting the same symptoms. The differential diagnosis includes infectious diseases as bilateral HZV or HSV infection, contact dermatitis with local superinfection. The clinical exam beside this atypical rash was normal. The ophthalmologic examination with slit-lamp biomicroscopy was quickly performed and showed lesions of epithelial keratitis. Laboratory findings included general blood test that was not discriminant & serology, among it HSV-1 for which IgM were found positive and IgG slightly positive too. Blood cultures were negative but ocular swab PCR and viral culture were positive for HSV-1. The patient was successfully treated with acyclovir, intravenously for 5 days until good clinical resolution of the lesions, and then the treatment was prolonged until keratitis lesions disappeared.

Learning Points/Discussion

Herpetic keratitis is still the leading cause of corneal blindness in children in developed countries. Although the clinical presentation of this case was quite atypical, diagnosis was made thanks to a thorough ophthalmologic exam and positive PCR on the eyelid swab. This condition is often misdiagnosed; we have to remember that children can present, more often than adults, with bilateral ocular HSV infections, and strong immune response often leading to keratitis lesions with severe consequences on the vision.

ESP16-0322
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

MIYASIS OF THE TOE AS THE COMPLICATION OF NEGLECTED WOUND: A CASE REPORT

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Title of Case(s)

MIYASIS OF THE TOE AS THE COMPLICATION OF NEGLECTED WOUND: A CASE REPORT

Background

Myiasis is an infestation of the tissues and organs of living vertebrates by the fly larvae which feed on host's necrotic or living tissue. It is a well-recognized complication of neglected wounds. Here to remind importance of wound care, we report a case with toe myiasis.

Case Presentation Summary

A 17 year-old boy was admitted to Pediatric Emergency Department for delayed wound healing on his left toe. We learned that he had been undergone left great toenail edge excision for ingrown toenail three months ago, after that operation he ignored wound care because of pain during dressing. At this current admission lateral edge of his left toe was hyperemic and swollen without pain or purulent material. On lesion at necrotic tissues larvae were observed. Orthopedist debridated necrotic tissues, removed larvae and antibiotic was initiated for secondary bacterial infection. During hospitalization the wound is kept clean and dry, no any microorganism grown in debridated necrotic material, antibiotic treatment completed to 10 days. Cure was achieved with proper wound care, a month later left great toenail edge excision again for ingrown toenail was done. No any complications or sequel occurred.

Learning Points/Discussion

To initiate prompt treatment for myiasis early diagnosis is important, when despite the appropriate antibiotic treatment open wound healing delay, especially in tropical or subtropical region myiasis should be suspected.

ESP16-0178
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

PERIANAL ABSCESS IN CHILDREN: PEDIATRICIAN PERSPECTIVE

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Background

Perianal abscess (PA) is a common disease that either heals without sequela or develops anal fistulas. We aimed to define characteristics of the children with PA in outpatient clinics, define the factors that influence the clinical outcomes and determine our experience in the perspective of pediatric infectious disease

Methods

The records of all patients who presented to our outpatient clinics with PA between January 2005 and July 2015 were reviewed retrospectively. Information was extracted regarding demographics; symptoms and signs; laboratory evaluation and treatment. Patients who developed PA during a previously known systemic disease were excluded.

Results

A total of 49 children (44 males, 5 females; $p<0.001$), whose data were eligible, were included in the study. Patients had insignificant symptoms at the admission; more than 50% of patients had no fever, no pain, no irritability. Recurrence rate was 51% in all population. All three of the patients with final diagnosis of inflammatory bowel disease (IBD) and all three of the patients with neutropenia at the admission had recurring abscesses. The patients who present with neutropenia were younger than 1 year of age and recovered from neutropenia in 6 months without specific final diagnosis. Three of the patients who were older than 2 years were diagnosed IBD, where all had high ESR at first evaluation. Of the thirty-five patients with culture results of drainage, 26.5% had no microorganisms identified. Sixty –seven percent of abscesses were treated by incision and drainage followed by antibiotics. Twelve of the abscesses subsided without any intervention or drained spontaneously

Conclusions

Further immunologic evaluation of the patients with PA seems unnecessary in the primary work-up. Inflammatory bowel disease should be kept in mind, particularly in patients with high acute-phase response

ESP16-1100
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

SEASONAL AND AGE GROUPS DISTRIBUTION OF HOSPITALIZED CHILDREN WITH ACUTE ROTAVIRUS GASTROENTERITIS AT COSTA RICA'S NATIONAL CHILDREN'S HOSPITAL, PERIOD JANUARY 2010 –DECEMBER 2014

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Background

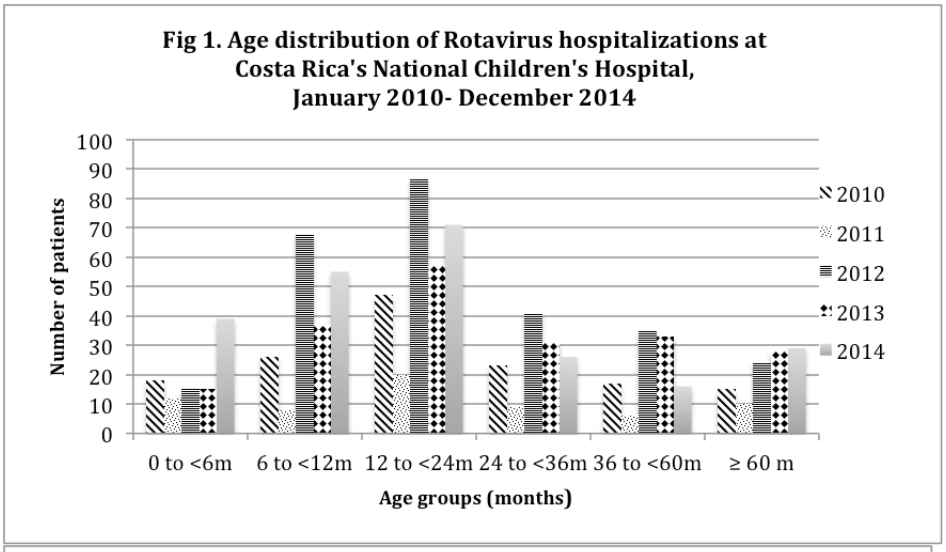
Prior to universal immunization, rotavirus represented one of the leading causes of infant morbidity and mortality in many Latin American countries. In Central America, Costa Rica and Belize are the only two countries without universal rotavirus vaccination. Our main objective was to describe the seasonal distribution and most common affected age groups of acute gastroenteritis due to rotavirus in children hospitalized at our center during 5 years.

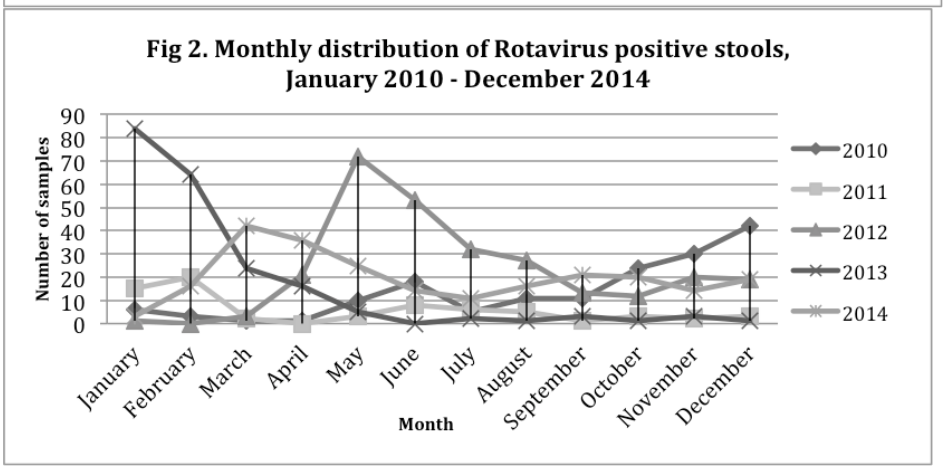
Methods

Retrospective descriptive study of children <13 yrs of age with a laboratory-confirmed episode of rotavirus acute gastroenteritis, period January-1-2010 to December-31-2014, who were admitted at the only national pediatric tertiary and academic referral hospital of Costa Rica.

Results

918 patients were analyzed, 557 (60.7%) were male. Most cases of rotavirus gastroenteritis occurred in children <2 years of age, particularly in those aged 12-24 months (Fig 1). Most episodes occurred during the summer months of Costa Rica (mid-November to mid-April) and the rest during the rainy season (mid-April to early-November) (Fig 2).





Conclusions

Rotavirus has variable seasonal distribution during each year in Costa Rica; however, two peaks occur during the year, the most pronounced during the summer months. Universal vaccination would prevent a significant proportion of these episodes, particularly in the first 2 years of life.

ESP16-0898
03. S - MUCOSAL/NON-INVASIVE BACTERIAL AND VIRAL INFECTIONS

THE BURDEN OF ACUTE ROTAVIRUS GASTROENTERITIS IN CROATIAN CHILDREN – A MULTICENTER PROSPECTIVE STUDY ON CLINICAL CHARACTERISTICS AND MOLECULAR EPIDEMIOLOGY (2012 – 2014)

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Background

Rotavirus *(RV)* infection is the major cause of infectious diarrhoea in children under age 5. The aim of the study was to determine the epidemiology, seasonality, disease severity and genotype distribution of RV strains causing young children's acute gastroenteritis *(AGE)* in Croatia. RV vaccine is not a part of NIP in Croatia.

Methods

1571 children with all-cause AGE, aged less than 5 years, were included in this prospective multicentric study from July 2012 to July 2014. Vesikari and Clark severity scores were calculated, routine laboratory tests were performed and one stool sample was taken for microbiological testing. RV positive samples were further molecularly analysed.

Results

A total of 735 (46.8%) samples were RV positive. RV was the most common cause of AGE in all age groups.The majority of RV AGE were recorded in January and February 2014 (93 and 90, respectively). RV-positive patients were younger than RV-negative ones ($p = 0.0168$). No sigificant differences in laboratory findings were found between two groups of patients. Comparing Vesicari score, more RV-positive patients had moderate to severe illness than RV-negative ($p = 0.0015$). Using Clark score, no differences were found between groups.

G1P8 was the most common RV genotype (60.5%), followed by G2P4 (21.2%), G1P4 (3.3%), G3P8 (3.3%), G2P8 (3%), G9P8 (2.5%).

There were significant differences in geographic distribution of RV genotypes (Table 1). Genotype G2P8 was associated with higher Clark and Vesikari scores compared with other genotypes.

No significant differences in genotype distribution by age groups and by different seasons were found.**Conclusions**

RV is the most common cause of AGE in Croatian children aged < 5 years. RV genotypes show differences in geographic distribution, as well as in clinical severity of disease.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0629
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

DETECTION OF 6 HUMAN HERPES VIRUS INFECTIONS BY MULTIPLEX PCR ASSAY AMONG PEDIATRIC LEUKEMIC PATIENTS

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Background

Our Pediatric leukemic patients are at higher risk of developing herpesviruses infection.

Several different antiviral are effecting for treating herpes viruses infections. However, since different herpes viruses infections presented with similar clinical manifestations, there is an increasing need for accurate and timely diagnosis of herpes infections particularly among immunologically impaired patients suffering from disease and its treatment. Therefore, we aimed at establishing multiplex PCR assay can detect and differentiate 6 types of human herpes viruses included: Herpes Simplex Virus 1 &2(HSV-1,2), Varicella-Zoster Virus (VZV), Human Cytomegalovirus (HCMV), Epstein Barr virus (EBV) and Human Herpesvirus 6 (HHV-6)

Methods

All patient's sera were subjected to multiplex PCR assay to detect 6 human herpes virus (HSV1,2, VZV, HCMV, EBV, HHV6) using specific sets of different primers at the same PCR condition. Thirty control siblings were served as a control group.

Results

An electrogram of multiplex PCR product showed we have amplified the 6 herpes viruses of the expected size when used the specific sets of different primers

A study group of 50 leukemia children, 40/50 showed to be positive for herpes virus DNA (HHSV1,2, VZV, EBV, CMV,HHV6) in WBCs or sera. Multiplex PCR results showed presence of Herpes simplex viruses 1& 2 in 2%, VZV in 16%, CMV in 54%, EBV in 20% and HHV6 in 8% of patient's sera versus 6.7% and 46% for VZV and CMV respectively in the control group with significant difference (p=0.009 and 0.021 respectively).

Conclusions

Multiplex PCR assay is a timely saving diagnostic tool showed that the most common herpes virus infection was CMV and HHV1&2 the lowest frequent viral infection among our symptomatic leukemic children

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0089
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

QUANTITATIVE REAL-TIMES PCR TEST FOR IDENTIFICATION BACTERIAL DISEASES IN PEDIATRICS PRACTICE

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Background

Infectious diseases are caused by microorganisms, such as bacteria, viruses, fungi, and parasites in children. Laboratory tests use a sample of blood, urine, sputum, or other fluid or tissue from the body. Quantitative real-time PCR tests have been extensively developed in clinical microbiology laboratories for routine diagnosis of infectious diseases, particularly bacterial diseases.

Methods

There are two main methods for detection of amplified qPCR products: the first using a fluorescent dye and second using fluorescent resonance energy transfer probes. The distance between the fluorophore and the quencher increases, allowing fluorescence emission detected by the real-time PCR instrument.

Results

Panbacterial qPCR has also been used for quantification of the eight bacteria as easy grow: Staphylococcus Aureus, Streptococcus Pneumoniae, Streptococcus Agalactiae, Streptococcus Pyogenes, Listeria Monocytogenes, Neisseria Meningitidis, Haemophilus Influenzae, Shiga Toxin-producing Escherichia Coli and rapid grow in more than twenty six species of bacteria: Mycobacterium Species, Chlamydia Trachomatis and Neisseria Gonorrhoeae, Chlamydia Pneumoniae and Psittaci, Rickettsia, Coxiella, Ehrlichia and Anaplasma, Bartonella, Mycoplasma Pneumoniae, Urogenital Mycoplasma and Ureaplasma Species, Helicobacter Pylori, Clostridium Difficile, Legionella, Bordetella, Corynebacterium Diphtheriae, Brucella, Francisella, Leptospira, Treponema Pallidum, Borrelia, Bacillus Anthracis, Yersinia Pestis, Tropheryma Whipplei. Test qPCR may allow rapid detection and identification of the antibiotic resistance genetic determinant including genetic alterations affecting structural or regulatory genes involved in antibiotic resistances.

Conclusions

The development of quantitative real-time PCR (qPCR)-based diagnostic tools allowing detection and optional quantification of bacterial DNA in clinical specimens. As compared with conventional PCR, a post-PCR step is unnecessary, which reduces the turn-around time of the analytical process and the risk of contamination with previously amplified nucleic acids.

Diagnostic tests of quantitative real-time PCR that hold promise for the improved management and control of infectious diseases in children.

Systematic Review Registration (Please input N/A if not registered)

ESP16-0616
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

REVIEW OF SPUTUM MICROSCOPY AND CULTURE RESULTS IN PATIENTS TREATED FOR ACTIVE PULMONARY TB IN A PAEDIATRIC TB CLINIC SETTING IN BIRMINGHAM, UK

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Background

Birmingham has one of the highest Tb rates in the UK with an annual rate of 35.2 per 100,000 between 2012-2014.

Tb culture still remains the gold standard for diagnosis.

UK NICE guidelines for Tb make recommendations for diagnosis of active pulmonary Tb. These include obtaining 3 sputum/ gastric washing samples.

The aim of this audit was to review numbers and results of sputum and gastric washing samples for patients that started treatment for pulmonary tuberculosis at the chest clinic in Birmingham between 2/2011 and 9/2014.

Methods

Retrospective audit.

38 children were identified who started treatment for pulmonary Tb between 2/2011 and 9/2014 at Birmingham Chest Cliniic.

Numbers of sputum and gastric washing samples were counted and culture and AFB results were reviewed.

Results

Samples were taken for 31 out of 38 patients.

103 sputum/gastric washing samples were taken overall (mean 3.3 per patient). Of these 20 were culture positive (19.4%). 10 out of 31 patients (32%) had positive Tb cultures. 3 out of these patients also had AFB positive samples.

1 patient with a positive Tb culture had only one sample taken. For the other 9 patients with at least one positive culture for M. tuberculosis 2-7 samples were obtained. All 9 patients had culture negative sputum samples as well as positive ones.

Conclusions

7 patients had no sputum samples sent (children 9-15 years, partly no productive cough).

A mean of 3.3 samples were sent for the other patients (in line with guidelines).

The audit highlights the importance of obtaining multiple samples for Tb culture. Even patients with one definite positive Tb culture also had culture negative samples. PCR testing for M. tuberculosis might improve diagnostic yield in the future.

ESP16-0734
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

RENAL FUNCTIONS AND SERUM ELECTROLYTES IN CHILDREN WITH ACUTE VIRAL HEPATITIS

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Background

Acute viral hepatitis is endemic in Northern India including the state of Punjab.It is usually caused by enterally transmitted Hepatitis A & E viruses.Most of the patients have benign course and don't require hospitalization but some land up in hospital and few developd frank hepatic failure also.Liver function tests have been studied a lot in these patients but renal functions and serum electrolyte levels have not been studied much.The aim of our study was to know the renal function tests and electrolyte levels in admitted patients of acute viral hepatitis.

Methods

This was a retrospective study in which case records of all the consecutive children admitted to the pediatrics department,Dayanand medical college and hospital,Ludhiana,Punjab over last 2 years and diagnosed as cases of Acute viral hepatitis,were included.Data regarding history,clinical examination and relevant investigations was entered in a structured proforma.

Results

A total of 110 cases with diagnosis of acute viral hepatitis were admitted during this time period.Out of these in 76 (69.1%) hepatitis A,13 (11.8%) hepatitis E,5(4.5%) hepatitis B,5(4.5%) hepatitis C and indeterminate in 11(10%) were seen.Serum creatinine was high in 21(19%) ,hyponatremia in 40(36.3%),hypernatremia in 2(1.8%),hypokalemia in 9(8.1%) and hyperkalemia in 35(31.8%) patients.Overall mortality was 6.3%.

Conclusions

Acute viral hepatitis is common cause of morbidity in children.Monitoring of renal functions and electrolytes can help in decreasing morbidity further in these children

ESP16-0633
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

THE ASSOCIATION BETWEEN ENTEROVIRUS SUB-TYPE AND CSF PARAMETERS IN ENTEROVIRUS MENINGITIS

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Background

Enteroviruses are responsible for up-to 50**%** of childhood aseptic meningitis and present with non-specific features, mimicking bacterial infections. Typical CSF changes, including moderate pleocytosis are expected in enterovirus meningitis but high pleocytosis resembling bacterial infection is also recognised and presents a clinical diagnostic challenge. Molecular advances in enterovirus sub-type identification offer an opportunity to explore associations between enterovirus sub-type and CSF parameters, providing further insight into this common childhood infection and aiding clinical decision making pathways.

Methods

A retrospective review of laboratory data for all children aged <16y with positive enterovirus PCR assays on CSF samples from September 2013 to September 2015. Positive CSF samples were typed by sequencing of VP1.

Results

73 enterovirus-positive CSF samples were identified, 71 from symptomatic children, median age 7 weeks, 2 days. 27 isolates underwent enterovirus sub-typing: two cases of mixed Enterovirus-bacterial meningitis were subsequently excluded from analysis Of those 25 with known subtype, Coxsackie-B5 virus (7/25, 28%) and Echovirus-9 (6/25, 24%) were most commonly isolated. The mean CSF white cell count was 238 $x10^6$/L with a significantly higher mean cell count incCoxsackie-B5 meningitis (623 $x10^6$/L, range 27 – 1060) compared to echovirus-9 (9.4 $x10^6$/L, range 1-41. P=0.0039) and other enteroviruses (109 $x10^6$/L, range 1 – 880. P = 0.0079). CSF protein in coxsackie-B5 was higher (mean 0.84 g/L) than other enteroviruses (0.50 g/L, p = 0.02). There was no significant difference in CSF red cell counts or glucose and all CSF samples were taken <24h after antibiotics.

Conclusions

Enterovirus sub-type influences the level of pleocytosis and coxsackie-B5 is associated with higher CSF protein and white cell count in the absence of bacterial co-infection. These results will be validated by analysis of the complete dataset (n=71).

ESP16-0308
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

A STUDY OF BACTERIAL MICROBIOME IN OME CHILDREN: METAGENOMIC ANALYSIS USING NGS TECHNIQUE

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Background

Otitis media with effusion (OME) is one of main causes of deafness in pediatric population. *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* are known as explainable bacterial agents, however, there should be more various commensalism in OME.

Methods

We collected effusion fluid samples from 27 OME children who underwent ventilation tube insertion operation. The sampling procedures were done in the course of surgery. Bacterial culture was done from the fluids. Metagenomic analysis was done by next generation sequencing method(16S ribosomal RNA).

Results

The average age of 27 subjects was 55.1±26.4 months. 11 were boys and 16 were girls. The average follow-up period duration in outpatient clinic before the surgery was 9.8±10.8 months. Antibiotics usage was 10.0±18.9 days within 6 months of follow up. The effusion fluids were mucoid in 11(55.6%), mucopurulent in 6(22.2%), serous in 5(18.5%), and purulent in 1(3.7%). Conventional bacterial culture revealed 11 positive results(Coagulase negative Staphylococcus 4, *H.influenza 2, H.parainfluenzae 1, M.catarrhalis 2, others 2).* Metagenomic analysis showed diverse results in all patients presenting various taxonomic abundance. In majority (n=16), *H.influenzae* was dominant. Other bacterial taxonomic results were as follows: *Moraxella*(n=5), *Propionibacterium*(n=8), *Staphylococcus*(n=3), *Streptococcus*(n=3), *Corynebacterium*(n=2), *Methylobacterium*(n=2), *Enhydrobacter*(n=2), *Sporolactobacillus*(n=1), *Pseudomonas*(n=1), *Bacillus subtilis*(n=1).

Conclusions

According to metagenomic analysis using 16s rRNA sequencing among 27 Korean children with OEM, *H.influenae* seems most important agent following *M.catarrhalis. Streptococcus* was detected scarcely.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0043
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

UTILITY OF MAGNETIC RESONANCE IMAGING IN THE FOLLOW-UP OF ACUTE OSTEOMYELITIS IN CHILDREN

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Background

Acute osteomyelitis is characterized, especially in children, by high morbidity due to extension of the infectious process or its chronicization, associated with permanent sequelae and disabilities. No guidelines exist for the follow-up of children affected by acute osteomyelitis, especially regarding the utility of magnetic resonance imaging (MRI), which has been evaluated so far in a single study.

Methods

We retrospectively reviewed MRI studies and medical records of children admitted to our Pediatric Department in Milan for acute osteomyelitis from 2008 to 2015. All children who had a follow-up MRI performed at least 10 days after diagnosis were included in the study. Exclusion criteria were age 18 years or more, more than 1 year time passed between MRI at diagnosis and at follow-up, tubercular osteomyelitis, subacute or chronic osteomyelitis. We analyzed if MRI follow-up prompted a change in patients' treatment.

Results

A total of 28 MRI studies were performed in 27 children (13 males and 14 females). Infection involved the appendicular skeleton in 64.3% of patients. Five (18%) of these studies prompted a change in patients' treatment. The only statistically significant indication for change in the therapeutic approach was MRI performed for persistence of worsening of the disease ($p=0.0058$). Change in bone signal at MRI, and time (more or less than 28 days) passed between MRI at diagnosis and follow-up were not significantly associated with change in the patients' treatment ($p=0.40$; $p=0.40$, respectively).

Conclusions

Routine MRI follow-up is not useful in children affected by acute osteomyelitis who adequately respond to antibiotic treatment. It can be useful, in adjunct to clinical evaluation, in those patients who do not promptly and adequately respond to treatment. Clinical monitoring remains the mainstay in the follow-up of these patients.

ESP16-0290
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

DOES AN EOSINOPHIL COUNT >200/µL RULE OUT A SERIOUS BACTERIAL INFECTION IN YOUNG FEBRILE CHILDREN?

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Background

Early diagnosis of serious bacterial infections remains one of the challenges for clinicians. The aim of this study is to assess the value of the eosinophil count to rule out serious bacterial infection (SBI) in young children with fever.

Methods

Retrospective cohort study with subject recruitment over a 24-month period, from January 2012 to December 2013. Children between 1 and 36 months with fever who had blood samples drawn for complete blood count and procalcitonin were included. The usefulness of the absolute eosinophil count to differentiate serious bacterial infection from non-serious bacterial infection (non-SBI) cases was studied.

Results

A diagnosis of SBI was made in 85 out of 574 cases. In 491 cases, the eosinophil count was <200/µl; a SBI was diagnosed in 13/83 cases with an eosinophil count >200/µl and in 72/491 cases with an eosinophil count ≤200/µl. Sensitivity, specifity, positive and negative predictive values (with their 95%CI) for an eosinophil count >200/µl were: 0.15 (0.09-0.25), 0.86 (0.82-0.89), 0.16 (0.09-0.26) and 0.85 (0.82-0.88), respectively. Among the 83 patients with an eosinophil count >200/µl only 3 had a procalcitonin level >1 ng/ml, and only one of these had a SBI.

Conclusions

Absolute eosinophil count is not a reliable marker of SBI in young febrile children but counts >200/µl make the possibility of a SBI less likely. Moreover, procalcitonin levels do not seem to add any information in these patients. Should these results be confirmed, a high eosinophil count could be used to rule out the need to perform a procalcitonin test, which would be of interest in settings of limited resources.

ESP16-0805
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

EVALUATION OF FILMARRAY MENINGITIS/ENCEPHALITIS PANEL PERFORMANCE FOR RAPID DIAGNOSIS OF MENINGITIS IN CHILDREN

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Background

Meningoencephalitis remains one of the most important infections in children and requires early diagnosis and immediate treatment. The FilmArray Meningitis/Encephalitis (ME) Panel is a multiplex PCR-based point-of-care system able to detect 15 of the most significant meningitis causative pathogens directly from cerebrospinal fluid in just one hour.

Objective
To evaluate performance of FilmArray ME Panel for etiological diagnosis of children with clinical suspicion of meningitis/encephalitis.

Methods

A retrospective study was performed evaluating 26 CSF samples, 20 of which were previously found to be positive by Real-Time PCR for Enterovirus (n=5), Herpes-1 Virus (n=1), Varicella Zoster Virus (n=1), Parechovirus (n=1), *N.meningitidis* (n=6), *S.pneumoniae* (n=5) and *S.agalactiae* (n=1). The remaining 6 samples were collected from patients with clinical suspicion of meningo/encephalitis and yielded negative results by bacterial culture and our routine monoplex real-time PCR profile of 8 target pathogens (*N.meningitidis, S.pneumoniae*, Enterovirus, Herpes-1, Herpes-2, Varicella Zoster, Epstein-Barr and Cytomegalovirus). The FilmArray ME Panel includes *E.coli K1, H.influenzae, L.monocytogenes, N.meningitidis, S.agalactiae, S.pneumoniae*, Herpes-1, Herpes-2, Varicella Zoster, Cytomegalovirus, Herpes-6 Virus, Enterovirus, Parechovirus*, Cryptococcus gattii* and *Cryptococcus neoformans.*

Results

Among 20 confirmed positive samples for meningoencephalitis, FilmArray detected all samples except for one (a low positive *N.meningitidis* DNA, Ct=39.6). In addition, it detected a coinfection of *S. pneumoniae* and Herpes-6 Virus in a sample that was only reported positive for *S.pneumoniae* by culture/PCR. Among 6 negative samples, FilmArray detected Herpes-6 Virus in one sample while the rest of samples tested negative. Sensitivity of FilmArray compared to our routine approach was 95.0% (95% CI, 75.1-99.9) and specificity was 83.3 % (95% CI, 35.9-99.6).

Conclusions

The FilmArray ME Panel showed to be a useful point-of-care system for rapid and accurate diagnosis of pediatric meningitis/encephalitis.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0702
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

INFLUENZA AS A CAUSE OF HOSPITALIZATION OF CHILDREN

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Title of Case(s)

INFLUENZA AS A CAUSE OF HOSPITALIZATION OF CHILDREN[1]

[1] *MCPE grant 501-1-20-19-14*

Background

Introduction: In Poland, according to the epidemiological period, there has been a few thousand to several million cases and/or suspected cases of influenza and/or flu-like infections. It seems that these figures may be underestimated due to the inadequacies of the monitoring of cases of infectious diseases and failure by physicians obligation to report suspicions of disease and illness to the State Sanitary Inspection.

Case Presentation Summary

Material and Methods: In the Clinical Department of Pediatric and Emergency Department of Bielański Hospital in 2013 hospitalized 65 patients (aged 0-18 years) diagnosed with influenza A and B. Influenza was diagnosed based on history, physical examination and the results of the rapid test RIDT diagnostic and / or test result by molecular biology (RT-PCR).

Results: Diagnosed 23 (35.4%) cases of influenza A, 39 (60%) of influenza B (60%). Three children (4.6%) test was positive for influenza A and B. 90.8% (59/65) children for 5 days, received oseltamivir (Tamiflu) in the dose recommended by the manufacturer. In 24 (40.7%) of them had complications requiring further treatment.

Learning Points/Discussion

Conclusions: Influenza is a disease that can be carried in a heavy, connecting with numerous complications. Currently, there are effective medications aganist flu. The best form of prevention against influenza is vaccination. In the study group, illness from the flu did not change the attitude of parents to vaccination. Only two (3.1%) children from the study group were vaccinated in consecutive seasons.

ESP16-0597
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

DETECTION OF THE EMERGING HUMAN PLASMODIUM KNOWLESI INFECTION IN NORTH SUMATERA, INDONESIA

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Background

After a large focus of *Plasmodium knowlesi* infecting humans reported in Borneo Malaysia in 2004, other reports of knowlesi infection in humans were documented in other Southeast Asian countries. Indonesia has limited documentation of human *P. knowlesi* infection, despite the wide distribution of the reservoir hosts and vectors across the country. Detection of *P. knowlesi* so far is identified and confirmed by molecular assay with a target on the small-subunit rRNA gene. However, studies have noted the possibility of cross-reactivity of the current standard primers with *P. vivax* isolates. This study aimed to determine the distribution of *P. knowlesi* cases in North Sumatera and to validate the novel PCR assay designed for detection of *P. knowlesi*.

Methods

Active and passive case screening were performed in 3635 participants in Batu Bara regency, Langkat regency and South Nias regency. Finger-prick blood samples were collected for RDT, microscopy examination and filter paper dried blood spots. DNA were extracted using Chelex and screened for all human *Plasmodium* infection using species-specific nested PCR described by Snounou. Additional hemi-nested PCR assay targeting other *P. knowlesi* gene was also performed to confirm *P. knowlesi* findings.

Results

P. falciparum, *P. vivax*, *P. malariae* and *P. knowlesi* each contribute to human malaria infections in North Sumatera province. Mixed-infections of *P. vivax* and *P. knowlesi* were identified using the standard assay. However, confirmation through other PCR method was failed in several samples indicating cross-reactivity with *P. vivax* isolates.

Conclusions

P. knowlesi occurs frequently in humans in North Sumatera province, Indonesia. Our newly designed PCR assay can be used for detection of *P. knowlesi* cases in areas where *P. vivax* and *P. knowlesi* are both sympatric.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0844
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

PROPOSAL OF ON-LINE APPLICATION FOR DIAGNOSTIC AND TREATMENT APPROACH TO THE PATIENT WITH ACUTE RHINOSINUSITIS AS AN EXAMPLE OF PRACTICAL RECOMMENDATIONS' IMPLEMENTATION TO MEDICAL PRACTICE

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Background

While acute rhinosinusitis (ARS) is a very common condition, only 0,5-3% of patients develop bacterial superinfection and need antibiotic treatment. Overprescribing antibiotics is a common problem in Poland. Our aim was to develop a practical solution in antibiotic therapy of ARS using on-line tools.

Methods

Our algorithm is based on data suggesting viral etiology or bacterial superinfection. Factors like age, anamnesis of beta-lactam allergies and previous treatment are considered. After completing basic data (age, weight, symptoms) algorithm redirects the user into the page with appropriate antibiotic therapy, with dosage automatically calculated or assesses the lack of indications for antimicrobial treatment. The system also attach the list of medications available on the Polish market and generates the sample prescriptions.

Results

We have designed our application with a user-friendly interface that helps doctors choose the best diagnostic and therapeutic approach to the patient with symptoms of ARS.

Conclusions

Our on-line tool which saves the doctor's time may facilitate clinical practice and enhance guideline adherence of physicians attending to children with ARS as well as may have a positive influence on antimicrobials resistance. We believe, that using actual recommendations in such practical facilitated way can improve antibiotics' regimen in Poland.

ESP16-1088
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

IMPLEMENTATION OF A POINT OF CARE MOLECULAR RESPIRATORY VIRUS TEST FOR PAEDIATRIC ADMISSIONS: STAFF PERCEPTIONS

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Background

The Enigma® MiniLab™ FluAB/RSV assay, a fully automated molecular assay with less than 2 minutes of hands on time and which requires no sample manipulation. We surveyed satisfaction in its use by ward staff on a Paediatric Respiratory ward of the Evelina London Children's Hospital during the winter of 2014/2015.

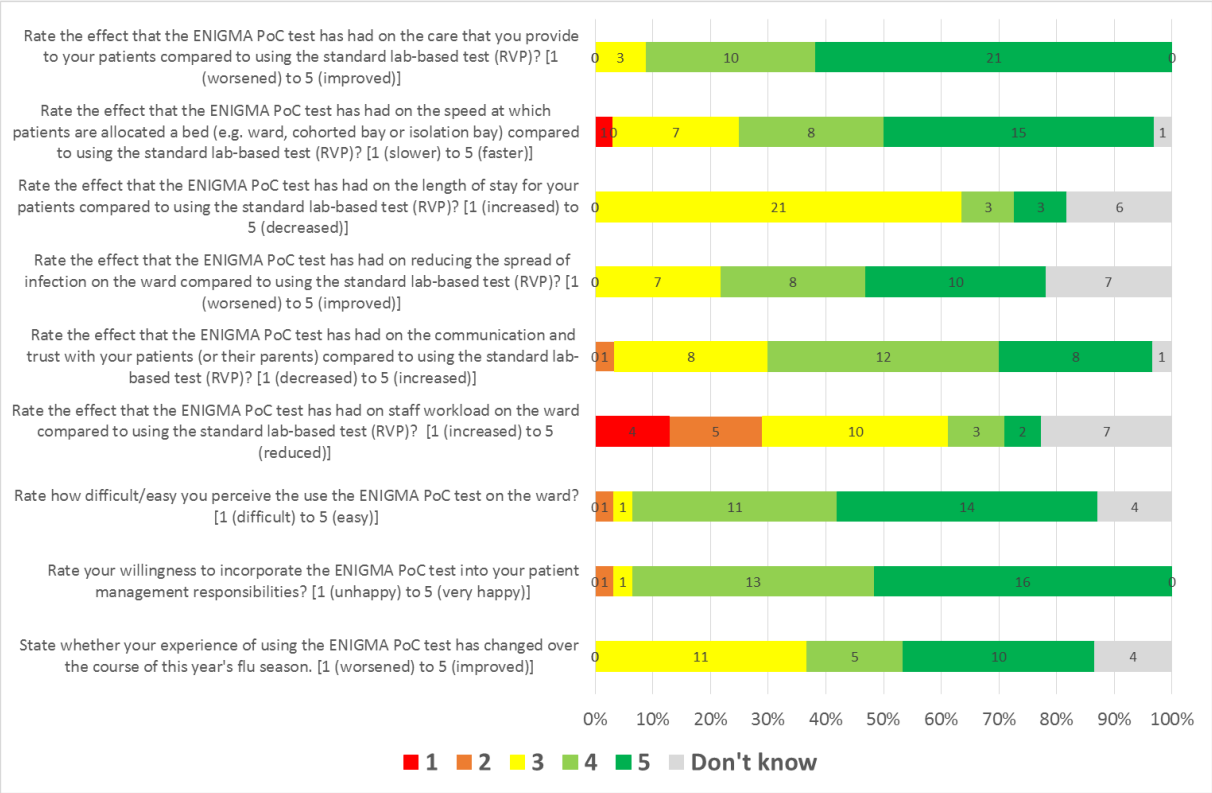
Methods

56 ward staff were trained to use the Enigma ML FluAB/RSV assay. Robust processes were put in place, prior to evaluation, to ensure results were acted on appropriately, recorded and communicated to appropriate teams. Staff satisfaction with the assay was assessed using an incentivised online staff satisfaction survey. The survey contained 9 Likert-scale questions and 15 open-ended questions.

Results

The questionnaire data revealed that staff thought that Enigma ML FluAB/RSV assay was simple to use (81% agree, 7% disagree) are willing to incorporate it into their responsibilities (94% agreeing, 7% disagreeing). The majority of respondents thought that it improved communication and trust with patients (67% agreeing and 3% disagreeing), and that patient care (91% agreeing, 9% disagreeing). However, most questionnaire respondents felt that

using the assay had increased their workload (29% agreeing, 16% disagreeing).



Conclusions

The clear positive review of this assay by staff, despite the increased workload it entails, shows the importance of improving turn around times for respiratory diagnostics. Such platforms are to be welcomed where robust processes can be implemented to ensure the appropriate governance of their output

ESP16-0751
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

CARE FOR CHILDREN WITH URINARY TRACT INFECTIONS ACCORDING TO DIFFERENT GUIDELINES: DIFFERENCES EXPLAINED

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Background and Objective

The aim of this study is to review different professional guidelines for diagnosis, treatment and follow-up of children with urinary tract infection. Furthermore, we aim to explain the differences between different guidelines.

Methods

We searched for guidelines and position statement papers about diagnosis, treatment and follow-up of children with urinary tract infection. Guidelines were reviewed on statements about methods of urine collection in incontinent children, therapy mode during the febrile phase of urinary tract infection and recommended investigations after diagnosis of urinary tract infection. Discrepancies in different statements are further explained by available studies.

Learning Points Discussion

7 guidelines were included for analysis, 1 of these guidelines was published by a urologic society, the rest were published by paediatric societies. 3 guidelines recommend a mid stream clean catch urine sample as preferred sample for urine culture, whilst the other guidelines recommend more invasive methods for collecting urine for culture (catheterization or suprapubic aspired urine). Almost all guidelines recommend oral antibiotics for most children with febrile urinary tract infection. The value of routine ultrasound screenings of children with febrile urinary tract infection has been challenged by the widespread implementation of antenatal ultrasound screening programs. Different strategies are described for performing voiding cystourethrogramme (VCUG) and nuclear scans after (recurrent) urinary tract infections, future research should select the optimal strategy.

Different guidelines can navigate the clinician in the care for children with urinary tract infection. Discrepancies between statements in these guidelines exist for issues as urine collection methods for incontinent children and invasive investigations after febrile urinary tract infection.

ESP16-1031
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

MOBILE APP – A NEW TOOL FOR DIAGNOSIS AND TREATMENT OF ACUTE OTITIS MEDIA (AOM)

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Background

Acute otitis media (AOM) is one of the most common infections of childhood. Despite this, GPs often have a problem with choice of appropriate treatment. Our aim was to create a simple on-line tool based on available European and local recommendations, that should facilitate the implementation of guidelines in AOM and could be used in daily practice.

Methods

The current guidelines were as the scientific groundwork.

Results

This application consists of “boards” presenting the successive steps of diagnostic process. First, there are questions about patient’s signs and symptoms, and otoscopy findings – answering these questions helps to diagnose AOM. The second step is the choice of appropriate way of treatment – answering the questions about patient’s age and presence of severe symptoms (such as: high fever, vomiting or ear leaking) appearing on the display, the doctor can decide whether the antibiotic therapy is necessary. If antibiotic therapy is necessary, then the next step is the choice of proper drug. The application provides information about available drug forms and doses, as well and possible treatment in the case of e.g. allergies to some drugs.

Conclusions

In the era of ubiquitous Internet access, there is a need to create on-line tools that can accelerate and facilitate doctors’ work. The online applications become more popular and probably in the future they will standardize medical practice about acute otitis media in accordance with current guidelines as well as reduce antibiotic overuse.

ESP16-0599
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

PROGNOSTIC VALUE OF SERUM PROCALCITONIN LEVELS UPON ADMISSION OF CHILDREN HOSPITALIZED WITH COMMUNITY-ACQUIRED PNEUMONIA

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Background

Procalcitonin(PCT) is an inflammatory biomarker that has been studied in children with community-acquired pneumonia(CAP) as a biologic predictor of bacterial infection. We aimed to evaluate the prognostic value of serum PCT levels on admission in relation to therapeutic response to aqueous penicillin G, stratified by aetiology, among children hospitalized with CAP.

Methods

Children under-5-years-old hospitalized with CAP were evaluated in a 21-month period. On admission, clinical and radiological data were collected as well as nasopharyngeal aspirates and blood to investigate 19 aetiological agents and serum PCT levels. Evolution and outcome were registered in standardized forms. Children with pleural effusion on admission were excluded.

Results

The study group comprised 89 patients. The median(interquartile range) age was 18(11-27) months and 53(60%) were boys. Viral (49.4%), typical bacterial (38.2%) and atypical bacterial (12.4%) infections were diagnosed. Overall, 25.8% were pneumococcal infections. In total, 75 (84.3%) children became afebrile within 48hr of treatment. Median serum PCT(ng/ml) levels on admission was higher in 14 children who remained febrile after 48hr of treatment (2.1[0.8–3.7] *versus* 0.6[0.1-2.2];P=0.025). In these children, pneumococcal infections were more common (71.4% versus 17.3%;P<0.001). PCT levels on admission were higher in children with pneumococcal pneumonia (2[0.7–4.2] *versus* 0.5[0.08–2.1];P=0.002). The ROC curve found that 0.25ng/ml of serum PCT had a high negative predictive value (93% [95%CI:80%–99%) for pneumococcal infection. All children that remained febrile after 48hr of treatment had PCT >0.25ng/ml on admission.

Conclusions

Serum PCT level >0.25ng/ml predicted delayed clinical response to antibiotic therapy and pneumococcal aetiology.

ESP16-1028
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

HERPES SIMPLEX VIRUS-2 ENCEPHALITIS IN A HEALTHY CHILD

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Title of Case(s)

Herpes simplex virus-2 encephalitis in a healthy child

Background

Herpes Simplex Virus (HSV), HSV-1 in particular, is the most common cause of viral encephalitis in children. HSV-2 encephalitis is usually described in neonates or in immunocompromised children.
We report an immunocomptent 23 month-old-boy with HSV-2 encephalitis, following a primary infection.

Case Presentation Summary

Previously healthy 23 month-old-boy presented with a five day course of fever and painful oral ulcerations, associated with multiple episodes of generalized non-febrile seizures. His father reported recent perioral herpetic lesions. The diagnosis of HSV-2 encephalitis was established by detection of HSV-2 DNA in cerebrospinal fluid (CSF) using polymerase chain reaction (PCR), associated with bitemporal paroxistic activity in electroencephalogram. The child was treated with a 21 day course of intravenous acyclovir. To monitor treatment response we repeated PCR for HSV in CSF, which was negative. A complete resolution of symptoms was observed.

Learning Points/Discussion

We report an unusual agent of encephalitis outside neonatal period in an previous healthy child, reminding that HSV-2 should be considered in the viral diagnosis of encephalitis. It also illustrates that the combination of clinical symptoms and CSF PCR for HSV DNA provides a rapid, specific and sensitive tool for early diagnosis, especially if there is a clinical evidence of a primary infection.

ESP16-1000
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

MOBILE APPLICATION TO GUIDE URINARY TRACT INFECTION THERAPY IN CHILDREN

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Background

Urinary tract infection (UTI) in children, although frequent, is still a subject of controversy concerning diagnosis, treatment and further evaluation. Recent development of mobile device-related application technology offers new possibilities of applying current recommendations and facilitating decision making in clinical practice.
The objective of this paper was to develop an algorithm suitable for a mobile application for clinicians to guide their diagnostic and therapeutic decisions in children with UTI.

Methods

Four current guidelines (NICE, AAP, Italian, Polish) concerning UTI in children were analyzed and compared, upon which a thorough algorithm was developed. The choice of antibiotic therapy took into consideration local epidemiology and antibiotic resistance patterns.

Results

After inserting age, weight and choosing clinical symptoms, the user will receive indications to perform urine tests with laboratory results interpretation and optimal antibiotics choice with automatically calculated dosage. The algorithm includes UTI risk factors, indications for hospitalization and for further diagnostics. It divides patients into three age categories: up to 28 days, 1-24 months and over 24 months. The system also attaches the list of antibiotics available on the Polish market and generates the sample prescription.

Conclusions

The offered algorithm is a proposal for clinicians and policy-makers interested in applying new technologies into clinical practice. This may moderately facilitate clinical practice and enhance guideline adhenernce of physicians attending to children with UTI.

ESP16-0743
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

A MOBILE DEVICE DIAGNOSIS AND TREATMENT AID APPLICATION FOR SEXUALLY TRANSMITTED DISEASES (STDS) FOR GENERAL PRACTITIONERS

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Pediatrics and Clinical Decisions Department, Warsaw, Poland

Background and Objective

Damian Okruciński, Dominika Pomorska, Ernest Kuchar

Title:
A mobile device diagnosis and treatment aid application for sexually transmitted diseases (STDs) for general practitioners.

Objective:

Effective diagnosing and treatment of STDs pose a problem in outpatient clinics due to the lack of quick laboratory tests and often times poor physicians' education in the matter in Poland, especially in children. Our aim was to streamline this process, creating an aid tool for diagnosis and treatment of STDs in the form of a mobile device application easily available to general practitioners.

Methods

Methods and results:

Our algorithm is based upon recommendations stemming from the Centre for Disease Control (CDC) and International Union Against Sexually Transmitted Infections (IUSTI). The application allows two types of input: either by known disease aetiology or by clinical symptoms. The 'known disease aetiology' path provides treatment recommendations after inputting the previously diagnosed disease, whereas the 'clinical symptoms' path can be utilized to obtain the same based upon the patient's signs and symptoms if the aetiology is not known. In both pathways the sex, age, weight, pregnancy and HIV status of the patient determine the suggested treatment plan and need for further auxiliary testing. The recommended dosage is automatically calculated based on weight and age, as well as presenting medications available on the Polish market. The application will be distributed solely among physicians and health care professionals.

Learning Points Discussion

Conclusion: Our intuitive, easy to use and time-sparing mobile device application can unify and improve STDs management in children in Poland, reduce antimicrobial resistance and raise STD awareness amongst GPs.

ESP16-0675
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

THE IMPORTANCE OF INCUBATION LATENCY AND 37^{0}C THE URINE PRIOR TO CULTURES

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Background

The purpose of this study is to demonstrate how transportation time and temperature prior processing urine samples have an increase on bacterial culture recovery. A modification to the gold standard technique -CLSI (Clinical and Laboratory Standards Institute -gold standard) was done. This novel approach reduces significantly the percentage of negative cultures; we sought to rule outa UTI.

Methods

All the 223 urines were smeared by the method of the CLSI and our new technique. These are modifications: 1. Samples were smeared as soon as possible, if not, they were kept in an incubator at 37^{0}C until smeared. 2. The urines were smeared as CLSI after 2 hours, 5-7 hours, and 24 hours of incubation.

Results

In the present study: 114 symptomatic, 109 asymptomatic patients, were tabulated and compared with the initial colony counts. Symptomatic patients had >100.000 CFU/mL CLSI 27.1%, by the new technique: after 2 hours incubation of 27.1%, 5 to 7 hours 39.4%, after 24 hours 82.4%. This novel approach can give from 24-48 hours earlier results than CLSI.

In asymptomatic group, they were >100.000 CFU/mL positive cultures by CLSI method 0.91% ($p<0.05$), and with the new technique-leaving urine 5-7 hours 7.3% and after 24 hours 43.1%. This percentage can be given because some people have an asymptomatic UTI.

Conclusions

This study suggests to leave the sample at 37^{0}C to keep the bacteria in a corporal temperature until is smeared. The new technique improves significantly the percentage of positive cultures, can help to reduce costs in days of hospitalization, diagnostic tests, plus it upgrades patients relieve in terms of urinary symptoms. Here we show that bacteria grow better in the same urine habitat rather than in artificial media.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0044
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

CAN PROCALCITONIN BE A DIAGNOSTIC MARKER FOR CATHETER-RELATED BLOOD STREAM INFECTION IN CHILDREN?

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Background

The potential role ofprocalcitonin (PCT) in the diagnosis of catheter-related blood stream infection (CRBSIs) is still unclear and requires further research. The diagnostic value of serum PCT for the diagnosis of CRBSI in children is evaluated here.

Methods

This study was conducted between October 2013 and November 2014, and included suspected patients of CRBSI from 1 month to 18 years of age who were febrile, with no focus of infection, and with a central venous catheter. Levels of PCT and other serum markers were measured, and their utility as markers of CRBSI was assessed. Additionally, the clinical performance of a new, automated, rapid, quantitative assay for the detection of PCT was tested.

Results

Among the 49 patients, 24 were diagnosed with CRBSI. The PCT-Kryptor and PCT-RTA values were significantly higher in proven CRBSI compared to those in unproven CRBSI ($p = 0.03$ and $p = 0.03$, respectively). There were no differences in the white blood cell counts and C-reactive protein (CRP) levels between proven CRBSI and unproven CRBSI. Among the 24 patients with CRBSI, CRP was significantly higher among those with gram-negative bacterial infection than in those with gram-positive bacterial infections. PCT-Kryptor was also significantly higher among patients with gram-negative bacterial infection than in those with gram-positive bacterial infections ($p = 0.01$ and $p = 0.02$, respectively).

Conclusions

We suggest that PCT could be a helpful rapid diagnostic marker in children with suspected CRBSIs.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0776
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

BACTERIAL IDENTIFICATION BY 16S RRNA GENE PCR IN CULTURE NEGATIVE MENINGITIS

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Title of Case(s)

Bacterial identification by 16S rRNA gene PCR in culture negative meningitis

Background

Bacterial meningitis is a life-threatening disease with a significant mortality and morbidity worldwide. The traditional diagnosis is based on bacterial cultures. However, prior use of antibiotics can result in false-negative cultures.

Case Presentation Summary

A previous healthy 8-year-old German boy, on holiday in Portugal, presented to the paediatrics emergency department with fever, vomiting and decreased level of consciousness. Two days earlier, he started with fever and right earache. He was then diagnosed acute otitis media and right hemotympanum - medicated with amoxicillin and clavulanic acid. Physical examination on admission revealed nuchal rigidity and petechiae (adding to the previous signs/symptoms). Cranial computerized tomography (CT) showed opacification of the right tympanic-mastoid. Cerebrospinal fluid (CSF) examination revealed 2342 leukocytes/mm3, elevated protein concentration (257mg/dL) and low glucose level (17mg/dL). With presumed diagnosis of bacterial meningitis and myringitis, he was administered ceftriaxone and vancomycin for 14 days and dexametason for 2 days. He underwent miringocentesis and tympanic ventilation tube insertion by the second day of hospitalization. Blood and CSF cultures were negative. Initial CSF was sent to bacterial identification by 16S rRNA gene PCR and revealed a positive result for Streptococcus pneumonia. Audiometric screening was normal.

Learning Points/Discussion

Nucleic acid amplification tests, such as PCR, act independently of agents' growth and are able to detect small amounts of pathogen DNA, directing antibiotherapy. The major benefit on this approach, compared to classical techniques, is on detecting infectious etiology, despite negative blood or CSF cultures.

ESP16-0465
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

NOVEL RAPID AMPLIFICATION TECHNOLOGY FOR POINT-OF-CARE DIAGNOSIS OF RESPIRATORY SYNCYTIAL VIRUS INFECTION IN CHILDHOOD

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Background

Acute respiratory tract infection (ARTI) caused by respiratory syncytial virus (RSV) is a frequent cause of hospitalization in young children. Early diagnosis can prevent nosocomial infections and reduce morbidity and mortality in patients with high risk for severe infection. The aim of this study is to apply novel isothermal amplification methods for point-of-care testing in children hospitalized with ARTI.

Methods

Currently, there are limited possibilities to diagnose RSV in a point-of-care setting. We evaluated a novel DNA amplification technique, called “Loop-mediated Isothermal Amplification” (L-AMP) allowing highly sensitive detection of RSV within approximately 30 min at comparably low costs. Results are compared with real-time PCR as a gold standard. The L-AMP test was first evaluated using patient samples in a laboratory setting during the winter season 2014/2015 and was then transferred to a routine application at the Paediatric Outpatient Department of the Heidelberg University Hospital during the winter season 2015/2016. Nasopharyngeal swabs were obtained from all hospitalized children presenting symptoms of ARTI.

Results

In a laboratory setting, the L-AMP test showed a test sensitivity of 73% compared to 58% sensitivity of the conventional point-of-care RSV rapid antigen detection test. Routine point-of-care application of L-AMP was successfully implemented in November 2015. A total of 111samples (mean age: 22 months; 40 % female) were collected. The LAMP test detected RSV in 25 samples, RSV real-time PCR revealed 33 RSV positive samples. The L-AMP test in the clinical setting showed a sensitivity of 75% when compared to laboratory testing with conventional PCR (95% CI: [61,1%; 90,4%]).

Conclusions

This innovative approach could substantially enhance the accuracy to detect ARTIs in a point-of-care setting, and thereby decrease the morbidity and mortality associated to nosocomial infection.

ESP16-0705
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

LUNG SEGMENTATION IN DIGITAL CHEST X-RAY IMAGES USING GRAPH CUT OPTIMIZATION METHOD

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Background

Chest X-Ray is performed to diagnose or monitor treatment for conditions of pneumonia, emphysema, lung cancer, line and tube placement and tuberculosis by Physicians. Lung Segmentation, is used in screening systems, is important for allowing timely treatment, and thereby increasing accessibility to and productivity of Lung diseases. The purpose is to present a supervised classification algorithm to detect large, irregular lung oriented diseases

Methods

This work is an attempt to extract the Lung Boundary so that it can trace severity of any infection. It presents a non-rigid registration driven segmentation of lung which uses retrieval based specific lung model to trace the boundary of lungs.This work consists of the following modules,

à Input X-ray

à Find the shape similarity for the CXR database using CBIR

à SIFT Flow Non-Rigid Registration

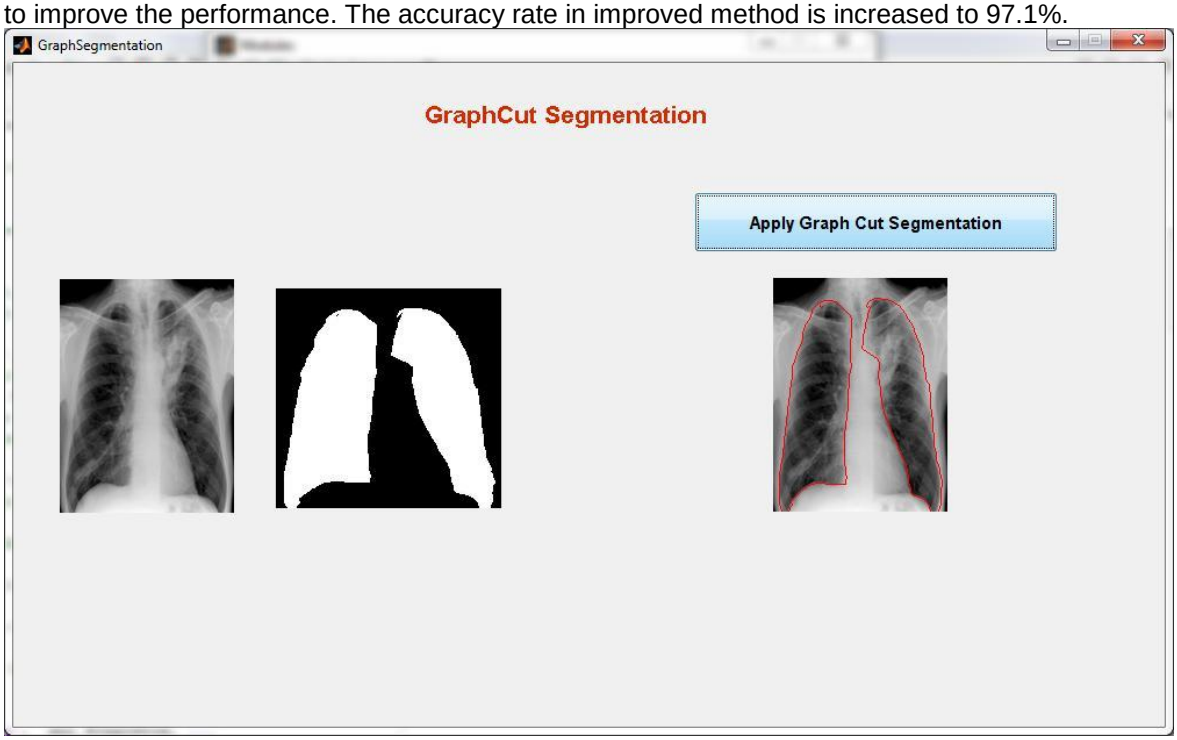
à Graph cut Segmentation

à Find Lung Boundary

Results

In earlier approach the accuracy rate was 95.4% with the Dice coefficient and Average contour distance metric were done. Objective Measures of Boundary Evaluation like Sensitivity & Specificity, Precision, Recall & Error Probability, and Accuracy are evaluated in the improved approach. In graph cut method, the energy function and kernel function are used

to improve the performance. The accuracy rate in improved method is increased to 97.1%.



Conclusions

Detecting the lung regions in chest X-ray images is an important component in computer-aided diagnosis(CAD) of lung health. In certain diagnostic conditions the relevant image-based information can be extracted directly from the lung boundaries without further analysis. This research work will help the Doctors to identify the severity of the infection with the chest X-Ray image itself, instead of going for other expensive diagnosis tests. This Lung Segmentation will help the physict to find any type of infection in the patients.

ESP16-0935
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

URINARY GROUP B STREPTOCOCCAL ANTIGEN TEST

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Background

Group B streptococcus (GBS) represents the leading pathogen causing neonatal infection. Isolation of GBS from usually sterile body fluids remains the gold standard for diagnosis, but urinary antigen latex agglutination (ALA) tests may play a role.
The aim of this study was to evaluate the sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) of this test.

Methods

Longitudinal retrospective study that included all infants who performed ALA tests between 2000 e 2015 in our hospital.
True positive (TP) was defined as positive ALA test in a child with positive culture, false negative (FN) as a negative ALA test in a child with a positive culture, true negative (TN) as a negative ALA test in a child with a negative culture and false positive (FP) as positive ALA test in a child with negative cultures. Cases with positive ALA test, negative cultures and clinical sepsis were excluded.

Results

Of a total of 3362 GBS urinary tests, 35 were TP, 3279 TN, 12 FN and 37 FP. This represents a sensitivity of 75%, a specificity of 99%, a PPV of 49% and NPV of 99%. Less than one third of confirmed SGB infections occurred in the second half of this period (13 cases).

Conclusions

Accordingly to previous studies, having a NPV of 99% makes this test a valuable tool on evaluating children at risk of GBS infection, a negative result in urinary GBS ALA test almost excludes GBS disease.
The low sensitivity of this test makes it inadequate as a screening test, although its high specificity may be of use in infants with clinical evidence of disease and a negative blood culture. There was a decrease in the confirmed SGB infections.

ESP16-0951
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

OSTEOMYELITIS –IS BONE SCINTIGRAPHY ACCURATE FOR THE DIAGNOSIS?

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Title of Case(s)

OSTEOMYELITIS

Background

Bone Scintigraphy (BS) is one of the most valuable radiologic methods in acute osteomyelitis diagnosis, especially in pediatrics when symptoms are poorly localized or there is a multifocal involvement. Only rare cases are not screened by this method. We present two cases of osteomyelitis in which BS was normal.

Case Presentation Summary

A fifteen-month child (case 1) and a 13-year-old adolescent (case 2) presented with fever and refusal to move the right limb, keeping the hip in a semi-flexion posture. No history of trauma. Case 1 blood tests (BT):WBC 9900/µL (neutrophils 6200/µL); ESR 93mm and CRP 262mg/L. Case 2 BT:WBC 5400/µL (neutrophils 4300/µL); ESR 22mm and CRP 122,8mg/L. Both blood cultures were positive for *S.aureus.* Hip ultrasound, plain radiographs and three-phase BS 99mTc-MDP were normal. Both had iv antibiotics (flucloxacillin and gentamicin) with clinical and analytical improvement. Case 1 MRI: “illiacus osteomyelitis with extense bone marrow involvement, some discrete abscesses, and psoas iliaccus, vastus externus and medialis muscles affected. There’s also arthritis, with joint effusion and synovial thickening”. Case 2 MRI: “right iliacus bone osteitis/ostomyelitis process with periostitis, right gluteus minimus and iliacus muscles miositis”.

Learning Points/Discussion

Confirmation of osteomyelitis diagnosis usually entails a combination of imaging techniques. Normal hip ultrasound/plain radiograph in a child presenting with fever and hip pain should be, ideally, followed by MRI. MRI is the most specific and sensitive imaging modality, providing excellent anatomic delineation of the infected area/surrounding soft tissues. Besides, it doesn’t expose the child to ionizing radiation. However, BS has a high sensitivity (~85%) and it's frequently done as first line, as the use of MRI is limited by the cost and the need of sedation in younger children.

ESP16-0895
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

THE PROGNOSTIC VALUE OF IL-6, IL-8, IL-10, PROCALCITONIN AND C-REACTIVE PROTEIN IN DETECTION OF INFECTIOUS ETIOLOGY OF FEBRILE NEUTROPENIA IN CHILDREN

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Background

Despite improvements in diagnosis and treatment, infections are still major cause of mobitity and mortality in children with febrile neutropenia. Many biomarkers have been proposed as predictors of high risk group, the most frequent used and accepted biomarker is still CRP. There are few studies in English literature in determination of prognostic value of cytokines in diagnosis of febrile neutropenia. The recent study was conducted for determination prognostic value of IL-6, IL-8 and IL-10 in children for diagnosis.

Methods

The medical records of the patients with ALL (n=30), AML (n=8) with 63 febrile neutropenia episodes who were treated at, Pediatric Hematology Division of Ege University Medical School between July, 2013 and March 2014 were prospectively recorded.

Results

Blood cultures revealed Gram(+) microorganisms in 11 patients, Gram (-) microorganisms in 8 patients. There is no statistically difference in CRP, procalcitonin, IL-6, IL-8 and IL-10 between culture positive and culture negative groups($p>0.05$).The most sensitive biomarker is IL-10 and the most sensitive biomarker is IL-6 and IL-8 for predicting bacteremia. There is no statisticaly difference in comparison of the groups with Gram (+) and Gram(-) microorganism for CRP, procalcitonin, IL-6, IL-8 and IL-10. In patients with clinically and micro-biologically documented infection, the most specific biomarkers were IL-6 and IL-10, the most sensitive biomarker was procalcitonin. The groups did not show statistically difference ($p>0.05$).

Conclusions

There is no unaccompanied biomarker for determination the risk groups for febrile neutropenia. For treatment both clinical signs, related risk factors, biomarkers should be evaluated together. In the current study, IL-6, IL-8 and IL-10 was found more sensitive and specific than CRP but further investigations needed for proposal of routinely usage of cytokines in children with febrile neutropenia.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0165
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

FECAL β-DEFENSIN CONCENTRATIONS AND DIAGNOSIS OF NECROTIZING ENTEROCOLITIS

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Background

Necrotizing enterocolitis (NEC) is most common acquried gastrointestinal and surgical emergency among patients in the neonatal intensive care unit, which acts as a leading cause of death among these patients.Among the many factors associated with NEC, mucosal innate immune response might play a role. Early detection of NEC is difficult and it is hard to distinguish from other gastrointestinal disorders and neonatal sepsis.The aim of this study was to evaluate the usefulness of fecal β-defensin in the diagnosis of NEC.

Methods

Patients were recruited from Shanghai children's Hospital neonatal intensive care unit between April 2014 and May 2015. All preterm infants were included. Meconium and stool samples were collected prospectively on alternate days for at least 28 days.We collected 680 stool samples from premature newborns. The stool samples were collected after birth and stored in -80℃, and the fecal β-defensin 1~3 level and fecal calprotein level was measured with the β-defensin enzyme-linked immunesorbent assay kit.

Results

Fecal β-defensin1~2 just show a slight raise in the NEC group than in the non-NEC group (P=0.12, P=0.21), but β-defensin3 levels were significantly higher in the NEC group than in the non-NEC group ($P < 0.001$). There was a significant positive linear relationship between the fecal β-defensin3 level and Bell stages of NEC ($P < 0.001$). Infants with NEC showed significantly increased fecal hBD3 concentrations before clinical symptoms. There was no difference in the fecal β-defensin levels according to the type and method of feeding between the NEC and non-NEC groups.

Conclusions

Fecal β-defensin levels were significantly increased in premature infants with NEC. The fecal β-defensin test might be a noninvasive, easy, and useful tool for the diagnosis of NEC.

ESP16-1108
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

REVIEW OF PAEDIATRIC HAEMATOLOGY/ONCOLOGY PATIENTS WITH A POSITIVE BLOOD CULTURE

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To review management of paediatric haematology/oncology patients with a positive blood culture (BC): (1) Audit antibiotic usage against local Trust and national NICE guidelines; (2) Review the microbiology; (3) Assess practice regarding central venous line (CVL) removal.

Retrospective analysis of all haematology/oncology inpatients with a positive BC between 1/5/2012 and 31/5/2014. Diagnosis, treatment, additional clinical and laboratory details were reviewed from paper and electronic hospital records.

There were 58 different isolates in 34 patients; 50% of patients were neutropenic. All patients with febrile neutropenia (FN) were started on appropriate 1st line antibiotics. 37% of patients with FN had a repeat BC after 72 hours of treatment. 24% of patients with FN had a BC 72 hours after finishing antibiotics. 35% of patients with FN had the appropriate duration of antibiotics from negative BC.

29/58 isolates were Gram-negative organisms, 27 Gram-positive organisms; 16 were coagulase-negative Staphylococci. 53% of organisms were susceptible to ceftriaxone, 76% to gentamicin and 75% to piperacillin-tazobactam. 74% of organisms were sensitive to the initial empirical antibiotics.

62% of positive BC were considered related to line sepsis. 43% of patients with suspected line sepsis had their CVL removed. 10 patients had CVL removed, 30% of whom were neutropenic; eight lines were removed after >72 hours from initial positive BC because of persistent bacteraemia and two lines removed < 72 hours in severely ill patients with the CVL as likely source.

All FN patients commenced on antibiotics in keeping with Trust/NICE guidance. Further education is needed to ensure BC is repeated 72 hours after starting treatment, 72 hours after finishing treatment and duration of antibiotics is based on first negative BC. All CVLs were removed in accordance with guidelines.

ESP16-0180
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

DIFFERENCES IN LABORATORY TEST RESULTS IN CHILDREN WITH NEUROBORRELIOSIS AND TICK-BORNE ENCEPHALITIS

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Background

Tick borne diseases, namely neuroborreliosis and tick-borne encephalitis (TBE), should be considered a possible cause of aseptic meningitis in children living in endemic areas. Diagnosing remains challenging because serology tests may produce false-positive results and the two-step approach in Lyme disease is time-consuming. Therefore we aimed to identify early-available findings suggestive of neuroborreliosis by comparing laboratory test results in children with neuroborreliosis or TBE, regardless of tick bite history.

Methods

A retrospective analysis of medical records of patients with neuroborreliosis or TBE hospitalized in The Medical University of Bialystok Children's Clinical Hospital between 2005 and 2015.

Results

A total of 50 children were included (20 with neuroborreliosis, 30 with TBE). There were no significant differences in mean CSF pleocytosis (178±34 vs 136±32 cells/μL) or CSF protein (55.6±9.4 vs 42.9±4.9 mg/dL) between the groups. In the neuroborreliosis group there was significantly higher percentage of mononuclear cells in CSF smear (91.0±2.06 vs 63.8±5.3 %, $p<0.005$), lower C-reactive protein concentration in serum (3.92±0.6 vs 11.7±2.6 mg/dL, $p<0.001$), lower white blood cells count (8.69±0.57 vs 14.32±0.81 $\times 10^3/\mu L$, $p<0.001$). Additionally facial nerve palsy was observed in 9 (45 %) patients with neuroborreliosis and in no one with TBE.

Conclusions

General CSF analysis results does not suffice to suspect neuroborreliosis, but high percentage of mononuclears in CSF and facial nerve palsy are suggestive. Additionally, in patients with a history of tick bite, C-reactive protein concentration and white blood cells count may be considered in differentiating TBE from neuroborreliosis.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0050
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

A COMPARISON BETWEEN C-REACTIVE PROTEIN AND IMMATURE TO TOTAL NEUTROPHIL COUNT RATIO IN THE DIAGNOSIS OF NEONATAL SEPSIS

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Background

A COMPARISON BETWEEN C-REACTIVE PROTEIN AND IMMATURE TO TOTAL NEUTROPHIL COUNT RATIO IN THE DIAGNOSIS OF NEONATAL SEPSIS

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Background :

Neonatal sepsis is one of the challenges among medical practitioners. Culture result will take 2 to 3 days and rapid deterioration of patient's condition may happen if medical treatment is not instituted early. This study aims to compare the sensitivity,specificity, PPV and NPV of C-Reactive protein (CRP) and the immature to total neutrophil count (I/T Ratio) in diagnosing symptomatic patients with sepsis.

Methods

Prospective cohort study of infants admitted from March 2013 to March 2014 in SGH. Inclusion criteria were gestational age < 34weeks, either symptomatic for suspected sepsis and/or perinatal risk factors including prolonged rupture of membranes, maternal pyrexia/leucocytosis/raised CRP and chorioamnionitis.

Results

201 infants were included. 423 episodes of sepsis evaluation were included, of which 17 episodes were confirmed sepsis, 232 episodes were probable sepsis and 174 episodes were of no sepsis.

For confirmed sepsis, sensitivity of CRP and I/T Ratio were 29% and 35% respectively, while specificity were 77% and 79% respectively. Positive predictive value (PPV) were 6% and 7% respectively. Negative predictive values (NPV) were high at 96% and 97% respectively.

For combined sepsis (probable and confirmed), sensitivity of CRP and I/T ratio were 33% and 26% respectively, while specificity were 97% and 84% respectively. Positive predictive value (PPV) were 96% and 70% respectively. However, negative predictive value (NPV) were low at 42% and 44% respectively.

Conclusions

Both CRP and I/T Ratio had low sensitivity but high specificity. Both can be used for monitoring of response to treatment but were not good screening tools by themselves for sepsis.

ESP16-0521
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

POINT OF CARE CRP TESTING IN PEDIATRICS INTENSIVE CARE UNIT

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Background

Recently attention has been turned to the use of portable instruments for point-of-care (POC), in order to get quicker results. However, few clinical studies support its use in pediatrics. We aim to ascertain the accuracy of POC analyzer (spinit®, biosurfit, SA) in the determination of C-reactive protein (CRP) from a sample of capillary blood or EDTA blood sample compared with CRP determined by the reference method.

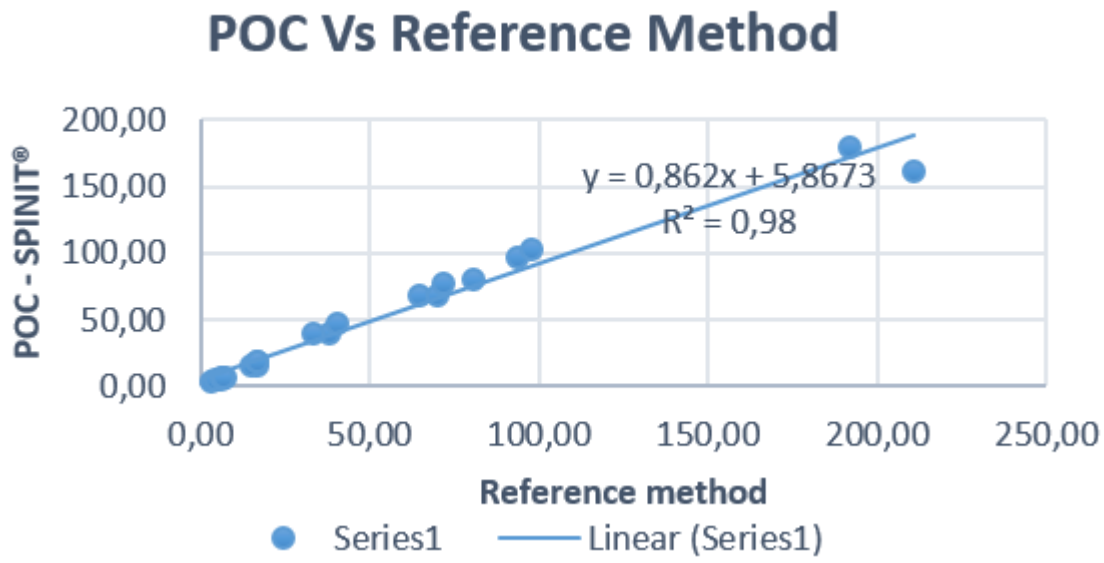
Methods

Prospective study, conducted at pediatric's intensive care unit (PICU) of São João Hospital, Oporto, Portugal, from October to December 2015. All children admitted to the PICU, regardless of their condition, age or gender were included. Data were analyzed using Statistical Package for Social Sciences (SPSS®).

Results

Our study included 43 samples. To validate the analyzer we compared the CRP values obtained by the reference method with CRP values obtained by POC (using the same EDTA blood sample) and considering the detection range. With the linear regression model we obtained r^2 0.98, $\surd r$ 0.97 (graphic 1). Comparing CRP values obtained by the reference method (from EDTA blood sample) with CRP value by POC (from capillary blood sample) we obtained r^2 0.94, $\surd r$ 0.88. A correlation was found between CRP obtained by POC using two

different samples (EDTA blood Vs capillary blood) and revealing an r^2 0.98, √r 0.98.



Conclusions

The results obtained by the POC analyzer were shown to be reliable and accurate. This may bring great advantages in its application in a PICU as it can reduce the need of catheter manipulation and blood spoliation in critical care patients. A limitation of our study regards to the reduced sample size. More trials are needed to assess the cost-benefit impact of CRP POC testing.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0358
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION IN DIAGNOSING INTRATHORACIC TUBERCULOUS LYMPHADENOPATHY: ALSO FEASIBLE IN PAEDIATRIC PATIENTS?

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Title of Case(s)

Endobronchial ultrasound-guided transbronchial needle aspiration in diagnosing intrathoracic tuberculous lymphadenopathy: also feasible in paediatric patients?

Background

Worldwide tuberculosis (TB) incidence in children is estimated to be 1 million/year and mortality 140.000/year. TB diagnosis in children remains a challenge and it is often difficult to obtain confirmation by culture.

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive technique for the diagnosis of mediastinal, paratracheal and peribronchial lesions with a high diagnostic yield in adults. This technique provides real-time sampling under direct visualization of the target lesion by ultrasound incorporated into the distal end of the bronchoscope. Data on children are lacking, probably because of hesitancy of clinicians to use EBUS-TBNA in children. The minimal diameter of the EBUS bronchoscope is 6.9 mm which is large compared to the diameter of the tracheal diameter of a child (11 mm in an 8 year old child compared to >20 mm in adults). We think that EBUS-TBNA could be performed safely in children from the age of 6 – 7 years old.

Case Presentation Summary

Case report: We present an 8 year old boy from sub-Saharan Africa with intrathoracic lymphadenopathy in whom initial TB investigations (sputum and gastric lavage) were negative. Samples were collected with the EBUS-TBNA technique. The procedure went uncomplicated. These samples were acid-fast bacilli smear positive and yielded *Mycobacterium tuberculosis* in culture, susceptible to Isoniazid and Rifampicin. Culture and susceptibility data provided guidance for confident regimen downscaling in the continuation phase of therapy.

Learning Points/Discussion

We conclude that EBUS-TBNA could be a valuable tool to diagnose intrathoracic tuberculous lymphadenopathy in the paediatric population from the age of approximately 6 – 7 years old.

ESP16-0761
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

LEVELS OF INFLAMMATORY BIOMARKERS AS A TOOL FOR PATIENT EVALUATION AND MANAGMENT

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Background

Despite major advancements in the recognition and management of sepsis, infectious diseases remain a significant burden on childhood health. Although mortality from sepsis in the developed world has decreased to approximately 10%, early diagnosis can be difficult because clinical and laboratory signs are similar to those presented in different severities of SIRS caused by infectious disease.

The aim was to determine if levels of inflammatory biomarkers can be used as an evaluation and management tool of patients with infectious disease.

Methods

A prospective descriptive study include children with infectious diseases from February to December 2015. For all the patients were taken following laboratory diagnostic tests: leukocyte count, immature granulocytes (IG%), C-reactive protein (CRP), IL-6, procalcitonin (PCT).

Results

The study included 51 patients. Median: age - 54 months, duration of hospitalization - 8 days. Pneumonia was diagnosed in 78%(40) patients. 62,7%(32) of all patients had SIRS, 78%(25) had sepsis. Patients were classified into three groups: SIRS positive with sepsis 78%(25), SIRS positive without sepsis 22%(7) and uncomplicated infections (SIRS negative) 37,3%(19).

	SIRS + 62,7% (32)		SIRS - 37,3% (19)	
Median	Sepse + 78% (25)	Sepse - 22% (7)		P value
Leu	17,96	12,64	9,96	< 0,05
CRP	150,9	8,35	21,46	> 0,05
PCT	1,73	0,43	0,49	< 0,05
IL-6	26,1	16,4	17,6	> 0,05
IG%	0,5	0,3	0,4	< 0,05

Conclusions

It is important to evaluate the SIRS criteria and SIRS positive patients to investigate in detail as 78% of SIRS positive are diagnosed with sepsis.

· In evaluation of biomarkers the most useful are recognized IL-6, CRP.

· PCT median rates were not statistically significantly different; this could be due to the size of the patient group.

· In IG% no significant statistical difference is found between the groups, however for sepsis positive group they are above the norm. This result demands a futher investigation.

Normal 0 false false false LV X-NONE X-NONE
Normal 0 false false false LV X-NONE X-NONE

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0041
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

TRANSCRANIAL MAGNETIC STIMULATION IN PROGNOSING THE COURSE OF ACUTE TRANSVERSE MYELITIS

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Background

Goal of our study was to evaluate motor pathways in children with viral myelitis using transcranial magnetic stimulation (TMS).

Methods

20 healthy children (7-14 years old, average 12) without signs of spinal disorders were enrolled as controls. Main group consisted of 24 patients (8-16 years old, average 11) with acute viral transverse myelitis, in 4 cases with cervical localization of the lesion, in 7 – thoracic and in 13 – lumbar. Etiology was enterovirus (n=20) Epstein-Barr (n=4) viruses. 18 children were unable to walk, lower paresis was seen in 6 cases. We used single-pulse TMS protocol.

Results

Three neurophysiologic patterns were observed in the myelitis group:

1. Presence of both cortical MEP and spinal MEP (n=15).

2. Presence of only spinal MEP without cortical one (n=6).

3. Total absence of both spinal and cortical MEP (n=3).

In follow-up period (2-5 years) 10 children (42%) were unable to walk 50 meters, 11 (46%) had normal motor function and 3 (13%) had total paraplegia without movements of lower limbs, no signs of recovery. Among those 11 who fully recovered only first TMS pattern (presence of both cortical and spinal MEPs) was registered. Those who recovered with sequelae had first or second pattern and in 3 patients who did not recover only third pattern was seen. ROC-analysis data revealed significant correlation between long-term (3-5 years) recovery of walk in patients with consequences of myelitis and CMCT value≥28,7 ms (seen on Fig. 1).

Conclusions

Acute transverse myelitis in 96% of the cases causes neurophysiologic changes which may be detected by diagnostic TMS. Method may be used as a predicting tool: absence of cortical and spinal MEP may be considered as a sign of highly probable poor clinical outcome.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0780
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

SMARTPHONE APPLICATION – BASED SYSTEM AS A DIAGNOSTIC AND THERAPEUTIC TOOL IN ACUTE GASTROENTERITIS MANAGEMENT IN CHILDREN

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Background

On-line applications can improve diagnostic and therapeutic approach to acute gastroenteritis, a common cause of general practitioners' consultations.

Methods

In association with the leading medical market IT service provider in Poland “Medycyna Praktyczna”, we created a smartphone application to facilitate management in acute gastroenteritis in children. We used the guidelines of international organizations (ESPID, ESPGHAN) as the scientific groundwork.

Results

Our intuitive algorithm takes into consideration: risk factors, diagnostic criteria, age, body weight and symptoms duration. Traveler’s diarrhea is distinguished as a separate category. After input of basic data, algorithm recommends the indication for microbiological tests and assesses the indications for antimicrobial treatment. If recommended, it presents appropriate antibiotic therapy and automatically calculates the dosage. The system also attaches the list of medications available on the Polish market and generates a sample prescription.

Conclusions

Creating an intuitive, easy to use and time-sparing smartphone application, as a diagnostic and therapeutic tool in acute gastroenteritis management in children can unify and improve diagnostic and therapeutic approach as well as reduce antibiotic consumption. Thereupon, this improvement can have a positive influence on antimicrobials resistance.

ESP16-0861
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

THE DIAGNOSIS DELAY ATYPICAL AND EXCEPTIONAL FORM OF KAWASAKI DISEASE IN A CASE REPORT

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Title of Case(s)

The diagnosis delay atypical and exceptional form of Kawasaki disease in a case report

Background

Kawasaki disease is the most common pediatric vasculitis, after rheumatoid purpura the second cause of acquired heart disease in children.

Its unusual shape was a pattern of multiple consultations and scalable for different symptoms.

Case Presentation Summary

The case of S. F boy aged 04 and a half years removed to our service for 02 members inferior lameness , who viewed it for the first time there's 15 days to neck pain with fever and treat as angina, persistent fever and the appearance of a rash with cervical lymphadenopathy led parents to see again new.

Despite the change to the clinical appearance of antibiotic persists and functional impairment requiring hospitalization and after discharge perform an EMG returned for a myogenic reached.

Kawasaki disease was chosen in front of a table with us in addition to the rebellious fever for more than 15 days and cervical lymphadenopathy, myositis, the presence of a rash act of a morbiliforme erythema and enanthema fact of cheilitis and installation of Arthritis 2 anchors with a strongly positive inflammatory balance.

The dramatic decline in fever immunoglobulin with the appearance of peeling gloves fingers and toes confirm our diagnosis

Learning Points/Discussion

The variety of clinical forms and the absence of specific biological criteria often leads to late diagnosis hence the need for information of health professionals to prevent life-threatening complications.

ESP16-0873
04. S - DIAGNOSTIC TOOLS FOR INFECTIOUS DISEASES

DIFFICULTY OF DIAGNOSIS BETWEEN A PRIMITIVE AND REACTION TO INFECTION HEMOPHAGOCYTIC SYNDROME, IN A CASE REPORT

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Title of Case(s)

Difficulty of diagnosis between a primitive and reaction to infection hemophagocytic syndrome, in a case report

Background

hemophagocytic syndrome is a serious disease, especially rare in children (1 case / million) and poor prognosis. Diagnosis is based on the combination of clinical and biological signs, non-specific, making it difficult to predict its primitive character despite exhaustive etiological investigation.

Case Presentation Summary

The case of one child (S.L); a girl of 55 days hospitalized in the pediatric ward CHU Batna for exploration splenomegaly stage II and hematologic reached first with a normochromic normocytic anemia, thrombocytopenia and neutropenia associated with secondarily, all operating in a context febrile.

Hypertriglyceridemia, hyperferritinemia and hyponatremia were remarkable, the puncture of marrow revealed a haemophagocytosis. An interstitial lung disease with bilateral diffuse infiltration and the chest radiograph and positive inflammatory balance, concluded in a secondary infection hemophagocytic syndrome

Antibiotic treatment with immunoglobulin infusion resulted in a regression of the disease and improved inflammatory balance but persistent pancytopenia and hemophagocytosis with death of the patient after 25 days of hospitalization

Learning Points/Discussion

In the absence of genetic study, the diagnosis of a primary macrophage activation syndrome type lymphohistiocytosis family before the young age and family history

Conclusion: in front of his character often triggering, infection is always difficult to remove in the case of a primitive hencemophagocytic syndrome the need to develop genetic diagnosis

ESP16-0971
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RSV INFECTION IN ISTANBUL: RISK FACTORS AND FREQUENCY

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Background

Respiratory syncytial virus (RSV) is one of the most common causes of acute respiratory infections in all age groups especially under two years. The aim of this study was to investigate the frequency and clinical features of RSV in hospitalized children under two years old with the diagnosis of lower respiratory tract infections (LRTI) in our region.

Methods

Hospitalized children aged 0-2 years with the diagnosis of viral LRTI at whom RSV antigen was investigated between September 2011- May 2013 were included in this prospective study.

Results

Among the total of 361 hospitalized children whom were investigated for RSV antigen, 138 (38%) were female and 223 (62%) were male and the male/female ratio was 1.6. The mean age of the group was 5,7±5,1 months (0-24 months).RSV antigen in nasopharengeal secretions was positive in 68 (19%) of 361 patients. RSV infection was detected significiantly higher in December and January (p=0.003). RSV positivity was significantly higher in patients; aging under 6 months (p=0.01), with shorter duration of breastfeeding (p=0.02), low socioeconomic status (p=0.02), and also born with spontaneous vaginal delivery (p=0.007). In RSV(+) LRTI group, children were associated with severe disease than RSV (-) LRTI group (p=0.014).

Conclusions

Since there is lack of data investigating the frequency and the risk factors of RSV respiratory infections in our region, our study has importance for providing new datas. Also it is the second study investigating the correlation between RSV positivity and meteorological conditions in Turkey.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0467
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

SUCCESSFUL TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA WITH AMPICILLIN AND AMPICILLIN-SULBACTAM IN HOSPITALIZED CHILDREN IN TURKEY, 2004-2014

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Title of Case(s)

SUCCESSFUL TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA WITH AMPICILLIN AND AMPICILLIN-SULBACTAM IN HOSPITALIZED CHILDREN IN TURKEY, 2004-2014

Background

Pneumonia is a leading cause of morbidity and mortality worldwide. Guidelines for the management of community-acquired pneumonia (CAP) suggest ampicillin for **uncomplicated** CAP and ampicillin-sulbactam for complicated CAP as first choice parenteral empiric antibiotic regimen alternatives in hospitalized children. A retrospective study was conducted to assess clinical response to empirical ampicillin and ampicillin-sulbactam among children hospitalized with CAP.

Case Presentation Summary

Medical records of 1,982 patients hospitalized in our center between 2004 and 2014 with the diagnosis of CAP were reviewed. Children between the ages of 1 month and 18 years without an underlying disease and treated with ampicillin or ampicillin-sulbactam were enrolled for the study. Clinical failure was considered with the persistence of fever, dyspnea or tachypnea beyond the first 48 hours of treatment or cough beyond the first 96 hours of treatment or signs of severe disease at the 5th day of treatment.
One hundred and twenty-seven patients were included in the study. There were 68 (53.5%) boys and 59 (46.5%) girls. The median age of patients was 20 months (range 5-64 months). Fifty-three (91.4%) of 58 patients were successfully treated with ampicillin and 64 (92.8%) of 69 patients were treated with ampicillin-sulbactam. Gender, age, tachypnea, body temperature, leukocyte and neutrophil counts at presentation were not associated with a high risk of treatment failure in both groups.

Learning Points/Discussion

Despite improved diagnostic techniques, treatment remains empirical in CAP. In current circumstances, the findings of our study encourage the use of narrow spectum antibiotic treatment like parenteral ampicillin or ampicillin-sulbactam as a first line option for children hospitalized with CAP.

ESP16-0781
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ACUTE ATAXIA AS RESULT OF ACUTE LABYRINTHITIS IN THE CONTEXT OF OTOMASTOIDITIS AND OTITIS MEDIA

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Title of Case(s)

ACUTE ATAXIA AS RESULT OF ACUTE LABYRINTHITIS IN THE CONTEXT OF OTOMASTOIDITIS AND OTITIS MEDIA

Background

Assessing a child presenting with ataxia can be challenging. Acute ataxia is uncommon in children. Central causes as cerebelous ataxia or post-infectious acute cerebelitis and intoxications are the most commonly mentioned. Peripheric vestibulopathies, as vestibular neuritis and labyrinthitis are rare etiologies. They are frequently related to upper airways viral inflammatory processes.

Case Presentation Summary

A previously healthy 3-year-old girl, with familial antecedents of febrile convulsions and epilepsy, had a first episode of febrile tonic-clonic convulsion. Posteriorly she initiated irritability, prostration and ataxia with imbalanced and wide step gait, without meningeal signs. In the previous 5 days she presented with rhinofaringitis and 37,5ºC. She had acute otitis media of the right ear and left seromucous otitis of the left ear. CTH revealed findings of bilateral otomastoiditis and ethmoid and maxillary sinusopathy. Lumbar puncture was normal. Toxicologic analysis was negative. MRI revealed important obliteration of mastoid air cells and tympanic cavity in relation to sinusoidal and ear inflammation. No alterations of cerebral parenchima, cerebellum and brainstem were revealed. Head impulse test and head shaking test caused discomfort bilaterally, without saccades or nistagmus. Tympanogram was bilaterally flat. Acute labyrinthitis was admitted. She received ceftriaxone and amoxicilin and clavulanate after discharge, neo-synephrine and topic nasal corticoid. Ataxia and vertigo reverted totally after 48 hours of therapy. Surgery will be further considered (ear grommets).

Learning Points/Discussion

Peripheric vestibulopathy in toddlers is difficult to diagnosis, for the subjectivity of clinical signs and symptoms, implying a high suspicion index. Diagnosis is usually clinical with acute onset of vertigo associated with nausea, vomits and gait alterations. It usually presents a benign and self-limiting course from days to weeks.

ESP16-0378
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RISK FACTORS FOR HOSPITALIZATION DUE TO INFLUENZA IN CHILDREN BELOW 6 MONTHS

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Background

The objective is to address risk factors for influenza infection in infants below 6 months of age requiring admission.

Methods

We performed a retrospective, case-control study. Infants ≤6 months without comorbidities admitted for influenza infections between October 2010 and March 2015 were included as cases. Controls without comorbidities were recruited among children admitted for non-respiratory diseases, matched for age and date of admission. Data were collected from medical records and phone interview. Logistic regression was used to identify independent risk factors for hospitalization.

Results

A total of 88 cases and 122 controls were included. Median age was 1.6 months [1.03-3.11] vs 1.87 [0.93-3.4], (p=0.9), males 55% vs 62% (p=0.29). From univariate analysis, differences were found in relation to maternal age (43.1±4.95 vs 32±5.3), paternal age (37±6.4 vs 34.5 ±6.1), having siblings (79% vs 24%), siblings < 4 years old (54% vs 15%) and having vaccinated grandparents (18% vs 39%) (all p<0.05). The 23.8% vs 14% lived with ≥3 relatives who weren't vaccinated (p=0.06). No difference was found in relation to breastfeeding (90% vs 79.3%; p=0.07) or assistance to the kindergarten (6.5% vs 1.6%; p=0.08). Vaccination during pregnancy was uncommon (3.5% vs 8.3%; p=0.3), despite indicated in 72% vs 71% (p=0.9).

After multivariate analysis, having siblings (OR 6.7 [IC95% 3.2-14.1]) and maternal age (OR 1.09 [IC95% 1-1.17]) were independent risk factors for Influenza-associated hospitalization. Having vaccinated grandparents was a protective factor [OR 0.3 (IC95% 0.1-0.84)].

Conclusions

-Having siblings was shown as the main risk factor forInfluenza-associated hospitalization in infants < 6 months, while having vaccinated grandparents was a protective factor.

-Immunization during pregnancy and in grandparents was rare. Increasing vaccination of them should be seriously promoted in order to reduce admission of the offspring.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0126
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CLINICAL COMPARISON OF RESPIRATORY SYNCYTIAL VIRUS INFECTIONS SUBTYPE A VS SUBTYPE B IN HOSPITALIZED CHILDREN

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Background

Although respiratory syncytial virus (RSV) infections are the most important cause of hospitalization in infants and has been extensively studied, is not well established if subtype A or B are associated to different severity. Our aim was to compare the severity between RSV subtypes in hospitalized children.

Methods

From September 2005 to August 2014 a prospective study was conducted on children, admitted with respiratory infection to the Severo Ochoa Hospital, in Spain. Specimens of nasopharyngeal aspirate were taken for virological study by using polymerase chain reaction, and clinical data were recorded. Infections associated to RSV A and RSV B were selected and compared.

Results

3278 episodes of viral respiratory infections were analyzed. RSV was detected in 1019(31%); 619(61%) cases were RSV A, 244(24%) RSV B and 156 could not be typed. Infections were present mainly in November-January, the mean each was 1 year (median 6 months), and the most frequent diagnosis was bronchiolitis (57.4%). 586(77%) of children had fever, and 611(70%) hypoxia. Infiltrate in Rx was present in 340 patients (49%). 35% of cases had a coinfection (mainly with rhinovirus). The hospitalization was of 4.7+ 2.5 days. Only 23(2.7%) infants needed PICU admission. We compared the clinical data of the total group, and also, the patients diagnosed of bronchiolitis, the patients diagnosed of recurrent wheezing and of pneumonia and we did not find any difference between the patients with RSV A or B. Single infections; 396 RSV A and 160 RSV B were also compared and no differences amongst them were detected.

Conclusions

Respiratory viral infections due to RSA virus in hospitalized children have no different clinical characteristics associated to type B or A. RSV B infections have not more severity.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0131
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RESPIRATORY INFECTIONS BY ENTEROVIRUS D68 IN OUTPATIENT AND INPATIENT CHILDREN.

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Background

The incidence of enterovirus D68 (EV D68) and the spectrum of clinical disease in children is not well known in European countries. Our aim was describing the clinical impact of EV D68 detected in children with respiratory tract infections.

Methods

As a part of a prospective study to identify the etiology and clinical characteristics of viral respiratory infections in children in Spain, we performed the analysis of the cases of EV infections in all children hospitalized in a secondary hospital in Madrid, during the epidemic respiratory season 2012-2013. A second group of samples corresponded to infants of the same area, with ambulatory respiratory infection or asymptomatic. Phylogenetic EV-D68 analysis was made using the VP1 gene. Clinical data of EV-D68 patients were compared with those infected by RV in the same period and population.

Results

The study population was 720 patients corresponding to 399 episodes of hospitalization for respiratory causes, 44 episodes of ambulatory infections and 277 asympotomatic children. A total of 22 patients were positive for EVs(3.05%); 12 of them were specifically typed as EV-D68(11/443 respiratory infections, 2.5%). The most frequent diagnosis in the 10 hospitalized children with EV-D68 detection was recurrent wheezing. Hypoxia was present in 70% of cases but admission in PICU was not required. No neurological signs or symptoms were observed. One patient had an ambulatory mild bronchiolitis and another was asymptomatic. No differences were found with RV infections except less duration of hypoxia and fever in EV D68 group.

Conclusions

EV-D68 infections were detected in 3.05% of respiratory studied samples(2.5% of admissions). The infection was associated to wheezing episodes with hypoxia and was similar to rhinovirus infections. No admissions to intensive care unit or neurological symptoms were found.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-1055
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

PREDICTING EVOLUTION OF VIRAL PNEUMONIA IN CHILDREN – IS IT POSSIBLE?

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Background

Viral pneumonia is an important cause of morbidity in children. Purpose: to evaluate the impact of clinical parameters/aetiology in evolution of children admitted with viral pneumonia.

Methods

Retrospective analytic study including all children with viral pneumonia admitted to a medical paediatric ward in Coimbra Paediatric Hospital (Portugal) between 2010 and 2015. Exclusion criteria: antibiotherapy 2 weeks before admission. Statistical analysis: SPSS Statistics 23 (α=0,05).

Results

A total of 86 patients (52% male) were included (age 6M-16Y, median 13M). Most patients were admitted from January to March (70%). The main reason for hospitalisation was hypoxemia (88%). Forty percent had comorbidities (mainly asthma - 23%). Virus screening in respiratory secretions was performed in 90% of patients, with a predominance for RSV (52%), adenovirus (22%) and rhinovirus (14%); coinfection was present in 43% of the cases (max 5 virus). Median hospitalisation period was 7 days (3-27d). The main complications were suspected bacterial infection (43%), respiratory insufficiency with ventilatory support need (15%) and atelectasis (10%). Eight per cent developed bronchiolitis obliterans (6 adenovirus, 1 VSR). Complications predominated in children with comorbidities (66% vs 25%, p=0.009) and, though not in a statistically significant manner, in younger children (60% ≤3M, 46%]3M, 12M], 47% ≥12M, p=0.636). No association was found between hospitalisation period and the aforementioned groups. The viruses most prone to lead to complications were RSV and adenovirus (60% and 58% associated with complication). No association was found between coinfection and complications (p=0.878) or hospitalization period (p=0.421).

Conclusions

We observed increased morbidity in children with comorbidities and a tendency to more complication rates in younger children or RSV/adenovirus infection. These factors must be considered in treatment and follow up of children with viral pneumonia.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0528
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CLINICO-EPIDEMIOLOGICAL PROFILE AND PREDICTORS OF OUTCOME IN CHILDREN WITH DIPHTHERIA: A STUDY FROM NORTH INDIA

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Background

Diphtheria, a vaccine preventable disease in children, is still being reported from India. Occurrence of the disease indicates failure to achieve satisfactory vaccination coverage. Poor socioeconomic status, illiteracy, lack of awareness and social taboos against vaccination are some of the causes for inadequate vaccination. This study was done to understand their clinical profile, effect of vaccination and predictors of outcome.

Methods

Details of 26 children with clinical diagnosis of diphtheria admitted to a general pediatric unit in a tertiary care centre between 2008 and 2015 were collected retrospectively and analyzed. Predictors were identified using multivariate regression.

Results

Mean (SD) age of study population was 6.4 (2.8) years and 57% belonged to a nearby district. Common clinical features: fever (92%), dysphagia (89%), greyish white membrane in oropharynx (85%), sore-throat (73%), dysphonia (62%) and bull-neck (58%). Throat swab culture grew C. diphtheriae in 11 (42.3%) samples. Airway compromise (58%) requiring advanced airway was most common complication followed by myocarditis (35%), renal injury (27%), thrombocytopenia (31%) and neuropathy (15%). Cardiac and renal involvement was less frequent in those who received at least one dose of DPT vaccine. Out of 26 children, 15(58%) survived, 6(23%) died and 5 discontinued care.

			Univariate analysis		Multivariate analysis	
Complication	Survivors	Poor outcome	Odd's ratio	p-value	Odd's ratio	p-value
Airway compromise	7	8	3.0	0.19		
Myocarditis	1	8	37.3	0.003	44.0	0.01
Renal injury	1	6	16.8	0.02		
Thrombocytopenia	1	7	24.5	0.008	29.0	0.03

Conclusions

Diphtheria still remains a fatal disease with frequent airway and cardiac involvement. Myocarditis and thrombocytopenia predicted poor outcome. Nearly two-third of the children were unimmunized and about 88% of them went on to develop myocarditis. Even partial immunization may have a protective role against cardiac complications.

ESP16-0933
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

A BAYESIAN DISCRETE-TIME MODEL TO PREDICT BRONCHIOLITIS INCIDENCE

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Background

Bronchiolitis is a lower tract respiratory disorder caused by viral infection. It is a common infection among young children that causes an elevated number of hospital admissions and a high demand for both primary care and emergency services. Consequently, the development of a predictive model that enables timely public health intervention is fundamental for the preparation of health systems.

Methods

We present a Bayesian model in discrete time to study bronchiolitis dynamics in a population of children aged less than 2 years-old in Valencia that has been divided into four age groups. New infections are described taking into account that previous cases of bronchiolitis in all age groups act directly on the probability of infection. The seasonality that explains the cyclical pattern of infected cases is treated through indicator variables that account for monthly effects.

Results

The model predicts well the dynamics of bronchiolitis.

Conclusions

The model has good predictive capacity, it can be adapted for other infectious diseases with seasonal pattern. The Bayesian analysis of the model allows us to calculate both the posterior distribution of the model parameters and the posterior predictive distribution, which facilitates the computation of point forecasts and prediction intervals for future observations.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0431
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RSV-HOSPITALIZATIONS IN INFANTS UNTIL 6 MONTHS OF AGE

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Background

90% of RSV-hospitalizations occur during the first 6 months of life, so a vaccine should be effective at very early ages. The objective of the study was to analyze the distribution of RSV-hospitalizations from birth to the age of six months in order to estimate the impact of different vaccination schedules.

Methods

A retrospective cohort of all children born between 2009 and 2012 in the Valencia Region was followed from birth to 6 months of age. We searched for all RSV hospitalizations from the regional hospital database (CMBD) using ICD-9 diagnosis codes for RSV. The population database (SIP) allows calculating incidences.

Results

The cohort consisted of 198,223 children; 2976 were hospitalizedwith a diagnosis of RSV during the first 6 months of life (incidence rate 3.2/100 children < 6 month – year). 76% of the hospitalizations occurred during the first 3 months of life. Most of the full term infants RSV-hospitalizations occurred during second month of life [945 (35.0%)], decreasing until sixth month of life [140 (5%)]. For preterm infants, most of the RSV- hospitalizations occurred during first month [84 (28.4%)], decreasing also until the sixth month of life [18 (6%)].

Conclusions

These results suggest that the most effective prevention of severe RSV infections in infants may be achieved by pregnant vaccination.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0706
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

NOVEL DESCRIPTION OF PULMONARY INFECTION CAUSED BY NEISSERIA ANIMALORIS IN A CHILD UNDERGOING BIOLOGICAL TREATEMENT FOR NON-HODGKIN AMIGDALIAN LIMPHOMA - CASE REPORT

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Title of Case(s)

PULMONARY INFECTION CAUSED BY NEISSERIA ANIMALORIS

Background

Neisseria animaloris, previously classified as CDC Group EF-4a, is part of the commensal oral flora of dogs and cats and can cause pulmonary and cutaneous infections in these animals. This group of bacteria has been identified as human pathogens fallowing animal bites, but several other infections have been reported in humans: chronic otitis media, bacteremia in a patient with hepatic carcinoid, endophthalmitis, sepsis after dog bite, peritonitis in a peritoneal dialysis patient.

Case Presentation Summary

We report the case of a 6-year-old male child undergoing maintenance therapy with Rituximab for over a year, for non-Hodgkin Lymphoma (Burkitt type), who developed Neisseria animaloris left inferior lobe pneumonia. Repeated samples of purulent sputum showed increased number of neutrophils and Gram-Stain revealed Gram negative coccobacilli, later identified as Neisseria animaloris using Vitek 2 Compact system. The patient had no pets and no history of animal bite.The patient initially received Meropenem and Linezolid, subsequently Ciprofloxacin after discharge for 3 weeks, with proven radiologic and clinical improvement. To our knowledge this is the first documented case of Neisseria animaloris pneumonia.

Learning Points/Discussion

Patients with lymphoma or other haemathological malignancy, during maintenance therapy with Rituximab, have increased risk of developing infections with both usual and uncommon

pathogens and the isolation of Neisseria animaloris from sputum should make microbiologists be aware of unusual isolates from immunocompromised patients.

ESP16-0154
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MANAGEMENT OF VIRAL BRONCHIOLITIS: 2015 SURVEY OF MEMBERS OF THE EUROPEAN SOCIETY FOR PAEDIATRIC INFECTIOUS DISEASE

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Background

In 1995 the European Society for Pediatric Infectious Diseases (ESPID) carried out a survey of its members to assess the variation in management of respiratory syncytial virus (RSV) bronchiolitis throughout Europe. The aim of the current study was to carry out a similar survey 20 years later to assess how the management of viral bronchiolitis has changed over time.

Methods

An electronic, structured, English language survey, based on the United Kingdom (UK) National Institute for Health and Care Excellence (NICE) bronchiolitis draft guideline (the full guideline was published in June 2015) was sent to members of the European Society of Paediatric Infectious Diseases (ESPID) (n=970) in March 2015. The questions asked included information on treatment practices of infants with bronchiolitis and doctor demographics.

Results

We received responses from 135 doctors (14% of ESPID members) who worked in 115 hospitals across the world. 56% doctors used a written guideline for the management of bronchiolitic infants. All doctors stated they isolated or cohorted all hospitalised bronchiolitic infants. The level of oxygen saturations suggested as an indication to administer supplemental oxygen varied between <89% to <95%. We found significant reductions in the use of ribavirin, bronchodilators and corticosteroids from 1995 to 2015 (ribavirin 57% to 13%, P<0.0001; bronchodilators 95% to 82%, P=0.0038; corticosteroids 81% to 45%, P<0.0001).

Conclusions

There remains wide variation in the management of viral bronchiolitis in infants within the members of ESPID, possibly due to only 56% of doctors referring to a guideline to manage bronchiolitic infants. Although variability in management remains high, encouragingly significantly fewer doctors are prescribing ribavirin, bronchodilators and corticosteroids than 20 years ago.

Acknowledgements: We would like to thank the members of ESPID for completing the questionnaire.

ESP16-0155
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

HUMAN METAPNEUMOVIRUS IN PAEDIATRIC INTENSIVE CARE UNIT ADMISSIONS IN THE UK

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Background

Human metapneumovirus (hMPV) is a common cause of hospital admission due to lower respiratory tract infections in children. It has also been associated with severe illness requiring children to be admitted to a paediatric intensive care unit (PICU). The aim of this study was to assess the clinical characteristics of children with hMPV infection admitted to United Kingdom (UK) PICUs.

Methods

Data were extracted from the UK Paediatric Intensive Care Audit Network (PICANet) database for all children with a hMPV diagnostic code between January 2006 and April 2015. PICANet is a UK national database that includes clinical and laboratory data on every child admitted to a PICU in the UK. Descriptive statistics were used to analyse the data using Microsoft Excel.

Results

There were 119 admissions involving 118 patients during the study period. The number of patients with a code of hMPV increased yearly from three in 2006 to 28 in 2014. Median age was 12 months and length of stay seven days. 34 (29%) patients received non-invasive ventilation (median of three days) and 95 (80%) received invasive ventilation (median of six days). 30 (25%) patients received inotropic support (median of three 3 days). Four patients required renal replacement therapy, two extracorporeal membrane oxygenation and seven died (median age 9 months).

Conclusions

hMPV is associated with significant morbidity in UK PICUs. The numbers of patients in UK PICUs with diagnostic codes of hMPV are increasing, which likely reflects increased awareness of hMPV and more frequent testing for hMPV by multiplex real-time reverse transcriptase PCR. Children with severe respiratory illnesses requiring PICU should be tested for hMPV as well as other respiratory viruses. **Acknowledgements:** The authors would like to thank PICANet for data extraction.

ESP16-0478
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

HOUSEHOLD COOKING PRACTICES AS RISK FACTOR FOR ACUTE RESPIRATORY INFECTIONS AMONG HOSPITALIZED UNDER-5 CHILDREN IN IBADAN, NIGERIA

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Background

In Nigeria, approximately 69% of households use solid fuels as their primary source of domestic energy for cooking. There is limited research that has examined how household cooking practices contributes to the acquisition of acute respiratory infections among under-five children in Nigeria. This study aimed to determine the association between households cooking practices and ARIs among under-5 children in Ibadan, Nigeria.

Methods

A hospital-based case-control study was undertaken. 220 U-5C with ARI (cases) and 220 without ARI (controls) were selected consecutively from children visiting Oni-Memorial Children Hospital and University College Hospital, Ibadan. A follow-up of 66 consented cases and controls each for household survey was carried out using a checklist to assess household cooking practices. Data were analysed using descriptive statistics, Chi-square and logistic regression at $p < 0.05$.

Results

Mean (SD) ages of cases and controls were 20.4 (14.7) and 20.3 (15.0) months respectively. Mean (SD) household size of cases was 6.0 (1.5) compared with 4.0 (1.7) for the controls ($p=0.001$). The odds ratios of ARIs were 8.15 (95% CI: 3.69-18.03) and 3.00 (95% CI: 1.29-6.95) in households using firewood and charcoal for cooking respectively. Children whose household cook in the bedroom were found to have a 3-fold greater risk of ARIs than children in houses that has its separate kitchen.

Conclusions

Inappropriate household cooking practices play an important role in the acquisition of acute respiratory infections among under-five children. Increase awareness of the importance of good cooking practices with regard to prevention and control of acute respiratory infections among under-5 children is therefore recommended.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0688
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ANTIBIOTIC TREATMENT IN NON-ALVEOLAR PNEUMONIA - A CONTINUOUS CHALLENGING IN CHILDREN < 1 YEAR

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Background

Pneumonia is still one of the most challenging diseases worldwide affecting mostly children younger than 5 year of age.

Aim: To identify the most relevant symptoms and lab exams that could suggest the use of antibiotic treatment for non-alveolar pneumonia.

Methods

retrospective study from 01.01.2013 through 31.12.2013. 448 children, under 1year of age admitted to Clinical Children Hospital Brasov with the diagnostic of non-alveolar pneumonia were enrolled.

Results

the age incidence peak of non alveolar pneumonia was <2 months of age with an admittance peak from January to March (44%) and a rural majority (62%) 14 % of the enrolled infants were premature babies. 44% were breast feed and 49 % had all vaccines according to the national immunization program (NIP), Romania is a non PCV vaccinating country), 70% had a proper admittance weight. Most common symptoms were nonproductive cough (71%), fever (31 %), respiratory distress (32%) and 25% presented concomitant AOM. Laboratory exams revealed anemia (77%), leukocyte above 15000/mm^3 (94%), CRP value <5 mg/dl (83%) and accentuated interstitial markings in 75% cases. More than 90% presented at least 1 risk factor (malnutrition, rahitism, passive smoking, older siblings, inadequate milk formula); only 8% had no antibiotic treatment; 1 antibiotic was administrated in 62% and 2 antibiotics in 22%, 3 antibiotic 5% and more than 3 antibiotics were used in 3 % of cases.

Conclusions

Despite the fact that antibiotics were given in more than half of the patients we conclude that we must evaluate properly the cases before administrating antibiotics in infants and toddlers with non-alveolar pneumonia.

ESP16-0568
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MYCOPLASMA PNEUMONIAE PRESENTING AS ERYTHEMA NODOSUM

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Title of Case(s)

***Mycoplasma pneumoniae* presenting as erythema nodosum**

Background

Erythema nodosum is a rare condition in childhood. Despite it is usually an idiopathic condition, it could have a treatable cause.

Case Presentation Summary

Introduction: *Mycoplasma pneumoniae* is a common bacterial agent of respiratory tract diseases. It has been observed that *Mycoplasma pneumoniae* can also give rise to extra-pulmonary manifestations, including cutaneous presentation.

Case presentation: We report a case of a healthy 5-year-old girl, who presented with acute painful nodules on lower members and ankle arthralgia. Also reported cough for seven days. Laboratory workout showed leukocytosis (18000/uL, with 84% neutrophils) and elevation of C-reactive protein (2.80 mg/dl). Streptococcal infection was ruled out. Chest radiography showed an interstitial infiltrate. The patient was treated with oral azithromycin, with resolution of respiratory and cutaneous manifestations. Serum specific immunoglobulin M antibodies for *Mycoplasma pneumoniae* were positive.

Conclusion: Erythema nodosum is a septal panniculitis, rare in childhood, characterized by painful inflammatory nodules. Despite it is usually an idiopathic condition, it could be a sign of a systemic disorder that is potentially treatable, including infectious agents. Although it is an uncommon cutaneous presentation of Mycoplasma, it must be considered when respiratory symptoms are also present.

Learning Points/Discussion

Erythema nodosum is a septal panniculitis, rare in childhood, characterized by painful inflammatory nodules. Despite it is usually an idiopathic condition, it could be a sign of a systemic disorder that is potentially treatable, including infectious agents. Although it is an uncommon cutaneous presentation of Mycoplasma, it must be considered when respiratory symptoms are also present.

ESP16-0214
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

EPIDEMIOLOGY, CLINICAL FEATURES AND MEDICAL INTERVENTIONS IN CHILDREN UNDER 12 MONTHS OF AGE HOSPITALIZED FOR RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS

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Background

The objective of this study is to describe the epidemiology, clinical characteristics and medical interventions performed in children under 12 months of age with respiratory syncytial virus (RSV) bronchiolitis admitted to our hospital.

Methods

Observational, descriptive and retrospective study of children younger than 12 months, admitted to Hospital Universitario La Paz (Spain), with the diagnosis of RSV bronchiolitis, from October 2013 to April 2015. Comparative of the clinical outcome according to the presence of factors associated to severe bronchiolitis (prematurity or underlying diseases: heart disease, broncopulmonary dysplasia, neuromuscular disease).

Results

A total of 449 infants were admitted: 360 full-term infants (4.8% with underlying disease) and 73 preterm infants (18% with underlying disease). The median age at diagnosis was 75 days. Palivizumab prophylaxis had been administered to 18 patients (4%), of whom 7 had received more than 1 dose. The infection was nosocomial in 59 of the patients (13.1%). The mean length of stay was 12.8 days; the presence of underlying disease was associated with longer duration of hospitalization in both preterm (mean 23.3 vs. 56.2 days, p=0.0048) and full-term infants (mean 7.6 vs 33.1 days, p=0.01). There were 113 patients (25.2%) who were admitted to pediatric intensive care unit (PICU). Mechanical ventilation was required in 122 patients (27.2%): 34 (7.6%) invasive mechanical ventilation, 27 (6%) CPAP or BPAP, and 95 (21.2%) High-Flow Nasal Cannula Oxygen (HFNCO). We found a positive correlation between prematurity and severity of the disease measured by admission and duration of stay in PICU, and necessity and duration of mechanical ventilation.

Conclusions

The majority of patients hospitalized due to RSV bronchiolitis were full-term healthy infants; prematurity and the presence of underlying disease were both associated with more severe disease.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0646
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CORONAVIRUS NL63- NOT SO INNOCENT

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Title of Case(s)

CORONAVIRUS NL63- NOT SO INNOCENT

Background

Respiratory tract infection is a major cause of morbidity/mortality, especially in children. The coronaviruses family has been associated with acute respiratory tract infection. Coronavirus NL63 was first isolated in 2004, being a recently identified virus. Since then it has been identified worldwide.It has been described as mostly associated with croup, bronchiolitis or asthma exacerbation in children, although some cases of pneumonia have been described.

Case Presentation Summary

We present a case of a 5 year old boy, with Dravet syndrome and refractory epilepsy, who presented with respiratory distress and fever. Clinically with tachypnea, retractions, hypoxemia, audible wheezing and crackles. Analytically with leucocytosis (21200x10^9/L), and hight CRP (258,6 mg/L.). He was admitted for O2 supplementation, bronchodilators plus penicillin and clindamycin. There was a progressive clinical and radiological deterioration, with worsening hypoxemia and hypotransparent parenchyma on the lower 2/3 of both hemithoraces with patchy opacities on the upper regions. Thoracic ultrasound confirmed bilateral pleural effusion. Non-invasive ventilation was needed. After D9 the patient gradually recovered. Multiplex real time PCR was positive for Coronavirus NL63.

Learning Points/Discussion

Identification of different coronaviruses' serotypes was initiated in June 2015 in our hospital. Since then, 10 cases of coronavirus 63 were identified. HCoV-NL63 is not rare and include some with lower respiratory tract involvement and severe disease, especially in children with underlying medical conditions Its uncommon but potentially severe manifestation should bring awareness to its identification.

ESP16-0417
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

A NOVEL PCR- CAPILLARY ELECTROPHORESIS (CapETyping) APPROACH FOR RAPID AND EASY IDENTIFICATION OF CAPSULAR TYPES OF S. PNEUMONIAE.

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Background

Pneumococcal infections remain a leading cause of serious illness that affects children and adults worldwide. Continuous monitoring of *S.Pneumoniae* capsular type distribution is necessary for epidemiological surveillance and evaluation of vaccines. The focus of this study was to develop and evaluate a PCR-automated capillary electrophoresis based serotyping assay with advantages of fast separation, high-resolution analysis, and small reagent consumption

Methods

Conventional PCR was performed using Qiagen Multiplex PCR plus kit which can amplify up to 80 targets. Twenty eight type specific primer pairs of prevalent Indian serotypes (1,2,3,4,5,8,10A,14,17F,19A,19F,20,23F,24B,35B,40,6A,7A,9A,9N,10F,11A,12F,15A,15B,18C,22F,33F)were designed from the sequence data available at http://www.cdc.gov/ncidod/biotech /strep/pcr.htm. Primer specific to the cpsA (wzg) gene were used as an internal positive control. The amplified product was categorized on Qiaxcel Capillary electrophoresis. The assay was standardized with 28 reference strains of Staten Serum Institute, Copenhagen. The CapETyping results of 112 invasive pneumococcal isolates were compared with the quellung results.

Results

CapETyping results of standard strains totally corresponded with the quellung reaction.

100% Correlation was also observed in the results of each one of the invasive pneumococcal isolates evaluated.

Conclusions

CapETyping for identification of capsular serotypes with improved speed and resolution is a useful alternative to conventional quellung test. The added advantage of the assay is the low cost and absence of subjective interpretation. Further studies are planned with larger number of samples covering other serotypes.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0915
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CAVITATING PNEUMONIA IN CHILDREN: EXPERIENCE IN A SECONDARY LEVEL HOSPITAL

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Background

Pneumonia is a common cause of admission in children, but cavitation is not an usual complication. We study onset symptoms, diagnosis, treatment and evolution of patients with diagnosis of Community-Acquired Pneumonia with Cavitation (CAPC), presented at admission or developed during hospitalization, in absence of pleural effusion, in a secondary level hospital.

Methods

Retrospective descriptive study of all patients diagnosed with CAPC since June 2004 to December 2015. CAPC cases are considered those that present cavitation areas at chest X-ray.
We collected demographic, symptoms, analytical and microbiological data, image test, treatment, evolution and complications, of each patient.

Results

We report 4 patients (2 girls), from 13 months to 4 years old (median 19.5 months). No pulmonary disease at past history, just one of them had full immunization with pneumococcal vaccine, and one patient developed varicella few days before hospitalization. Symptoms started a median of 7 days before admission (p25-75, 3.25-23.5), and all cases presented fever and cough, 2 cases polypnea. Acute phase reactants were elevated in all patients (PCR maximum median value 19.3 mg/dL), as well as they developed thrombocytosis. One patient had Pneumococcal Urinary Antigen and Mycoplasma IgM positive results, but there were no other microbiogical findings.

Antibiotic iv therapy was 3rd generation cephalosporin plus clindamycin, in 3 of 4 patients. Median length of stay was 14.5 days (p25-75, 11-23.5). All cases recovered ad integrum.

Conclusions

Age of presentation of CAPC in our serie of cases is under 5 years old. Patients had no relevant medical past history, nor history of aspiration, but one patient suffered from varicella. Length of admission and iv treatment are prolonged. We haven't detected any long term respiratory problems.

ESP16-0125
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

A SINGLE DOSE MONOCLONAL ANTIBODY (MAB) IMMUNOPROPHYLAXIS STRATEGY TO PREVENT RSV DISEASE IN ALL INFANTS: RESULTS OF THE FIRST IN INFANT STUDY WITH MEDI8897

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Background

RSV is the most common cause of lower respiratory tract infection (LRTI) among infants. A significant unmet need exists for RSV prophylaxis in healthy infants. Our goal is to develop a MAb with an extended half-life ($t_{½}$) to protect infants through an entire RSV season with a single intramuscular (IM) dose. The purpose of this study was to evaluate the safety profile, pharmacokinetics (PK), and anti-drug antibody (ADA) responses for MEDI8897 in healthy 32 – 35 weeks' gestation preterm infants.

Methods

Infants were randomized to receive a single IM injection of MEDI8897 10 mg (n=8), 25 mg (n=31), 50 mg (n=32) or placebo (n=18) and will be followed for 360 days. Enrolment occurred during the 2015 RSV seasons in the US, South Africa, and Chile. Blood was collected at multiple timepoints. Infants who met criteria for a medically-attended (MA) LRTI had nasal samples obtained for RSV RT-PCR.

Results

At the interim analysis 30 days after the last subject was dosed, 88 infants remained in the study. Adverse events (AEs) were reported in 12/18 (66.7%) placebo and 51/71 (71.8%) MEDI8897 recipients. One serious AE (LRTI) was reported in a MEDI8897 recipient. Model-based simulations predict MEDI8897 median $t_{½}$ torange from 83 - 94 days for the 50 mg dose in infants with normal clearance. ADA post-dose was detected in 12.5% of placebo and 4.4% of MEDI8897 recipients. MA-LRTI was reported in 4 MEDI8897 recipients, and 1 was RSV positive.

Conclusions

In healthy preterm infants, the safety profile of MEDI8897 was favorable. The interim PK results support the feasibility of a single IM dose to provide protection for the duration of the RSV season.

This study was sponsored by MedImmune.

Clinical Trial Registration (Please input N/A if not registered)

NCT02290340

ESP16-0494
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

PILOTING A SHORT EPIDEMIOLOGICAL SURVEY TO EVALUATE THE VARYING CLINICAL MANAGEMENT OF CHILDREN WITH BRONCHIOLITIS ACROSS EUROPE

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Background

The optimal clinical outcome measure to study the efficacy of antivirals for Respiratory Syncytial Virus (RSV) bronchiolitis remains unclear. The aim of this study was to determine the utility of a short epidemiological survey (SES) in assessing clinical presentation and management of clinical bronchiolitis in young infants across a range of European countries.

Methods

Seven centres (from 7 countries) participating in the PREPARE network (Platform for European Preparedness Against Re-Emerging Epidemics), completed a bronchiolitis SES during the winter of 2014/2015.This focused on infants <24 months of age presenting with lower respiratory tract infection (LRTI) to participating emergency departments (EDs), as a large proportion of these infants were likely to be suffering from bronchiolitis.

Results

In infants <24 months old presenting with LRTI and subsequently discharged home, RSV was tested routinely in only 3/6 centres, while all tested for RSV in admitted infants. The proportion of infants who attended with bronchiolitis and were admitted ranged from 5 to 71% between the centres, and was highest for the youngest infants (28%). The proportion of infants who were discharged from ED then re-attended within 14 days varied between 13-21% according

to age.

Table 1: Summary of key clinical management features for infants with bronchiolitis presenting to 7 European centres during a 72-hour short epidemiological survey

	Infants <6 months of age	Infants 6-12 months of age	Infants 13-24 months of age
ED attendances	87	110	95
Re-attendances within 14 days	18 (21%)	19 (17%)	12 (13%)
Confirmed RSV	23 (26%)	14 (13%)	9 (9%)
Ward admissions	24 (28%)	15 (14%)	13 (14%)
Confirmed RSV	17 (71%)	11 (73%)	6 (47%)
Admissions to PICU	0 (0%)	3 (20%)	1 (8%)

*These data refer to a surveillance period of a total of 72 hours per centre during December 2014 to March 2015.

Conclusions

Useful clinical data that will help to design interventional trials can be collected using rapid SES. Re-attendance is frequent amongst infants with bronchiolitis (1 in 5 infants <6 months of age), although the number of secondary admissions after re-attendance and the proportion of RSV-positive cases amongst re-attenders are unknown. Further development of the SES may provide information about potentially relevant target groups and end-points for clinical trials.

ESP16-0402
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

CHILDREN WITH PERSISTENT COUGH SHOULD UNDERGO LABORATORY EVALUATION TO EXCLUDE PRESENCE OF PERTUSSIS

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Background

Cough is common complaint in children to visit a doctor. We aimed to determine the prevalence of pertussis and parapertussis in children with cough of unknown aetiology lasting for ≥7 days in highly immunised population and to define symptoms that best predict either disease.

Methods

Children and adolescents (<18years) were enrolled between 23. April 2012 and 31. December 2014 in 25 general practitioner practices and three hospitals in Estonia. The recorded symptoms were paroxysms, inspiratory whooping, posttussive emesis, apnoea and fever (axillary ≥37.3°C). Pertussis was confirmed by culture and/or PCR and/or presence of pertussis toxin (PT)-IgG antibodies >100 IU/mL or PT-IgG 40-100 IU/mL and PT-IgA ≥ 12 IU/mL. Parapertussis was confirmed by culture and/or PCR. Four statistical analyses shown in Table were performed.

Results

Of 151 patients with cough of median duration of 19 days 12 (7.9%; 95%CI: 4.2-13.5%) had pertussis and 7 (4.6%; 95%CI: 1.9-9.3%) parapertussis. The prevalence of pertussis was highest in partly or non-immunised children <1 years (44.4%; 95%CI: 13.7-78.8%). The prevalence of parapertussis was similar across paediatric ages. According to four statistical analyses the presence or absence of recorded symptoms did not definitely confirm or exclude pertussis, but children with pertussis had more often inspiratory whooping and posttussive emesis than other patients (Table). No symptoms to predict parapertussis was revealed, except presence of inspiratory whooping in a classification tree analysis.

Table:

The statistical tests and symptoms that occurred more in patients with pertussis and parapertussis than in patients with cough of another/unknown aetiology.	Children with pertussis (n = 12)	Children with parapertussis (n = 7)
Prevalence of symptoms	Posttussive emesis (p = 0.059)	No specific symptoms
Multiple correspondence analysis	Inspiratory whooping, posttussive emesis, apnoea, fever	No specific symptoms
Classification tree analysis (CART) (minimum splitting criteria univariate p<0.3)	Inspiratory whooping	Inspiratory whooping
Step-wise multiple regression analysis	Posttussive emesis	N/A

N/A-not available

Conclusions

With the exception of children below one year a low prevalence of pertussis was observed in patients with persistent cough. Still, we recommend laboratory testing for pertussis (PCR and/or serology) in all children with persistent cough due to poor predictability of clinical symptoms in distinguishing pertussis.

(Funded by Estonian Science Foundation, grant 9259)

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0353
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

DETECTION OF RESPIRATORY VIRAL INFECTIONS IN INFANTS TREATED FOR SUSPICION OF SEPSIS: A PRELIMINARY RESULTS

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Background

To determine frequency and significance of respiratory viral infections in infants who were treated for suspicion of sepsis in Hacettepe University Faculty of Medicine, Ankara, Turkey.

Methods

We performed a prospective screening method for detecting respiratory viral infections in infants (from one month of age to two year old) treated with suspicion of sepsis from November 2014 to December 2015. The diagnosis of viral infection was confirmed by real-time positive viral polymerase chain reaction from nasopharyngeal swabs. Demographic, clinical, radiographic and laboratory data records were reviewed.

Results

During 13 months, nasopharyngeal swabs was collected in 36 infants. Twenty-two (61,1%) of the 36 infants had a respiratory virus detected from the nasopharyngeal swab that included 6 (16,7%) of the 22 infants had concomitant positive blood culture. All of the respiratory viruses were detected at the time of the first sepsis evaluation. Gender was equally distributed (16 males and 20 females) and median age was 5 months (range 1 to 23 months). Rhinovirus and influenza A were the most common viruses in 8 cases and in 4 cases, respectively. December was the month that sepsis and respiratory viral infection seen most frequently. Four patient dead, one of had respiratory viral infection, two of had both respiratory viral infection and bacterial infection, and one of had no positive test results.

Conclusions

A total of 61.1% of infants had a respiratory virus detected and 19.5% had blood stream infection when evaluated for bacterial sepsis. These findings put forth for more respiratory viral investigations of infants with suspected sepsis to establish accurate diagnoses, and inform antibiotic approaches.

ESP16-1053
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

LARGE PULMONARY ABSCESS DUE TO TUBERCULOSIS AND POLYMICROBIAL COINFECTION CONSERVATIVELY CURED ONLY WITH ANTIBIOTICS IN AN ADOPTED CHILD

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Title of Case(s)

"Large pulmonary abscess due to tuberculosis and polymicrobial coinfection"

Background

Pulmonary abscess is a rare, serious condition in children. Coinfection with tuberculosis (TB) and bacteria is not common. We report the case of a 6-year-old Ethiopian girl who presented a massive lung abscess, due to TB and polymicrobial coinfection.

Case Presentation Summary

The patient, whose parents died from TB, was adopted 3 years before admission. She received BCG vaccination and had a normal work-up before her adoption. She had an ENT surgery with possible aspiration two weeks prior to her hospitalization. She was admitted for high vesperal fever since 20 days, associated with cough. Her blood investigations revealed only a mild inflammatory syndrome. A large lesion in the right lower lung field was found on chest X-ray. A chest CT scan showed an important abscess of the middle and lower right lobe (8 cm x 5,7 cm x 7,3 cm). No extra-pulmonary lesions were found. The Mantoux test showed a 13 mm induration but the direct analysis of gastric intubation was negative for AFB. She received a 3-week IV antibiotherapy with Amoxicillin-Clavulanate of 150 mg/kg/day with an oral relay. The chest ultrasound, after 4,5 weeks of treatment, was normalized except for a thin cavity rind. At that point, the culture of gastric intubation grew for *Mycobacterium tuberculosis*. A four-drug therapy was initiated (INH- RIF- PZA- EMB). The child fully recovered without any sequelae.

Learning Points/Discussion

The coinfection of tuberculosis and bacterial infections in lung abscesses in immunocompetent children is not a commonly reported entity. Detection of one infection could mask the diagnosis of the other. Early adequate treatment can prevent further complications and reduce the need for surgical intervention even in the presence of large abscess.

ESP16-0841
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MODERN ON-LINE DIAGNOSTIC TOOL IN STREPTOCOCCAL PHARYNGITIS - OLD DISEASE, NEW APPROACH

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Background

Streptococcal pharyngitis can be easily mistaken with viral infection, which still constitutes the vast majority of pharyngitis etiology in children.

Methods

To help doctors in therapeutic decisions in acute pharyngitis we created our on-line application with the algorithm based on Centor/McIsaac Score and recent European and local guidelines.

Results

It requires input of basic patient data - age, weight, important medical history: risk factors and antibiotic allergy. By the typing in presented symptoms the result of Centor Score is presented as well as the probability of diagnosis of streptococcal pharyngitis.

The application includes indications to microbiological testing like pharyngeal swab or rapid strep tests. If antimicrobial therapy is necessary, it suggests the first line treatment, provides information about available drug forms on Polish market and adjusts doses to patients body weight. Exemplary prescription is also generated. The extraordinary situations like, for example, streptococcal carriage, treatment in case of allergy for beta-lactams are included.

Conclusions

The main purpose of this IT tool is the unification of management in acute pharyngitis according to current recommendations. We hope that it will increase the availability of reliable data for every healthcare professional as well as limit antibiotic misuse and development of drug resistance. It seems to be a handy, effortless form of e-learning using modern technology.

ESP16-0260
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

SIGNIFICANCE OF CONCOMITANT RESPIRATORY INFECTION IN RESPIRATORY SYNCYTIAL VIRAL DISEASES IN THE RURAL AREA OF SOUTH KOREA

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Background

This retrospective survey was designed to elucidate the clinical and laboratory significance of concomitant respiratory infection in respiratory syncytial viral(RSV) illness.

Methods

Two hundred RSV infected infants, who were admitted from Oct. 1, 2014 to Apr. 30, 2015, were enrolled. Nasal secretion swab and blood sampling took placed immediately after admission. Thirteen different viruses were detected from nasal secretion by multiplex RT-PCR, while serum Mycoplasma pneumoniae IgM was measured from serum. We compared various parameters between two groups: Group1 with RSV only infection and Group2 with RSV infection with concomitant respiratory infection. Patients with history of prematurity, congenital heart disease, RDS, or immunodeficiency were considered as high risk group.

Results

Among 200 infants, 146 were included as group1, 54 as group2. Rhinovirus was the most common concomitant pathogen(19 cases). Expression rate of severe symptoms such as fever or dyspnea were 63.7%(Group1), 59.3%(Group2)($p>0.05$) and 14.4%(Group1), 13.0%(Group2)($p>0.05$), respectively. White blood cell(WBC) count (Group1: $9.65\pm3.55X10^9/L$, Group2: $11.30\pm3.49X10^9/L$), absolute neutrophil count(ANC) (Group1: $3.63\pm2.49X10^9/L$, Group2: $4.72\pm2.91X10^9/L$) were higher in Group2 ($p<0.05$). The Large unstained cell(LUC) was higher in Group1 (Group 1: $5.24\pm1.69X10^9/L$, Group2: $4.81\pm1.61X10^9/L$)($p<0.05$). The duration of hospital stay, duration of OPD follow up showed no significant difference between 2 groups.

Conclusions

In RSV disease, concomitant respiratory infection can cause elevation of WBC and ANC count without any clinical or prognostic significance.

ESP16-0692
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

PATIENTS WITH SEVERE RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN PEDIATRIC INTENSIVE CARE UNIT (PICU) AND THEIR ELIGIBILITY FOR PALIVIZUMAB PROPHYLAXIS- A RETROSPECTIVE MULTI-CENTER STUDY

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Background

Palivizumab (PZ) prophylaxis has shown to reduce hospitalization caused by severe respiratory syncytial virus (RSV) infection in high-risk children. The guidelines for PZ prophylaxis vary in different countries and region. This study was performed to compare the PZ eligibility according to different guidelines in patients hospitalized in pediatric ICU (PICU) with RSV infection.

Methods

This was a retrospective, multi-center study in Korea. Children (< 18 years) with RSV infection diagnosed within 48 hours in PICU admission were included from September 2008 to March 2013. Patients having underlying hematology-oncology diseases were excluded.

Results

A total of 92 patients from six hospitals were identified and 47 patients (51.1%) had risk factors. Hemodynamically-significant congenital heart disease (40.4%, 19/47) was most frequently observed, followed by chronic lung disease (23.4%, 11/47), neuromuscular disorder (NMD) or congenital abnormalities of the airway (CAA) (19.2%, 9/47) , prematurity (14.9%, 7/47), and primary immunodeficiency (2.1%, 1/47). Sixty-two patients were less than 2 years of age at the beginning of RSV season. Among those, eligibility for PZ indication was 35 % by Korean guidelines, 42 % by EU guidelines, and 47% by 2014 US guidelines. Compared with US guidelines, there was 25.5% relative decrease and 10.6% relative decrease by Korean and EU guidelines, respectively. Patients with NMD/CAA who were included only in US guidelines as possible PZ prophylaxis had a more prolonged duration of mechanical ventilation than babies without risk factors (the median days, 26 days [range, 24 to 139] vs. 6 days [range 2 to 68], $P = 0.031$)

Conclusions

Eligibility for PZ prophylaxis varied according to guidelines of different countries and region. Further study such as cost benefit analysis in the community may help updating guidelines.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0501
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

HOSPITALIZATION FOR FLU IN INFANTS: CLINICAL EVOLUTION AND RISK FACTORS

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Background

To describe risk factors associated with admission due to influenza infection in a cohort of infants below 1 year of age, as well as clinical course and complications.

Methods

Retrospective study including children below1 year of age, admitted in a tertiary care hospital with confirmed influenza virus infection over 5 years (October/2010 - April/2015). Epidemiological and clinical data were collected.

Results

139 patients were included, 60% male. The median age was 82 days [IQR 36-176] being 75% younger than 6 months and 17% (24) neonates. 78% of infections were due to influenza A, 19% to type B and 2% were coinfections. 42% of children had any medical background (21% bronchial hyperreactivity, 7% prematurity,5.7% heart disease, 8% others). Nevertheless, only 7% of children older than 6 months had been immunized against flu. The average stay was 3 days [IQR 2-5], and 90% received oseltamivir treatment for 5 days without registering adverse reactions. 38% of patients required oxygen therapy (65% of those over 6 months vs 31%, P <0.01) for an average of four days [IQR: 2-7]. IN 32% of cases antibiotics were prescribed. The complication rate was 35%, mainly pneumonia (26%). Eleven patients (10%) required admission to CIP (5 infants under 3 months), with an average stay of 4 days [IQR 2-8], 4 requiring mechanical ventilation.

Conclusions

40 % of infants hospitalized for flu had medical history or pre-existing disease, mainly bronchial hyperreactivity. However, the rate of vaccination was very low. The complication rate among infants hospitalized for flu is high, despite antiviral treatment, which was well tolerated, even in patients below one month of age.

ESP16-0506
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

OSELTAMIVIR FOR TREATMENT OF INFLUENZA VIRUS INFECTION IN NEONATES AND INFANTS

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Background

Infants below 6 months of age are considered at risk of complications from influenza virus infection. Early treatment with neuraminidase inhibitors appears to decrease the duration and severity of the process, but data on tolerance and safety are scarce in neonates and infants. Oseltamivir is the only antiviral approved by the EMA for the treatment of influenza in children of all ages, and by the FDA in infants over 15 days of age.

Methods

Retrospective study including all children below 6 months of age with confirmed influenza virus infection admitted to a tertiary care Hospital in Spain between October/2010 and April/2015, and treated with oseltamivir. Epidemiological, clinical and therapeutic data were collected.

Results

A total of 92 infants below 6 months of age were included, 60 % males. 19 of them were neonates (20.6 %). The median age was 49 days [IQR 32-90] . A 79 % of them were positive for influenza A virus , 17% for influenza B and there were 2 cases of coinfection. 21% of patients had any medical background, mainly prematurity and cardipathy. The average stay was 3 days [IQR 2-5] and 32% of children required oxygen therapy (3 patients High-flow nasal cannula (HFNC) oxygen therapy and 2 mechanical ventilation). 26% suffered from complications and in 30% of cases antibiotics were prescribed. The mean dose of oseltamivir was 4.3 ± 1.2mg/kg/12h [range: 1.6-6.4] . No treatment was discontinued because of intolerance, and no adverse effects were reported.

Conclusions

There was a wide variation in Oseltamivir dosage in our cohort, despite recommendations by EMA and FDA. Nevertheless, tolerance was good in this population, including neonates, and no adverse reactions were reported.

ESP16-0697
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

SEROTYPE DOES NOT INFLUENCE DISEASE SEVERITY IN RESPIRATORY SYNCTIAL VIRUS BRONCHIOLITIS

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Background

RSV bronchiolitis remains the most common cause of hospital admission in infants. RSV genetic variability is mostly within the G gene. A 72 bp repeat in the G protein of RSV-A was noted in Ontario in 2010 (ON1) and has since spread worldwide but had not been studied in Ireland. Conflicting data exists about its effect on disease severity. The aim was to determine if the RSV subtype is associated with severe disease in children hospitalized with bronchiolitis.

Methods

RSV positive samples for 571 patients admitted to a tertiary paediatric hospital between 2009-2014 were typed into A and B by real-time PCR. 55 patients infected with RSV type A were successfully subtyped into ON1 or non ON1 variants by PCR amplification of the glycoprotein (G) gene and Sanger sequencing. RSV subtypes were compared with retrospective chart review data including requirement for PICU and length of stay. Stata version 11(College station, Texas) was used for statistical analysis.

Results

Two thirds of cases were RSV A (379). RSV A and B co-circulated each season with RSV B causing between 22% and 39% of cases. 15% of patients with RSV A required PICU and 20% of those with RSV B. This was not statistically significant (p value 0.35). Median length of PICU stay was 7 days for RSV A and 6 for RSV B (p value 0.34). ON1 subtype represented 75% of tested specimens in the 2013/14 season, 2/7 ON-1 required PICU compared to 9/48 non ON-1 (p=0.16).

Conclusions

There was no association between RSV type A and B and disease severity. The RSV ON1 variant is circulating in Ireland, however, was not associated with a more severe bronchiolitis presentation.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0250
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

BRONCHIOLITIS CLINICAL SCORE TO PREDICT HOSPITALISATION IN CHILDREN: A PROSPECTIVE COHORT STUDY

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Background

Objectives: We wished to determine the risk factors and develop a score to predict hospitalization in children with Bronchiolitis.

Methods

Prospective Cohort study. Children aged 2-24 months with clinical diagnosis of bronchiolitis were prospectively enrolled in two time epochs (from December 2011-14thDecember2012 and from 30thDecember 2013-31st December 2014) in a Pediatric emergency ward of a tertiary-care hospital in India. Twenty six clinical risk factors were identified *'a priori'.* Data regarding these 26 risk factors was collected in all enrolled children. The primary outcome was need for hospital admission. Association between each independent risk factor and hospitalization was tested by calculating OR and 95%CIs. We determined independent predictors of admission through multivariable logistic regression analysis and assimilated them into a simple clinical score using regression coefficients.

Results

266 children (136 admissions) with Bronchiolitis were enrolled. Eleven clinical risk factors associated with hospital admission were identified via univariate analysis ($p<0.1$) and incorporated into multiple logistic regression analysis. Five factors retained their independent association. Our predictive score consisted of Age < 6 months (score of 2), Tachypnea RR>60/- (score of 3), Temperature >37.8°C (score of 3), SpO2 <92% @ room air (score of 6), GCS <15 (score of 6). The total score was 20. Area under receiver-operator characteristic curve was 0.84 (95% CI 0.80 to 0.89, $p<0.001$).

Conclusions

We present a novel score to predict hospitalization in children with bronchiolitis. Age< 6 months, Tachypnea, fever >37.8°C, SpO2 <92% and GCS <15 were significantly associated with risk for hospital admission in Bronchiolitis

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0143
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

MICROBIOLOGICAL DIAGNOSIS, TREATMENT AND OUTCOME OF 19 CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA WITH ASSOCIATED PLEURAL EFFUSION

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Background

Community acquired pneumonia (CAP) with associated pleural effusion appears to be on the rise in recent years. We present our experience in the management of children with CAP and associated pleural effusion.

Methods

Between 1/1/2010 and 2/28/2015, 19 children (10 females) with a median age of 4 years (1.5-14 years) required hospitalization for CAP with associated pleural effusion. The presence of pleural effusion was confirmed by ultrasonography. In cases of effusions with associated fever not settling after 48 hours of intravenous antibiotics and/or with associated signs of respiratory compromise, tube thoracostomy was performed.

Results

All patients received intravenous antibiotic for 7-21 days, while a thoracostomy tube was required in 15 cases. Two patients had positive blood cultures for *Streptococcus pneumoniae* (serotype 22F identified in the first, no serotyping was performed in the second). Bacterial cultures of the pleural fluid revealed the responsible organism in 4 patients (*Staphylococcus aureus* in 2, *S. pneumoniae*, serotype 3 and S*. pyogenes*, 1 case each). In 2 patients, polymerase chain reaction of the pleural fluid disclosed *S. aureus* and *S. pyogenes* (1 case each). In 5 other patients, urinary pneumococcal antigen was detected despite negative blood and pleural fluid cultures for *S. pneumoniae*. Two more patients had positive serological studies for recent *Mycoplasma pneumoniae* infection in conjunction with detection of urinary pneumococcal antigen. Finally, in 4 patients no pathogen was identified by all microbiological investigations. Only 1 patient required referral to thoracic surgery for further management. All 19 patients had favorable outcomes.

Conclusions

Microbiological diagnosis should be attempted in children with CAP with associated pleural effusion. The prognosis of children with CAP and associated pleural effusion is excellent with conservative management.

ESP16-0593
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

THE USE OF C-REACTIVE PROTEIN AND PROCALCITONIN IN THE DIAGNOSIS OF BACTERIAL INFECTION IN INFANTS WITH SEVERE BRONCHIOLITIS

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Background

Background and aims: Bacterial infection (BI) is related to one of the complications in severe bronchiolitis (BQ). The need of discriminate the patients who require antibiotics from the ones who don't is essential to reduce their use, therefore, biomarkers may be useful.

Methods

Methods: A prospective and observational study of patients with BQ admitted to the Pediatric Intensive Care Unit (2011-2014). Objective: to define a cut off value of procalcitonin (PCT) and C-reactive protein (CRP) during the patient evolution that would be useful to identify BQ with BI as sepsis, pneumonia or urinary tract infection (UTI), with CDC definitions. SPSS 20.0 was used.

Results

Results: 425 patients, 244 (57.4%) males were collected. The median age was 52 days (P_{25-75} 21-99). The median score of severity (HSJD score) was 10 points (P_{25-75} 7-13), it is defined as a severe stage. Respiratory Syncytial virus (RSV) was identified in 285 (67.0%) patients. BI was diagnosed in 128 patients (30.1%): 39 sepsis (9.2% of the total), pneumonia 96 (22.6%) and 23 ITU (5.4%). The percentage of patients receiving antibiotics at the time of admission was 320 (75.3).

It was observed significant differences between the level of PCT at admission and 48 hours in patients with BI with respect to uninfected ones, p=0.032 and p= 0.048 respectively. CRP value was significantly higher only in BI at admission, p=0.009. ROC curve for BI diagnosis of was significantly higher for PCT than for CRP, at admission and 48h, p= 0.002 and p= 0.015. Optimal cut off for PCT about BI diagnosis was 2.3ng/ml.

Conclusions

Conclusions: BI is common in severe BQ in PICU patients. CRP and specifically of PCT can help to confirm the clinical suspicion and adequate the antibiotic treatment.

ESP16-0707
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RESPIRATORY PATHOGENS IN YOUNG NEPALESE CHILDREN HOSPITALIZED WITH SEVERE PNEUMONIA

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Background

Acute lower respiratory tract infections in children are most commonly viral in origin, yet in many cases no cause of infection could be determined.

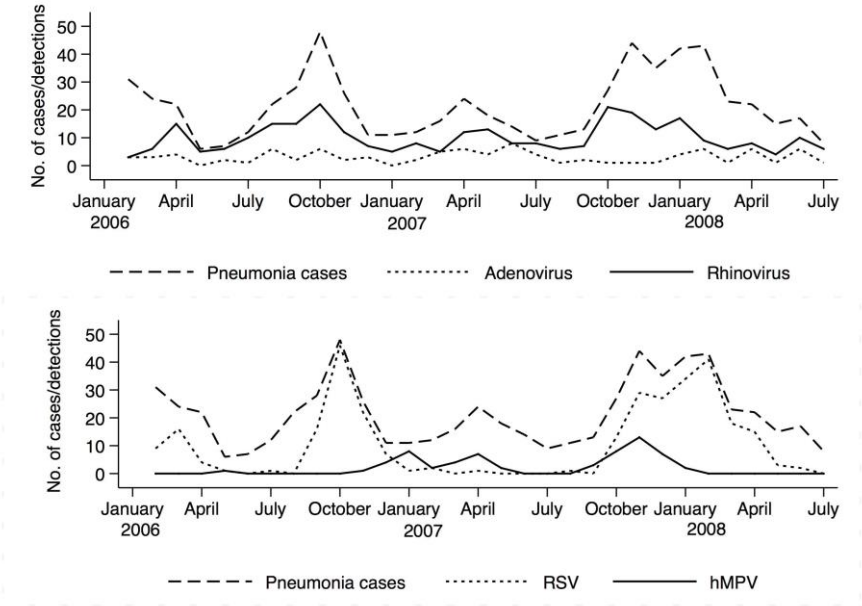
Methods

We employed 15 PCR-assays and retrospectively re-analyzed 610 nasopharyngeal specimens from children aged 2 to 35 months admitted with severe pneumonia (WHO) to Kanti Childrens's Hospital in Kathmandu, Nepal, from January 2006 through June 2008.

Results

Previously one or more of seven viruses had been detected by multiplex RT-PCR in 30% (188/627) of cases. In this reanalysis, we detected one or more microbes, including 12 respiratory viruses and three atypical bacteria, in 97% (592/610) of cases. Respiratory syncytial virus (RSV) and rhinovirus (RV) were the most common pathogens in this population,and were detected in 307 (50.3%) and 292 (47.9%) cases, respectively, followed by adenovirus (15.2%), human metapneumovirus (hMPV, 10.2%) and parainfluenza virus type 3 (8.9%). The remaining pathogens were detected in less than 5%. Among the atypical bacteria, *Mycoplasma pneumonia* was most common (4.3%). Single detections of RSV and hMPV were observed in 44% and 45% of cases, respectively, whereas RV was the sole microbe in 27% and ADV in 14%. During the 30 month study period, RSV outbreaks occurred at the end of the monsoon or during winter. RSV and hMPV were not detected between

epidemics, whereas RV and ADV were detected throughout the study, with varying epidemic



peaks.

Conclusions

An expanded diagnostic PCR-panel greatly increased the detection of respiratory pathogens in young Nepalese children hospitalized with severe pneumonia. RSV and RV were most frequent. RSV and hMPV were more often encountered as single detections and demonstrated a more epidemic seasonal pattern compared to RV and ADV, which were more often involved in co-detections.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0696
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

HUMAN METAPNEUMOVIRUS AND RESPIRATORY SYNCYTIAL VIRUS IN HOSPITALIZED NORWEGIAN CHILDREN WITH LOWER RESPIRATORY TRACT INFECTIONS

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Background

Human metapneumovirus (hMPV) and respiratory syncytial virus (RSV) are two dominating pathogens causing childhood respiratory tract infections (RTI) in need of hospitalization. Studies have implied that hMPV and RSV are quite similar viruses, in regards of disease severity and diagnosis, but few have compared them.

Methods

Children hospitalized with RTI at Department of Pediatrics, St.Olavs Hospital, Trondheim University Hospital, Norway, were prospectively included from November 2006 to July 2015. Nasopharyngeal aspirate (NPA) was analyzed by polymerase chain reaction tests for hMPV, RSV and other viruses. Children with lower RTI (LRTI) diagnosis and single virus positive for hMPV (n=106) or RSV (n=540) were compared.

Results

hMPV-infected children (median, months, 14.7. IQR 8.1-25.7) were older than RSV-infected (5.4. IQR 1.95-14.3) ($p<0.001$). The LRTI diagnoses differed between hMPV- and RSV-infected children (Table).

There were no significant differences in disease severity measures between hMPV and RSV: (1) Days at hospital: both median 4.0 vs 4.0 days. (2) Need of oxygen supply: 60.4% vs 65.0%. (3) Need of stay at Intensive Care Unit: 13.2% vs 12.0%. (4) Severity score: both median 1.0 (IQR 0.0-

2.0).

LRTI	hMPV (n = 106)		RSV (n = 540)		*p-value*
-pneumonia	36	34.0%	99	18.3%	
-bronchiolitis	43	40.6%	384	71.1%	
-asthma	15	14.2%	40	7.4%	< 0.001
-obstruct. bronchitis	6	5.7%	14	2.6%	
-unspecified LRTI	6	5.7%	3	0.6%	
Total	106	100%	540	100%	

Conclusions

Children with hMPV-infection were older than children with RSV. hMPV was more often associated with pneumonia, whereas RSV more often was associated with bronchiolitis. There was no difference in disease severity measures between hMPV and RSV infected children.

Clinical Trial Registration (Please input N/A if not registered)

N/A (not needed)

ESP16-0679
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

LUNG ABSCESS AFTER DELIBERATE DRUG OVERDOSE

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Title of Case(s)

Lung abscess

Background

Lung abscess is a rare infectious condition in paediatric patients. Aspiration is the most important predisposing factor for lung abscess, which may develop 1-2 weeks after the event.

Case Presentation Summary

We present the case of a 16-year-old female presenting with cough for ten days, right chest pain for 4 days and mild fever. One month before she had attempted suicide with drug overdose, presenting as coma, with a normal chest X-ray. On admission she was afebrile, with normal respiratory rate, SpO_2 of 97% and decreased respiratory sounds on the right. Leucocyte blood count was 16800/mm^3 with 80% neutrophils, C-reactive protein was 14.3 mg/dL. Chest X-ray showed a large, round and well-circumscribed hyperdense lesion on the lower half of the right lung field. Chest computed tomography confirmed the presence of a cavitary lesion containing an air-fluid level in the superior segment of the right lower lobe, consistent with lung abscess. Parenteral antibiotic therapy with amoxicillin and clavulanic acid and clindamycin was initiated. Blood culture was sterile and the tuberculin skin test was negative. The adolescent became afebrile within 2 days of administration of antibiotics and asymptomatic within 7 days. Intravenous therapy was continued for 2 weeks and the patient was then discharged on oral antibiotics for another 2 weeks. X-ray was performed 60 days after presentation showing no evident parenchymal changes.

Learning Points/Discussion

Antimicrobial therapy is the cornerstone off lung abscess treatment and it should include antibiotics with anaerobic bacteria and Gram-positive cocci coverage. Our patient was successfully treated with a 4 week course of antibiotics.

ESP16-0985
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

COMMUNITY-ACQUIRED PNEUMONIA AND MODIFICATION OF ASTHMA SYMPTOMS IN CHILDREN

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Background

Problem of early asthma and community-acquired pneumonia (CAP) diagnosis in children remains relevant because of variation of symptoms, late detection and inadequate treatment that leads to development of complications and disability in patients.

Methods

118 children aged 1-18 years with asthma were observed. Relationship between variations in the study was analyzed by Pearson correlation with determination of strength of linear association between the variables.

Results

Atopic asthma was diagnosed in all patients, 35 children (29.7%) had CAP, caused in 18(51.4%) by Mycoplasma pneumonia(Mp), in 21(60%) – by Cytomegalovirus(CMV), in 4(11.4%) - by Epstein-Barr virus(EBV), in 3(8.6%) – by Chlamydophilla pneumoniae(Cp), with polyetiology of CAP in 34(97.1%) patients.

Development of pulmonary hypertension (PH) and fibrosis (PF) in children with CAP and asthma occurred in 37.1% of patients. In 38.4% of patients with asthma, CAP, PH and PF CT scans revealed emphysematous bullae (EB). In 17 of 20 patients older than 3 years with asthma and CAP (85%) signs of connective tissue disorders (CTD) in osteoarticular system (95.8%), skin (35.8%), cardiovascular (82.2%), gastrointestinal (40%), urinary system (19.5%) were determined with strong positive correlation ($r=0.9$, $P \ll 0.001$) between CAP frequency and presence of CTD signs in children with asthma that significantly complicated asthma and CAP diagnosis and caused development of complications and disability due to inadequate treatment.

Conclusions

1.One-third of asthmatic patients had CAP caused in 97% by association of pathogens (Mp,CMV,Cp,EBV), that led to more severe and prolonged asthma exacerbations.
2.Strong positive correlation between CAP frequency and CTD signs in children with asthma was revealed.
3.Variety of clinical symptoms associated with involvement of multiple systems in CTD process in children with CAP and asthma complicated diagnosis of both asthma and CAP and worsened prognosis.

ESP16-0998
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ASTHMA HIDES BEHIND AN «ACUTE RESPIRATORY INFECTION»

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Background

Acute respiratory infections (ARI) are significant in asthma symptoms in children. Heterogeneity of asthma causes considerable difficulties in its diagnosis, leading to the development of complications, quality-of-life deterioration in patients.

Methods

118 children aged 1-18 years with asthma were observed within groups: Group A(n=25) - asthma diagnosed in first 2 years since onset, with adequate therapy; Group B(n=86) - 3-5 years after onset; Group C(n=7) - later than 5 years after onset.

Results

Asthma in Group A was considered as ARI in 21.2% of children. In 56% of them CAP was diagnosed, in 35.7% – CAP with episodes of bronchial obstruction; in 28% - recurrent laryngotracheitis (RLT); in 36.5% - acute obstructive bronchitis. 3-5 years after onset asthma was diagnosed in 72.9% of patients, after 5 years and more – in 5.9%. In Group B "frequent ARI" occurred in 48.8% of patients; in 12.7% - recurrent bronchitis (RB); in 22.1% - recurrent CAP; in 2.3% - RLT. RB was diagnosed in 71.4% of parients of Group C, RLT - in 28.6%. Complications developed 2 years after asthma onset: pulmonary hypertension (PH) - in 22% of cases, pulmonary fibrosis (PF) in 59.1% of asthmatic children with CAP and PH and emphysematous bullae (EB) in 38.5% of them. Strong positive correlation between late-diagnosed asthma and the frequency of complications ($r=0.9$; $P \ll 0.001$) was determined.

Conclusions

1.The diagnosis of ARI should be viewed as universal in the late diagnosis of asthma.
2.Late asthma diagnosis (after 2 years of its onset) leads to development of complications: PH, PF, EB.
3.Close relationship between asthma exacerbations with CAP and development of PH, PF, EB was revealed.
4.Thorough examination of patients with frequent ARI is required for asthma excluding.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1009
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN WITH ASTHMA AND DIFFERENT DURATION OF INHALED CORTICOSTEROID THERAPY

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Background

Controller treatment of asthma includes inhaled corticosteroids(ICS), as effective anti-inflammatory agent. Frequent community-acquired pneumonia(CAP) in asthmatic children makes it necessary to examine relationship between CAP and ICS therapy.

Methods

118 children with asthma aged 1-18 years were observed within 3 groups: Group A(n=87) - children received ICS therapy for more than 2 years; Group B(n=25) - from 2 to 5 years; Group C(n=6) - for 5 years and more.

Results

Atopic asthma was diagnosed in all patients, in 29.7% of them CAP was revealed, caused by Mycoplasma pneumonia(Mp) in 51.4% of children; cytomegalovirus(CMV) – in 60%; Epstein-Barr virus(EBV) – in 11.4%; Chlamydophila pneumoniae(Cp) - in 8.6%. Polyetiology of pneumonia was determined in 97.1% of cases. Development of complications (pulmonary hypertension (PH) and fibrosis (PF) in asthmatic children with CAP occurred in 37.1% of cases. In 38.4% of patients with asthma, CAP, PH and PF CT-scans revealed emphysematous bullae (EB). CAP was diagnosed in 14.9% of patients of group A, in 64% of children of group B; recurrent episodes of CAP 2-3 times a year were observed in all patients of group C. Strong positive correlation between duration of ICS therapy in asthmatic children and frequency of CAP in them was observed($r=0.9$; $p \ll 0.001$).

Conclusions

1.29.7% of asthmatic patients had CAP, caused by association of pathogens (Mp,Cp,EBV,CMV) in 97% of them, with the development of complications (PH,PF,EB).
2.Strong positive correlation between frequency of CAP in children and duration of ICS treatment in children for more than 2 years was revealed.
3.It is necessary to continue the study of relationship between CAP in children receiving long-term ICS therapy and duration of the treatment for prevention of possible complications of hormone therapy.

ESP16-0672
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

THE PREVALENCE, CO-DETECTION AND SEASONAL DISTRIBUTION OF UPPER AIRWAY VIRUSES AND BACTERIA IN CHILDREN WITH ACUTE RESPIRATORY ILLNESSES WITH COUGH AS A SYMPTOM

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Background

Cough in children is the most common reason for presentation to medical practitioners. We aimed to describe the upper airway microbes detected in children presenting with cough as a symptom to a tertiary emergency department .

Methods

A prospective cohort study of children aged less than 15 years presenting to an emergency department in Brisbane, Australia with cough as a symptom. Bilateral anterior nasal swabs were collected at baseline and PCR tested for 7 bacteria and 17 viruses at the Queensland Paediatric Infectious Diseases Laboratory.

Results

Between Dec 2011 and August 2014, 876 children were enrolled; swabs were collected from 827. Median age was 27.7 months (IQR 13.9 – 60.3) and 498 (61%) were male. 75.3% of children were positive for any bacteria; *M. catarrhalis* (53.4%), *S. pneumoniae* (46.5%) and *H. influenzae* (29.6%). Detection of ≥ 2 bacteria occurred in 43.7% of children. 60.4% of children were positive for any virus, ≥ 2 viruses were detected in 10.5%. *B. pertussis* and influenza viruses were uncommon (0.8% and 3.9% respectively). 48.5% were both virus and bacteria positive. H. influenza dominated bacteria-virus pairs. Factors associated with co-detection were age (adjusted odds ratio (aOR) for age <12-months=4.9 [95%CI 3.0, 7.9], age 12 to <24-months=6.0 [95%CI 3.7, 9.8]; and age 24 to <60-months=2.4 [95%CI 1.5, 3.9]), male gender (aOR=1.46, 95%CI 1.1, 2.0), childcare attendance (aOR=2.0, 95%CI 1.4, 2.8) and winter enrolment (aOR=2.0, 95%CI 1.3, 3.0).

Conclusions

Bacteria are more commonly identified in the upper airways of children with cough than viruses however co-detection occurs in almost a half of children. Viral-H. influenzae interactions in ARI should be investigated further, as the contribution of non-typeable H. influenzae to acute and chronic respiratory diseases is being recognised increasingly.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0678
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

DO UPPER AIRWAY VIRUSES AND BACTERIA PREDICT COUGH DURATION AND NEED FOR HOSPITALISATION IN CHILDREN WITH ACUTE RESPIRATORY ILLNESSES WITH COUGH AS A SYMPTOM

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Background

Cough is symptomatic of a broad range of acute and chronic pediatric respiratory illnesses. No studies in children have tested for an extended panel of upper airway respiratory viruses and bacteria to identify whether they predict cough outcomes, irrespective of clinical diagnosis at the time of acute respiratory illness (ARI). We therefore determined whether upper airway microbes independently predicted hospitalization and persistent cough 28-days later in children presenting with an ARI, including cough as a symptom.

Methods

A cohort study of children aged <15-years were followed for 28-days after presenting to a pediatric emergency department with an ARI where cough was also a symptom. Socio-demographic factors, presenting clinical features and a bilateral anterior nasal swab were collected at enrolment. Polymerase chain reaction assays tested for 7 respiratory bacteria and 17 viruses. Predictors of hospitalization and persistent cough at day-28 were evaluated in logistic regression models.

Results

817 children were included in the analysis; median age 27.7-months. 116 (14.2%, 95%CI 11.8, 16.6) children were hospitalized and 163 (20.0%, 95%CI 17.2, 22.7) had persistent cough at day-28. The only microbial predictor of hospitalization was having RSV A or B detected on nasal swab (aRR 1.8, 95%CI 1.0, 3.3). *M. catarrhalis* (aRR 1.8, 95%CI 1.2, 2.7) was the only organism associated with cough persistence (aRR 1.8, 95%CI 1.2, 2.7).

Conclusions

An etiologic role for *M. catarrhalis* in the pathogenesis of persistent cough post-ARI is worth exploring, especially given the burden of chronic cough in children and its relationship with chronic lung disease.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0285
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

PROBIOTICS FOR THE PREVENTION OF PEDIATRIC UPPER RESPIRATORY TRACT INFECTIONS: A SYSTEMATIC REVIEW.

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Background

Acute upper respiratory infections (URTI) contribute substantially to pediatric morbidity and mortality worldwide. Prevention of these infections in childhood is a very important public health challenge. Previous systematic reviews including both adult and childhood populations have reported that probiotics seem promising with modest evidence. This study aimed to focus on prophylactic probiotic use in the prevention of URTIs in childhood.

Methods

Relevant trials on two databases were identified in a systematic review from inception to June 2014. Study selection, data extraction and quality assessment were carried out by two reviewers.The Jadad score was used to assess the methodological quality of studies. In this review, the effects of probiotics, particularly *Lactobacillus* and *Bifidobacterium* strains, on the incidence and symptom scores of URTIs in otherwise healthy children were evaluated for the first time. This review comprised 14 RCTs applied to a paediatric population with high-quality methodology.

Results

A significant decrease in the incidence of URTIs was reported in 7 of the 12 RCTs. A significant reduction regarding the severity of symptoms of RTIs was found in 7 of 11 RCTs. At least one beneficial effect of prophylactic probiotic use was observed in the majority (10/14 RCTs) of these high-quality studies.

Conclusions

This systematic review suggests that probiotics in immunocompetent children have a modest effect both in diminishing the incidence of URTIs and the severity of the infection symptoms. Even a minimal reduction of 5-10% in the incidence of URTIs would have an important clinical and economic mpact on societies. Furthermore, the long-term administration of probiotics appeared to have a good safety profile in childhood and none of the studies reported any serious adverse events related to the probiotic strain.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESP16-0047
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

VIRUSES AND ACUTE RESPIRATORY INFECTIONS IN CHILDREN UNDER TWO YEARS OLD IN BLIDA - ALGERIA

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Background

The aim of the study is to investigate the incidence of 10 viruses in children less than 2 years of age admitted with lower ARI at a tertiary teaching hospital and study demographic and clinical differences among virus.

Methods

Children < 2 years old hospitalized for lower ARI were prospectively enrolled between December 2010 and April 2011. Nasal or nasopharyngeal swap sample was collected from each patient. These samples were tested for the detection of RSV, influenza Virus A and B, human Rhinovirus (RV), human Metapneumovirus (HMPV), human rotavirus, Adenovirus, Parainfluenza 1-3, by reverse-transcription-polymerase chain reaction multiplex RT-PCR. Outcome measurements were age, breastfeeding history and clinical severity score.

Results

117 children (68 Males) < 2 y were recruited. The median age was 3 months (± 0.9) with 50% being < 3 months and 90% < 12 months. Risk factor for severe ARI included malnutrition (14%) and significant comorbidities (20%). Virus was detected in 82.9% of the 117 infants. The most frequently detected viruses were RSV (48%), Human Rhinovirus (23%), Human Metpneumovirus (22%), Adenovirus (7.5%), Influenza (5%), Parainfluenza 3 (2.5%). Co-infections were particularly common being detected in 25 children (21.4%). A unique virus infection was present in 72 children (62%). Clinical features associated with RSV infection were similar to those of other respiratory viruses. Presenting symptoms between the RSV positive and RSV negative groups were similar.

Conclusions

The study underlines the important of viral pathogens in lower ARI in hospitalized children less than 2 years old. Overall RSV was the most frequently identified virus. HMPV and RV are also important cause of acute respiratory infections in children in Algeria. Positive viral identification will reduce the inappropriate use of antibiotics.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0695
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RECOGNIZING IMMUNODEFICIENCY IN CHILDREN WITH FREQUENT INFECTIONS: WHAT ARE THE PREDICTIVE FACTORS?

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Background

The aim of this study was to evaluate the children presenting with the complaint of recurrent infections and to determine the possible predictive factors foreseeing the requirement for further investigations.

Methods

This study is a retrospective analysis of 507 children (221 female, 43.6%) with median age of 46 (range 4-190) months, who attended to our department with the complaint of recurrent infections between January 2013 and December 2014 during two years period.

Results

The majority of the patients were the preschool age children (n=380,75%), the number of patients presenting with LRTI was 117 (23.1%). The patients were divided into 4 diagnostic groups; as atopic children (n=148, 29.2%), children with PID (n=54, 10.7%), patients with chronic disorders (n=40, 7.9%) and the majority, healthy subjects (n=265, 52.3%). Among school age patients, the incidence of atopic children was significantly high (p=0.016). Presenting at adolescent age group, growth retardation and hypogammaglobulinemia were the predictive risk factors for primary immune deficiency. Antibody (B cell) deficiencies (n=43, 80%), and among those, selective IgA deficiency (n=23, 4.5%) constituted the majority of the patients in PID. Rheumatological diseases (n=9, 1.8), mainly periodic fever syndromes, were the most common chronic disorders. Malignancy, acute lymphoblastic leukemia and lymphoma, was obtained in two patients (0.4%).

Conclusions

Complaint of recurrent infections is very common among children attending to health care facilities. It is crucial for clinicians to differentiate the children who need further investigations and urgent medical attention.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0458
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

INCIDENCE OF ACUTE OTITIS MEDIA (AOM) IN RUSSIA: AN EPIDEMIOLOGICAL STUDY IN CHILDREN UNDER 5 YEARS OF AGE

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Background

Acute otitis media **(**AOM) is one of the most common diseases in children. However, there is limited data on the incidence of AOM in children under 5 years of age in Russia. We evaluate the incidence of clinically confirmed AOM in this age group, severity of AOM, described disease management and estimated healthcare costs.

Methods

The study was conducted in three Russian cities (Barnaul, Yekaterinburg, Murmansk). Healthy children were randomly selected from rosters of out-patient clinics and actively followed-up for 12 months. Suspected episodes of AOM had to be confirmed clinically by a pediatric ENT using otoscopy. Incidence was estimated using person-time method.

Results

During the period October 2013 to March 2014, 1294 children were enrolled into the study. During the 12 months follow-up period, 158 ENT -confirmed AOM cases were collected. Incidence of clinical AOM was 18.6 per 100 person-years. Mean duration of parent sick leave was 12.2 days and the cost of treatment (money spent by parent) was 1159 Rubles. Hospitalization rate due to AOM was 2%, and duration of hospital stay varied from 3 to 30 days. Tympanocentesis was performed in 7.1% (8 cases). No complication of AOM was registered in our study. 64 cases of AOM were treated by antibiotics, most frequently the following were used: amoxicillin/clavulanic acid - 33 (51.5%), amoxicillin - 10 (15.6%) and ceftibuten - 7 (10.9%).

Conclusions

AOM disease burden in Russian children under 5 years of age in Russia is high, and underestimated by official statistics. Modern pneumococcal conjugate vaccines are the most rational strategy of the disease prevention.

ESP16-0722
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

ETIOLOGICAL STRUCTURE OF ACUTE OBSTRUCTIVE BRONCHITIS IN CHILDREN

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Background

Definition of etiological structure of a cute obstructive bronchitis in children was the purpose of our work.
Acute obstructive bronchitis are one of the most widespread forms of diseases of the bottom respiratory ways in children of early age (till 3 years) that is caused as anatomo-physiological features of respiratory ways in children of this age, and action of the viruses causing these diseases.

Methods

Nasal swabs samples from 115 children hospitalized at Children Infection Diseases Hospital (Minsk) for acute obstructive bronchitis (AOB) were studied for the detection of influenza virus A and B, parainfluenza virus 1-4 types, respiratory syncytial virus (RSV), adenovirus, rhinovirus, human coronavirus (HCoV), human bocavirus (HBoV), human metapneumovirus (HMPV) by multiplex PCR assay.

Results

One or more respiratory viruses were detected in 96 of 115 (83,5%) cases. Mono-infection was diagnosed in 90% cases and at 12 (10%) patients were proved mix-infection. The most often etiological agents of AOB were RS-virus (41%), Rhinovirus (14%) and Influenza virus 1-4 types (14%). Parainfluenza virus was detected in 5%, HBOV – 7%, HMPV – 9%. Among mix-infections were HBoV+Rhino (3 cases), HboV+HMPV (1), HBoV+Adeno (1), HBoV+Parainfluenza (2), Parainfluenza+RSV (3), Influenza A (H1N1) pdv-09+RSV (1), InfluenzaB+HMPV (1).

Conclusions

This study demonstrates that main etiological agents of acute obstructive bronchitis in children are respiratory viruses among which PSV belongs the most important role.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0733
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

RHINOVIRUS INFECTION IN CHILDREN

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Background

The most cold and flu–like illnesses are caused by human rhinoviruses (HRVs). HRVs is a major cause of acute viral respiratory tract infections in hospitalized children and is among the leading causes of childhood mortality. Main symptoms of rhinovirus infection may include runny nose and nasal congestion, headache, cough, sneezing, sore throat, rhinorrhea, croup in infants, tracheit and fever may occur in infants and young children. The clinical complications related to all rhinovirus infections include acute otitis media, acute sinusitis, and acute bronchitis.

Methods

Virusological examination of nasal swabs by OT PCR method was performed in 607 patients aged <18 years from October 2009 till June 2012.

Results

In 397 specimens (61%) were determined respiratory viruses. HRVs was detected in 15,6% of patients with ARVI. 98% of patients were children between the ages of one to three years. The disease started with the rise of body temperature (38,7^{0}C (from 37,0 to 40,2^{0}C) for 62,5% of patients (2/3 - febrile numbers), the duration of fever lasted 2 days (from1 to 5). Among respiratory syndromes were pharyngitis (8,5%), rhinopharyngitis (16,5%), rhinopharyngotracheitis (25%), pharyngotracheitis (8,5%), bronchitis (16,5%), 25% patients had symptoms of affection of larynx. Complications (acute otitis media, pneumonia) were registered in 17% of patients with HRVs.

Conclusions

The rare of detection rhinoviruses in structure of respiratory viruses is 15,6%. Clinical manifestations of HBoV-infection in children are characterized by respiratory syndrome with lesion of upper respiratory tract (in 83,5% cases) with high rate of development of complications (45%).

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0623
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

FAMILY HISTORY OF CROUP, ASTHMA, AND ALLERGY IN CHILDREN WITH CROUP AND CHILDREN WITH ASTHMA

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Background

There are data about relationship between croup, allergy and asthma. Due to various reasons the results of researches are not always consistent.

Methods

It was investigated 575 children with a history of croup, 60 children with asthma, and 369 controls (without croup and asthma) aged 6-14 years. Standardized questionnaires were used to obtain family history of croup, asthma, and allergy in first-third-degree relatives of children. We compared the frequency of croup, asthma, and allergic disorders in family history of patients.

Results

In family history of patients with croup and patients with asthma significantly higher prevalence of asthma and allergic disorders was found than in controls (for asthma prevalence 19.0% and 33.3%, respectively, vs 4.6%, for allergic disorders prevalence 25.9% and 51.7% respectively vs 16.0%). Asthma and allergy were found significantly higher in family history of patients with asthma compared to patients with croup. Croup was found higher in family history of patients with croup compared to controls (8.3% vs 1.1%, $p < 0.01$) and compared to patients with asthma (8.3% vs 1.7%, $p < 0.1$).

Conclusions

Our results are evidence of hereditary susceptibility not only for asthma, but for croup as well.

ESP16-0613
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

WHOOPING COUGH IN PEDIATRICS: A REVIEW OF THE PAST TWENTY YEARS

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Background

The purpose of this study is to characterize the clinical and epidemiology of pediatric pertussis cases admitted to our hospital over the past two decades.

Methods

Retrospective observational study; review of cases of pediatric patients diagnosed with whooping cough admitted to the Hospital General Universitario de Castellon, Spain, from 1992-2015.

Results

A total of 86 patients was detected, 55% girls. 67% were infants under 3 months (1% under 1 month).

85% presented with classical symptoms but 16% had nonspecific symptomatology, especially infants under 1 month of age.

In 37% microbiological confirmation was made, 9% serology and 29% with RT-PCR, implemented since 2007.

The index case was unknown in 55% of cases and in the 29% was a first-degree relative.

Treatment with macrolides was made in 93% of patients (44% erythromycin, 33% clarithromycin and 11% azithromicyn).

The outcome was favorable in most cases despite the 21% required ICU admission (90% of them children under 3 months).

76% of patients had complete vaccination schedules for their age.

Conclusions

Whooping cough remains a public health problem. Our series confirms that is most common in children under 3 months, more vulnerable to severe forms of the disease and in whom symptoms cannot be classical, 16% of the cases in our series, a high index of suspicion still necessary though.

Familiar transmission is the main route of infection, especially in infants.

24% of children did not complete vaccination coverage, updating calendars still needed.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0572
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

THREE YEAR SURVEILLANCE OF VIRAL RESPIRATORY INFECTIONS, IN A PEDIATRIC ONCOLOGY UNIT AND COMPARISON TO A GENERAL POPULATION COHORT

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Background

A prospective observational study was conducted over 3 consecutive seasons to examine viral respiratory epidemiology in pediatric oncology/hematology patients.

Methods

Inpatients and outpatients with respiratory symptoms were included. A nasopharyngeal aspirate was obtained and tested with a multiplex PCR (PneumoVir-kit, GENOMICA, Spain), detecting 18 respiratory human viruses. We concurrently collected data on immunocompetent children, by documenting number of ER outpatients and nasal-antigen detection data at the adjacent children's hospital.

Results

Between 09/2012-08/2015, 282 samples were obtained from 240 patients (186 boys) with respiratory symptoms. A season was defined from 01/09 to 31/08. Underlying illness included: hematological malignancy (67%), lymphoma (5.5%), solid tumors (25%) and other hematological disorders (2.5%). Eight children (3%) died, 6 of whom were virus-positive.
On the 1stseason, 113 samples from 104 patients were obtained. A viral pathogen was detected in 58%, the most frequent being RSV (27.5%), followed by Influenza, Parainfluenza-3, Bocavirus, Rhinovirus, Human Metapneumovirus and Adenovirus. Viral co-infections were

detected in 15%.
On the 2nd season, 97 samples were collected from 80 patients. The positive-virus percentage was significantly lower (19%) with predominant agents being Parainfluenza-1 and RSV (5% each), followed by Parainfluenza-3, Bocavirus, Rhinovirus, Influenza and Coronavirus. No co-infections occurred.
On the 3rd season 73 samples were gathered from 56 patients. Only 5% were positive, with Parainfluenza-3, Parainfluenza-4, Bocavirus, Rhinovirus in equal distribution.
Number of outpatients visits of otherwise healthy children were similar between seasons. Viral antigen detection was markedly decreased during 2nd season, as noted for our cohort.
However, during the 3rd season a brief surge of RSV infections among general population, was not captured in our cohort.

Conclusions

Our cohort seems to broadly follow epidemiologic trends of the immunocompetent population. Increased vigilance is warranted in order to safeguard these fragile patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0227
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

SURVEILLANCE FOR BURKHOLDERIALES BACTERIA – THE MAIN AGENTS OF CROSS-INFECTION

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Background

The emerging nonfermenting Gram-negative microorganisms, especially from order Burkholdriales are dangerous for the patients with cystic fibrosis (CF) and congenital lung malformation (CLI). The acquisition of these respiratory pathogens is associated with the chronic pulmonary colonization, an increase in morbidity and respiratory exacerbations in patients. The transmissible strains may cause cross-infection which influences patient's quality of life, opportunities for social contact, future prospects for transplantation, disease progression. So the surveillance for Burkholdriales bacteria by the genomic fingerprinting was the goal of our investigation.

Methods

Bacterial identification and genotyping were performed by amplification and sequencing of *16S rDNA*, genes according tothe MLST (Multi Locus Sequence Typing) protocols for *Burkholderia cepacia* complex (*Bcc*), *Achromobacter spp*. (http://pubmlst.org/), and genes from in home elaborated protocol for *Lautropia mirabilis.* Analysis of sequences was made by Launch MUSCLE, MEGA6.0 and BLAST NCBI programs.

Results

Patient sampling included 400 persons aged 2 - 69 years (most with CF). Children aged 2-18 formed separated group. 42.7% patients were infected by Bcc, 23.0% - *Achromobacter spp.*, 5.3% – *Lautropia mirabilis.* From Bcc presented by 4 species and 18 ST the most transmissible was the strain *B. cenocepacia* ST709 (69.3% from all patients with Bcc). The proportion of *A. ruhlandii* between 6 *Achromobacter* species was 52% and *A. ruhlandii ST36 – 37%* between 27 ST. In the children group *B. cenocepacia ST709 and A. ruhlandii* ST36 also dominated, but the proportion of *B. cenocepacia* ST208 rose from 12.4% to 21.2% and *Lautropia mirabilis t*o 11.3%*.*

Conclusions

B. cenocepacia ST709 and *A. ruhlandii ST36* may be considered as the Russian epidemic strain. Surveillance for Burkholdriales bacteria must include stains with tendency to infection growth in the children group too.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0942
05. S - UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

THE MANAGEMENT OF COMMUNITY-ACQUIRED PNEUMONIA COMPLICATED BY PARAPNEUMONIC EFFUSION IN CHILDREN: A SINGLE CENTRE EXPERIENCE

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Background

Community-acquired pneumonia is a commonly diagnosed disease in childhood. Parapneumonic effusion is its well-known complication. The management for parapneumonic effusion consists of antibiotic therapy, drainage of pleural fluid via chest tube, intrapleural fibrinolytics and surgical intervention with debridement and decortication. A recent debate covers the optimal timing of an operative approach, certainly with the emergence of new surgical techniques. This study describes the management and outcome of pediatric parapneumonic effusion in our institution over a period of 5 years.

Methods

We retrospectively reviewed the demographic data, vaccination status, clinical presentation, bacteriological findings, management and disease outcome of all pediatric patients (0 to 16 years old) admitted with parapneumonic effusion as a complication of community-acquired pneumonia to the Pediatric Intensive Care Unit of the Ghent University Hospital from January 1st, 2009 till December 31st, 2013.

Results

167 patients met the inclusion criteria. Of the 35 patients with an isolated S. pneumoniae, 15 (42.9%) had no or an incomplete vaccination with pneumococcal conjugate vaccine. Of the 167 patients, 155 (92.8%) received a chest drain. Of these, 117 (75.4%) were also treated with intrapleural fibrinolytics. In only 3 children surgery was the primary approach. Thoracotomy was the chosen technique in all of them. Of the 155 patients treated with chest tube drainage +/- fibrinolytics, 20 (12.9%) needed secondary surgery. Thoracoscopy was performed in 11 patients, thoracotomy in the other 9. None of the patients with primary surgery needed a re-intervention.

Conclusions

In our institution conventional therapy with intravenous antibiotics and chest tube drainage +/- fibrinolytics remains the treatment of choice for the management of parapneumonic effusion as a complication of pediatric community-acquired pneumonia.

ESP16-1063
06. CONGENITAL AND PERINATAL INFECTIONS

ABUSE OR CONGENITAL INFECTION?

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Title of Case(s)

Is a real abuse ?

Background

Congenital syphilis is preventable and curable if maternal infection is detected early. Congenital syphilis is a disease that continues to persist in France despite its preventable nature. Diagnosing of congenital syphilis and determining the therapeutic course can be challenging. But diagnosis is not easy because of the many clinical forms of the disease. We present a difficult diagnostic case of congenital syphilis.

Case Presentation Summary

A 1-month-old girl presented with a several-week history of progressive cutaneous lesions with fever and inconfort. She was the second of a Cape Verde ‘s couple. Examination revealed a painful infant with cutaneous eruptions with palmo plantar lesions and right elbow’s edema. Radiography showed metaphysis lesions on the distal part of right humerus. First the diagnosis of abuse was made. But the clinical presentation and long bones films with typical Winberger sign lead to congenital syphilis's diagnosis. The diagnosis was confirmed by maternal and infant serologies. Treatment by a full course of intra venous Penicillin G was performed. Evolution at 2 months was favorable with absence of recidive of the infection.

Learning Points/Discussion

This case shows that the complexity of clinical presentation can tighten the diagnosis and can conclude wrongly to abuse. Long bone films revealed multiple bony changes, including destruction of the medial metaphysis of both tibias (Wimberger sign) and diffuse symmetrical periosteal reactions. Wimberger sign is due to destructive metaphysitis and is highly suggestive of congenital syphilis, though it has been reported with other conditions such as osteomyelitis and neonatal hyperparathyroidism.

ESP16-0636
06. CONGENITAL AND PERINATAL INFECTIONS

CONGENITAL CMV INFECTION: EARLY TREATMENT...LATER BENEFITS!

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Title of Case(s)

"CONGENITAL CMV INFECTION: EARLY TREATMENT...LATER BENEFITS!"

Background

Congenital cytomegalovirus (CMV) infection is common worldwide. Seroconversion rates during pregnancy range from 1-7%. It is the leading cause of nonhereditary sensorineural hearing loss (SNHL) and can cause other long-term neurodevelopmental disabilities.

Case Presentation Summary

Female newborn with maternal seroconversion to CMV in first trimester of gestation. Morphological ultrasound showed brain cystic lesions and periventricular calcifications.PCR for CMV was positive in amniocentesis fluid. In the second day of life, PCR for CMV was positive in urine. Physical examination was unremarkable. Neonatal hearing screening showed bilateral SNHL, moderate (50 dB) in left ear (LE) and severe (80 dB) in right ear (RE).On D11, she had 580 copies/mL in blood and 4053983 copies/mL in urine, moderate thrombocytopenia, normal transaminases and no cholestasis. Brain ultrasounds neonatal showed mild ventriculomegaly and thalamus striated vasculitis and brain MRI showed multifocal white matter lesions. EEG and ophtalmologic evaluation were normal. Ganciclovir was started, resulting in a decrease of the blood viral load in blood and urine and platelets count normalized. At D18 she started oral valganciclovir. At 1st month, blood viral load was negative, urine viral load was 391464 copies/mL and she showed improvement in serial brain ultrasounds. After 6 months of therapy with no side effects, she showed a total recovery of LE hearing and at 12 months she achieved an adequate neurodevelopment.

Learning Points/Discussion

Documented maternal seroconversion is useful for optimal approach, allowing early diagnosis and treatment. Early anti-viral treatment has been shown to improve long-term audiologic and neurodevelopmental outcomes. Valganciclovir seems to be a good alternative to ganciclovir due to its efficacy and few side effects**.** These infants should have long-term follow-up because they are at risk of delayed manifestations of CMV.

ESP16-0909
06. CONGENITAL AND PERINATAL INFECTIONS

LOCALIZED LATE-ONSET STREPTOCOCCUS AGALACTIAE INFECTION: CASE REPORT

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Title of Case(s)

LOCALIZED LATE-ONSET *STREPTOCOCCUS AGALACTIAE* INFECTION: CASE REPORT

Background

Streptococcus agalactiae (GBS) is a major perinatal pathogen until 3 months of life. Late-onset infection is more frequently localized. GBS maternal colonization is the single most important risk factor for infection and intravenous ampicilin is an effective prevention method.

Case Presentation Summary

A healthy 28-day-old full-term newborn, whose mother was submitted to adequate intrapartum prophylaxis for GBS colonization, was admitted with subfebrile temperature (37,7ºC), intermittent moan and refusal in mobilizing the left hip. Initial examination revealed a newborn with good general condition, mild pain on the edge of hip mobility bow, calm in rest. Hip ultrasonography showed a thin layer of joint effusion and analysis revealed white blood cells count (WBC) of 15000/uL with 56% neutrophiles, CRP of 39mg/L and an ESR of 50mm/h. 12 hours later he maintained joint pain and CRP increased to 45mg/L and ESR to 52mm/h, so ultrasound guided arthrocentesis was performed in the operating room. As the aspiration fluid looked thick and turve, an anterior mini-open lavage arthrotomy was performed and fluid was sent to culture. Empirical antibiotherapy with cefotaxime and flucloxacilin 200mg/kg/day was initiated. At day 6 GBS was isolated in blood culture so antibiotics were changed to endovenous Penicilin and Gentamicin (14 and 5 days course respectively). Joint fluid culture was negative. At day 20 he was discharged with full recovery of hip mobilization and analytic normalization.

Follow-up was performed in orthopedic consultation with monitorization of joint dysfunction. Six months later he was discharged with normal hip ultrasound and symmetric mobilization of hips.

Learning Points/Discussion

This case illustrates that prophylaxis does not modify the course of late onset infection, and GBS must be excluded in an infant with suspected bacterial infection.

ESP16-0852
06. CONGENITAL AND PERINATAL INFECTIONS

EARLY DETECTION OF PERINATAL INFECTIONS IN NORMOINMUNE PREGNANCY, IMPACT ON NEWBORNS

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Background

Considering that due to delayed access to programmed consultation, studies and results, opportunities of an early detection were lost, we conducted this study in an acute general hospital in Ciudad Autónoma de Buenos Aires. Argentina.

Objectives: It is a descriptive study of perinatal infections prevalence, diagnostic opportunity, treatment and impact on Newborns.

Methods

As from June 2014, an obstetrics-infections consulting service without previous appointment was created, receiving pregnant women after their first obstetric visit with basic serological laboratory for the following pathologies: Toxoplasmosis, Syphilis, Chagas, HVB, HVC, CMV, and VIH. Infection is here defined with 1st line serology (IGG-IGM) and /or 2nd line e.g:IgG Avidity Assay, MHATP,PCR test. Timely treatment is indicated, including the couple if necessary. Median gestational age is assessed at the moment of the infectology consultation, median age of patient and gestational number.

Results

In the period June 2014 – December 2015, 152 pregnant women were received

Acute cases started specific treatment: Syphilis 14, Toxoplasmosis 23, HVB 1. From these cases, impact on the newborn was: Syphilis symptomatic 1 asymptomatic 13 (no infection), toxoplasmosis symptomatic 1 asymptomatic 22 (no infection), HVB asymptomatic 1.

Detected as positive without treatment, it was not corresponding during gestation were: HVC 2, Chagas 2, CMV 1 acute (dead fetus 37wk). All VIH negative.

Mean gestacional number: 2

Median age: 25.8 years (r: 15-44)

Median gestational age at infectology consultation: 24.7 weeks (r: 10-39)**Conclusions**

From 152 patient, 38 (25%) were treated for acute infections pathology. 36(94.7%) empiric treatments on newborns were avoided.

This screening in pregnancy with joint obstetric and infectology control, with quick definition and timely specific treatment, made perinatal transmission definition easier, reducing the number of lost opportunities and the use of empiric treatments unnecessary for the newborn.

ESP16-0428
06. CONGENITAL AND PERINATAL INFECTIONS

SPARING BABIES THE NEEDLE: WORKING TOWARDS A BETTER PARADIGM FOR EXCLUDING CONGENITAL SYPHILIS

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Background

The 2008 UK national syphilis guidelines, written by the British Association of Sexual Health and HIV (BASHH), recommend that all infants born to mothers with positive syphilis serology, should have both treponemal and non-treponemal syphilis serology tests undertaken at birth, 3, 6 and 12 months of age (or until all tests become negative) in order to exclude a diagnosis of congenital syphilis (CS). These recommendations were felt to be excessive. An updated BASHH guideline was released in draft version in 2015 stratifying infant testing based upon previous maternal treatment.

Methods

A retrospective case note review was performed on all infants who had syphilis serology tests (Syphilis screening enzyme immunoassay, *Treponema pallidum* haemagglutination assay, Venereal Disease Research Laboratory, rapid plasma reagin or treponemal enzyme immunoassay) undertaken between January 2008 and February 2015 at the Leeds Teaching Hospitals NHS Trust. Clinical practice was compared to the 2008 UK BASHH guidelines and then to the draft 2015 BASHH guidelines.

Results

Of the 93 infants identified, our study did not find any evidence of CS. Comparison of local practice to the UK 2008 BASHH guidelines revealed that 88% of infants did not have the full set of recommended serological tests. In 27 cases, infants were discharged prior to the completion of all the recommended tests due to clinical judgement. Comparison of clinical practice to the draft 2015 guidelines showed a significant increase in adherence (12% versus 31%, OR 3.42 (95% CI 1.215 to 9.671) p= 0.0199).

Conclusions

The 2008 UK BASHH guidelines were excessive and in need of amendment. The draft 2015 guidelines reduce such testing to enable clinician time and resources to be focused upon those infants that are most at risk.

ESP16-0736
06. CONGENITAL AND PERINATAL INFECTIONS

UNUSUAL REPORT OF TWO EPISODES OF CELLULITIS-ADENITIS SYNDROME IN YOUNG INFANT

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Title of Case(s)

Background

Cellulitis-adenitis syndrome (CAS) is a rare late-onset clinical manifestation of group B Streptococcus (GBS) infection in neonates and young infants. Due to its uncommon presentation it may not be recognized by physicians leading to wrong diagnosis and poor prognosis.

Case Presentation Summary

A female, AGA neonate was born at 40 weeks of gestation (vaginal delivery) without GBS screening during pregnancy. At 20days of life, the neonate presented fever and was admitted to a pediatric department. She was treated with ampicillin and amikacin after full sepsis workup. The next day a submandibular swelling appeared and the ultrasound examination showed lyphadenitis. Treatment was continued for a total of ten days; meanwhile blood and CSF cultures were negative. Eight days after release at home, the mother noticed irritability and groin area swelling. The infant was admitted to our department 24hours after the symptoms began. At clinical examination, the groin swelling had completely disappeared and there was submandibular erythema and edema. The patient received ceftriaxone after full sepsis workup. The submandibular ultrasound showed cellulitis with multiple small lymph nodes. The clinical and imaging presentation matched with CAS whereas CSF culture yielded GBS. The swelling improved on the second treatment day and had completely disappeared on day three. The infant received 14-day treatment with ceftriaxone and was released at home.

Learning Points/Discussion

Physicians should be aware of unusual forms of neonatal GBS-infections and the need to exclude CNS involvement. The classic location of swelling in the submandibular region at first hospitalization suggests the diagnosis of GBS-cellulitis. However, all cultures at first episode were negative (which is not uncommon,so a PCR for GBC detection is recommended) to aid in distinguishing between recurrent or persistent GBS versus a new occurrence of disease

ESP16-0766
06. CONGENITAL AND PERINATAL INFECTIONS

NATIONAL NEWBORN SCREENING FOR CONGENITAL TOXOPLASMOSIS IN IRELAND: OUTCOME OF A COHORT FOLLOWED UP FOR A DECADE

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Background

SURVEY
Most newborns with congenital toxoplasmosis (CT) in Europe are asymptomatic and CT can remain undetected during routine postnatal care. Postnatal screening for CT facilitates early diagnosis, targeted therapy and intervention to optimise neurodevelopmental outcome.

To determine the visual and neurodevelopmental outcomes of CT infants detected by newborn screening.

Methods

From 7/05-7/07, a 2-year pilot screening programme was undertaken using dried heel blood spots obtained 72 -120 hours after birth. A 2-step screening protocol was employed (AutoDELFIA and ISAGA IgM assays). Diagnosis was confirmed using paired mother/infant serology. Detailed clinical evaluation, 1-year antiprotozoal therapy and clinical follow-up was offered to all diagnosed infants.

Results

15 cases were identified giving an incidence 1 per 10,000 births.2/15 (13%) were symptomatic: 1 significant hydrocephalus, intracranial calcifications and unilateral chorioretinal scar; 1 ventriculomegaly, intracranial calcifications and unilateral blindness. 13/15 (87%) were asymptomatic, 4 (31%) of whom had detectable clinical signs: 4 inactive chorioretinal scars (2 unilateral, 2 bilateral), 2/4 intracranial calcifications. 14/15 accepted antiprotozoal treatment; 1 asymptomatic was untreated due to non-confirmatory serology up to 9 months.

Median follow-up is 9 years (range 2-10 years). 14/15 have normal neurodevelopmental outcome and visual acuity including 1 asymptomatic infant who had a unilateral inactive retinal lesion at birth that reactivated requiring retreatment at age 2 years. Regression of intracranial calcifications was noted in 3 children. 1/15 with hydrocephalus and ventriculoperitoneal shunt has minor co-ordination deficits but normal cognition and attends main stream school.

Conclusions

A third of asymptomatic infants had significant CT lesions detected only because of screening. Better than anticipated visual and neurodevelopmental outcomes were demonstrated in children with CT where early treatment was facilitated by a postnatal screening program.

ESP16-0533
06. CONGENITAL AND PERINATAL INFECTIONS

TREATMENT OF CONGENITAL CYTOMEGALOVIRUS INFECTION WITH GANCICLOVIR AND HUMAN SPECIFIC CYTOMEGALOVIRUS IMMUNGLOBULIN

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Title of Case(s)

TREATMENT OF CONGENITAL CYTOMEGALOVIRUS INFECTION WITH GANCICLOVIR AND HUMAN CMV IMMUNGLOBULIN

Background

Congenital cytomegalovirus infection is associated with significant brain lesions and late neurological consequences. There are some controversies about the most effective treatment. We present a clinical case of successfully treated congenItal CMV infection with a combination of antiviral drug and human specific immunglobulin.

Case Presentation Summary

Female neonate born after uneventful second pregnancy with a birth weight 3000 g, head circumference 35 cm, gestational age 41 weeks.After delivery were noted enlarged liver and spleen, blood count showed marked thrombocytopenia, biochemistry - elevated aspartataminotransferase and alaninaminitransferase, negative C reactive protein.Virological assessment found elevated CMV IgM and positive CMV DNA - 93 960 copies/ml. Clinical symptoms of the baby were presented mainly by abnormal neurological signs - hyperexcitability, increased tone of neck extensor muscles, clonic seizures. Brain ultrasound showed mild dilation of the lateral ventricles, periventricular hyperechogenicities, bilateral subependymal cysts and one larger cyst in the occipital area. The treatment consisted of five weeks course of intravenously applied ganciclovir (Cymevene) in conventional dose regimen and four infusions of human CMV immunglobulin (Cytotect, Biotest). There was marked improvement of the clinical condition, normalization of platelet numbers and liver enzymes and negative CMV -DNA results. Brain ultrasound at the age of seven months showed only mild ventricular dilation and three small periventricular calcifications without any cystic lesions. Neurological and sensorial assessment revealed mild abnormalities of the muscle tone, moderate hearing impairment and normal ophtalmological examination

Learning Points/Discussion

Treatment of congenital cytomegalovirus infection with ganciclovir and human CMV immunglobulin possibly could reduce the neurological consequences of the disease.

ESP16-0763
06. CONGENITAL AND PERINATAL INFECTIONS

PATHOGENS IMPLICATED IN SYSTEMIC INFECTIONS IN PREMATURE INFANTS

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Background

The neonatal infections are common in premature babies. As lower is the gestational age, greater the susceptibility of infection is. The paper aims to highlight common infections in premature infants, incriminated pathogens, predisposing factors, and also treatment and evolution.

Methods

The study was conducted at the Maternity Bega Timisoara , for a period of 3 years. This study included all preterm infants with gestational age below 37 weeks.

Results

During this period, 565 preterm were born, of which 40% had positive blood cultures. The most common pathogens were Candida albicans (25%), Coagulase-negative Staphylococcus (22%), Klebsiella pneumoniae (15%), Staphylococcus aureus (17%). Prolonged hospitalization, and also invasive maneuvers increase the risk of infections. From this group, 183 premature infants were hospitalised more than 14 days. From the total number of preterm 122 required mechanical ventilation. The treatment quickly established can change the evolution of premature infants. In our study, 84% of premature infants received antibiotics.

Conclusions

Newborns are susceptible to infection, particularly premature infants who require prolonged hospitalization. Invasive maneuvers, small gestational age, and also low birth weight are risk factors in the occurrence of neonatal infections. The pathogens most incriminated were Candida albicans and Coagulase-negative Staphylococcus. Antibiotics make the prognosis of this group of infants to be better.

ESP16-0289
06. CONGENITAL AND PERINATAL INFECTIONS

STUDY OF MONITORING OF NEWBORNS TO MOTHERS HBS ANTIGEN AND VIRAL LOAD POSITIVE

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Background

Hepatitis B virus (HBV) infection remains a global health problem. The mother-child transmission of HBV is a major cause of maintaining the global epidemic, despite the availability of an effective vaccine.

The objective is to achieve, from an analysis of practices, an overview of monitoring and serovaccination quality in newborns to mothers who were HBs antigen and viral load positive.

Methods

Retrospective, multicenter (Nice, Grasse and Cannes) study conducted over five years. Neonates received the included serovaccination scheme according to the « Réseau Sécurité Naissance PACA Est-Haute Corse-Monaco » protocol. It consisted of two serovaccinations. 200 IU of anti-HBs immunoglobulins (IgHBs) associated with Engerix B10® at birth; then 100 or 200 IU IgHBs depending on lactation associated with Engerix B10® at one month life. A third injection of Engerix B10® was administrated at six months and serological testing (HBsAg and anti-HBs antibodies) was carried out one to four months after the last dose of vaccine. The children were considered well monitored if they received serovaccination at birth and at one month, if the serology was realized and if a fourth Engerix B10® was done if needed.

Results

All the 118 infants included received the first serovaccination. At one month, 109 had a second IgHBs injection and 111 had a second Engerix B10®. Serology was done on 71 infants (60.17%). One child was infected with a viral load of 200 million IU/ml. Follow-up was well-done for 66 children (56%). Serovaccination was effective at 96.9%.

Conclusions

Infant monitoring is imperfect. The practices should be improved in order to manage optimal care.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1098
06. CONGENITAL AND PERINATAL INFECTIONS

ACUTE CONCURRENT PAROTITIS AND EPIDIDYMITIS IN A NEONATE WITH BACTEREMIA: A CASE REPORT

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Title of Case(s): A rare case of a neonate with concurrent acute bacterial parotitis and epididymitis.

Background: Acute parotitis is not a common infection in the neonatal age (3.8/10000 of neonatal admissions). Bacteria are the most important causes with predominance of Staphylococcus aureus (approximately 55% of cases). Higher incidence of acute bacterial patotitis is observed in premature infants and males. Epididymitis is a rare etiology of acute scrotum in the neonatal age. In infancy, acute epididymitis can be a systemic disease (haematogenously spread of bacterial or viral infection) or can be associated with an underlying genitourinary abnormality. Despite the well known association between viral parotitis and epididymitis, no cases of bacterial concurrent parotitis and epididymitis have been reported in infants.

Case Presentation Summary: A 7-day-old twin preterm (35+3 weeks) male, delivered by cesarean section with a birth weight of 2180 g, was transferred from a maternity hospital to our Neonatal Unit because of fever and right pre-auricular swelling. On examination, the neonate was irritable and presented fever and tachycardia; capillary refill time was >3'', while a warm, tender, erythematous swelling was noted over the right parotid gland region extending to the right mandibular angle and neck. Laboratory findings revealed leucocytosis and increased serum C-reactive protein levels, whereas Staphylococcus aureus (MSSA) grew in blood cultures. The baby was put on antibiotics intravenously and his general condition, as well as parotidic swelling, improved. However, on day six of hospitalization the neonate presented swelling of the right scrotum with inflammatory characteristics. Ultrasound revealed acute epididymitis.

Learning Points/Discussion: Bacterial acute parotitis should be suspected in neonates presenting with facial swelling. Epididymitis may be associated with bacterial parotitis in neonates.

ESP16-0192
06. CONGENITAL AND PERINATAL INFECTIONS

CHARACTERISTICS AND RISK FACTORS FOR STAPHYLOCOCCUS AUREUS BLOOD STREAM INFECTION IN NEWBORNS ADMITTED IN LEVEL III NEONATAL UNIT NEW DELHI

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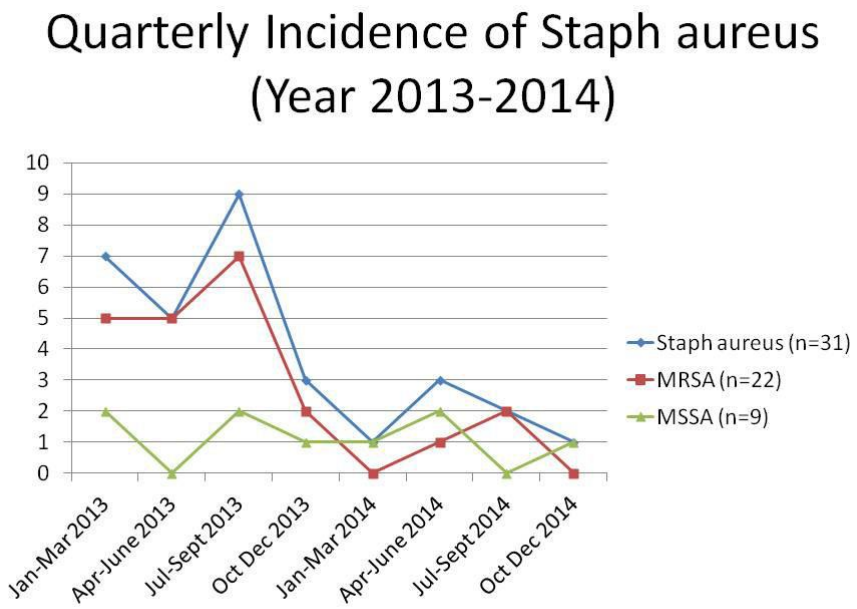
Background

Background: Blood Stream Infection (BSI) contributes significantly to neonatal morbidity and mortality. The *Staphylococcus aureus* (*SA*) is a significant cause in these babies.The data on burden of *SA* disease in hospitalized newborns is limited. It is perceived that Methicillin Resistant *Staphylococcus aureus* (*MRSA*) is a more virulent or more serious pathogen than Methicillin Sensitive *Staphylococcus aureus* (*MSSA*). Newborns are unique in the sense that *MRSA* and *MSSA* infections may have comparable morbidity and mortality
Objective was to determine the annual proportion of S aureus infections that were *MRSA* and *MSSA* and to find the risk factors for *MRSA* BSI

Methods

Retrospective cohort study (January 2013 and December 2014) in a NICU in New Delhi. Study population included babies who grew *Staphylococcus aureus* (*SA*) in blood culture. Data on patient demographics, underlying diseases, medications, central catheters, nutrition, ventilator use etc. was retrieved. Data was analysed using SPSS Version 20.0. Risk factors were assessed using Univariate analysis. P values<.05 were taken as significant. Odds Ratios (O.R.) and 95% Confidence Intervals (C.I.) were calculated

Results



31 out of 4038 admitted newborns developed *SA* BSI (22 by *MRSA* and 9 by *MSSA* incidence of 77 and 54 per 10000). There was steady decline in the incidence of *SA* and *MRSA* during the study period. Examination of conditions associated with morbidity in these infants e.g. birth-weight, gestation, asphyxia, ventilation, central catheters, vasopressors, surfactant, steroid etc did not reveal any notable differences between newborns infected with *MRSA* or *MSSA.* Mortality caused by *MRSA* and *MSSA* (11/22 vs 3/9 p 0.4 OR 2.0 C.I. 0.39-10.1) were comparable.

Conclusions

There was reduction in incidence of *SA* and *MRSA* BSI. Both type of infections (*MRSA* and *MSSA*) had similar morbidity and mortality.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0031
06. CONGENITAL AND PERINATAL INFECTIONS

THE LATENT PERIOD DURATION OF PROM WAS NOT ASSOCIATED WITH NEONATES WHETHER INFECTION

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Background

This study attempts to survey the relationship between latent period duration of premature rupture of membranes (PROM)and fetal-neonatal infectious rates by large scale clinical epidemiological investigation.

Methods

From January 2007 to December 2014, 51,313 cases of neonatal clinical data were retrospectively analyzed.

Results

①There were 27,336 cases full-term neonates (53.3 %) and 23,977 cases of preterm infants (46.7%) in total of 51,313 newborns, there were 12,899 (25.1 %) cases with history of PROM. Among them, there are 7405 cases(30.9%) hospitalized preterm infants with PROM and 5494 (20.1 %) cases of hospitalized term-infants with the history of PROM. ②The incidence rates of infectious diseases in PROM infants was 27.1%, which is 12.3 times of those without PROM infants (2.21%). ③The blood culture was perform in 9475 PROM infants, there were 1431 cases infants with bacterial growth with a positive rate of15.1%. The blood cultures positive rate was 20.7% (1066/5154) in preterm infants and 8.45 % (365/4321) in full-term neonates, respectively (χ^2=18.370,p=0.000). ④Among the cultured bacteria, G^+ cocci accounted for 58.5% while G^- bacilli accounted for 33.8% with a statistically significant (χ^2=31.7,P=0.000). The most common pathogens were Staphylococcus epidermidis, **Staphylococcus homini**, Klebsiella pneumoniae, E.coli and hemolytic staphylococcus. The incidence of fungal infections were 7.7%, which were seen only in preterm infants.⑤The blood culture positive rate in infants with latent period duration of PROM ≤24h, <72 h ,0, <7d and > 7d were 14.6% , 15.1% , 15.8% and 15.5 %,the difference was not statistically significant (χ^2= 2.301, p=0.359) .

Conclusions

Infants with the history ofPROM account for more than 25% of the total hospitalized infants, the latent period duration of PROM is no correlation with whether fetal-neonatal infection.

Clinical Trial Registration (Please input N/A if not registered)

n/a

ESP16-0265
06. CONGENITAL AND PERINATAL INFECTIONS

VERTICAL TRANSMISSION OF CYTOMEGALOVIRUS IN A RURAL MOZAMBICAN HOSPITAL

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Background

Congenital cytomegalovirus(CMV) infection is the most prevalent worldwide, varying the prevalence from 0.2% to 2%. This is higher in developing countries and among HIV infected newborns, although it is decreasing among exposed-not infected infants, following the increased use of antiretroviral therapy for prevention of mother-to-child transmission(MTCT).We aimed to assess CMV vertical transmission prevalence and risk factors associated among newborns born in a rural Mozambican maternity.

Methods

A cross sectional descriptive study was conducted on pregnant mothers attending Manhiça District Hospital at delivery. Blood cord samples in filter paper were collected for CMV detection measure by PCR. HIV rapid test was done to pregnant women with negative or unknown previous test.

Results

120 mothers were recruited at delivery, mean age was 25,1 (±7,6) years and mean of gestational age at recruitment was 38,8 (±0,6) weeks. Prevalence of HIV infection among them was 27.5% (33/120) and only 28.3% was taking antiretrovirals to prevent MTCT. Of 120 pregnancy outcomes, 5.8% (7/120) were premature, 1.7% (2/120) stillbirths, 2.5% (3/120) born with malformations (polydactyl and spina bifida) and 12.5% (15/20) had low birth weight. CMV PCR was positive in 3/116 cord samples collected (2.6%) and only one child was exposed but not infected to HIV. 100% of them were asymptomatic at bitrth and at 6 months follow-up. Risk factors associated to vertical transmission of CMV were not found.

Conclusions

Our results showed a higher prevalence of congenital CMV than studies in developed countries but lower than reports from low-income countries. Although it is an important cause of hearing loss completely neglected, it would be premature to consider newborn CMV screening in resource-poor settings because the disease burden and the cost/benefit of long term follow-up have not been defined.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0784
06. CONGENITAL AND PERINATAL INFECTIONS

EARLY-ONSET NEONATAL SEPSIS DUE TO ESCHERICHIA COLI: SHOULD WE CHANGE ANTIBIOTIC EMPIRICAL THERAPY?

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Background

Escherichia coli (*E coli*) early-onset sepsis (EOS) is a major cause of mortality and morbidity in neonates, especially on premature newborns. Most studies have shown an increased rate of antimicrobial-resistant strains, especially to ampicillin. Our aim was to evaluate changes in the clinical and microbiological characteristics of *E. coli* EOS over the past two decades, specially focusing on VLBW premature infants.

Methods

Epidemiological, clinical and microbiological data of *E. coli* EOS from Hospital Universitari Vall d'Hebron (Barcelona, Catalonia, Spain) were retrospectively collected from January 1994 to December 2014. Data were stratified for gestational age and birth weight and compared for four 5-year periods.

Results

Seventy-nine *E. coli* EOS were included. Fifty-five cases (70%) were preterm newborns, 34 (43%) of them with VLBW. Maternal risk factors were observed in 88.6% cases. Fourteen patients presented with meningitis. Overall mortality rate was 22.7% and remained stable over the study period; mortality rate in VLBW was 35%. The overall incidence of *E. coli* EOS remained stable for all the period (0.98 per 1 000 live births), and in the VLBW group for the last 10 years (12.7 per 1 000 VLBW live births). The rate of antimicrobial-resistant strains did not increase significantly. In the last 5 years, ampicillin resistance rates reached up to 93%; cefotaxime 13% and gentamicin 33%. One ESBL isolate was observed. No significant correlation was found between antimicrobial-resistant *E. coli* EOS and gestational infection, intrapartum antibiotic therapy or clinical severity.

Conclusions

The epidemiology and microbiology of *E.coli* EOS has remained stable during the past 20 years. High resistance rates, especially to ampicillin but also gentamicin, should be considered on empirical antibiotic therapy for next years.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0532
06. CONGENITAL AND PERINATAL INFECTIONS

PHARMACOKINETICS (PK) OF GENTAMICIN COMPONENTS (GC) IN NEONATES

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Background

Gentamicin consists of three main components C1, C1a and C2, differing in chemical structure almost as much as gentamicin differs from tobramycin or netilmicin. The content of GC in commercially available gentamicin preparations varies. Very few data are available on the PK of GC in humans.

Methods

Post-hoc analysis of a PK study recruiting neonates with gestational age (GA) ≥ 32 weeks, treated with gentamicin plus penicillin or ampicillin, was performed. Gentamicin was administered in a dose of 4 mg/kg q24h as 1-hour infusion. Blood samples were collected after the 2nd to 8th dose before and on five time-points during the dosing interval. Serum concentrations were measured by UHPLC with MS/MS detection. Population PK analysis was performed using the Pmetrics package (software R).

Results

Final analysis included 176 samples from 30 patients with median (range) GA of 37 (32-42) weeks, birth weight (BW) 3120g (1285-4660g) and postnatal age 2 (1-5) days. Gentamicin C1, C1a and C2 fractions in the study drug were 25.1%; 25.9% and 49.0%, respectively (measured by Estonian Drug Administration). Two-compartmental model best described the PK of all GC (Table). Incorporating BW as a covariate provided the best model fit for volume of distribution (Vd) of GC C1a and C2, whereas height improved fit for C1 and C2. Allometric scaling for BW improved the model fit for clearance (CL) of all GC with further improvement for GC C1 and C1a by adding creatinine.

Table 1. Final population parameter estimates for GC C1, C1a and C2.

Parameter	Gentamicin component C1		Gentamicin component C1a		Gentamicin component C2	
R^2 obs vs indiv predicted/obs vs pop predicted	0.84/ 0.50		0.79/ 0.17		0.77/0.63	
Parameter estimates						
	mean (SD)	CV	mean (SD)	CV	mean (SD)	CV
V0 (L)	2.26 (1.79)	79.2	2,66 (1.65)	62.2	2.96 (1.63)	55.1
CL0 (L/min)	0.27 (0.06)	34,2	0.46 (0.46)	99.9	0.26 (0.19)	74.6
Q (L/min)	0.31 (0.31)	118.1	0.17 (0.35)	211.8	0.13 (0.10)	75.1
Vp (L)	2.18 (1.76)	80.6	1.46 (1.45)	99.1	2.42 (1.60)	66.1
Theta2	-0.05 (0.03)	248.4	0.08 (0.65)	849.0	0.02 (0.02)	116.5
theta3	-0.02 (0.03)	139.9	-0.61 (0.52)	85.4	-0.06 (0.11)	192.7

CL-clearance; V0-volume of distribution, central compartment; VP-volume of distribution, peripheral compartment; TH-theta

Conclusions

We found significant variations in the PK profile of GC. Together with recent data on possible differences in their nephrotoxicity, understanding of the underlying mechanisms may hold the potential for improving the safety profile of the drug.

Clinical Trial Registration (Please input N/A if not registered)

EudraCT number 2012-002836-97

ESP16-0635
06. CONGENITAL AND PERINATAL INFECTIONS

INCIDENCE AND OUTCOMES OF MYCOPLASMA HOMINIS, UREAPLASMA UREALYTICUM AND CHLAMYDOPHILA TRACHOMATIS RESPIRATORY COLONISATION AMONG PRETERM INFANTS IN MALAYSIA

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Background

There have been numerous studies on the burden of disease caused by *Ureaplasma urealyticum*, *Mycoplasma hominis* and *Chlamydophila trachomatis* but reports on the incidence, clinical features and outcomes among premature infants affected by these organisms in Southeast Asia are scanty.

Methods

This is a cross sectional study conducted in Tuanku Jaafar Hospital, Malaysia. The objective of this study is to determine the incidence of *Ureaplasma urealyticum*, *Mycoplasma hominis* and *Chlamydophila trachomatis* respiratory tract colonisation in preterm babies less than 37 weeks of gestation who required assisted ventilation and clinically important outcomes associated with it. Nasopharyngeal or tracheal aspirate sample taken within the first 7 days of life for polymerase chain reaction test. Relevant clinical and laboratory data were collected using a standard case report form.

Results

Only 15 (7.5%) of 200 infants were detected to have these organisms in their respiratory tract. 8 (4.0%) were positive for *Ureaplasma urealyticum* and *Mycoplasma hominis* respectively while 2 (1.0%) had *Chlamydophila trachomatis.* There is no statistical significant association between the presence of these organisms and mortality, respiratory distress syndrome, bronchopulmonary dysplasia, duration of ventilation, hydrocephalus, necrotising enterocolitis and length of stay. 73 (36.5%) were given antibiotic for presumed atypical infection, out of which only 3 were positive for these organisms. Among those who were treated, duration of ventilation was 3 days longer than those who were not (p=0.001).

Conclusions

The incidence of *Ureaplasma urealyticum r*espiratory colonisation among preterm infants in Malaysia is lower than other published reports while the frequency of *Mycoplasma hominis* and *Chlamydophila trachomatis* isolation is comparable to many studies. Larger studies are needed to determine the clinical relevance of *Ureaplasma urealyticum* and *Mycoplasma hominis* infection in Malaysian preterm infants.

Clinical Trial Registration (Please input N/A if not registered)

NMRR-13-620-16788

ESP16-1039
06. CONGENITAL AND PERINATAL INFECTIONS

VESICLES ON NEWBORN SKIN – A SIGN NOT TO BE MISSED

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Title of Case(s)

Vesicles on newborn skin – a sign not to be missed

Background

Neonatal herpes simplex virus infections, which affect one in every 3,200 – 10,000 live births, cause significant morbidity (0.2% of all newborn hospitalizations) and in-hospital mortality (0.6%).

Case Presentation Summary

A term male newborn was presented with jerking movements of the left arm and left leg with reluctance to suck on his postnatal day 14.

The infant was very ill-looking and hypoactive. His vital signs, systemic examination, complete blood count with peripherals, routine chemistries, even transfontanel ultrasound scan revealed almost no signs that may be interpreted as “pathological” except for vesicles on frontotemporal skin.

Cerebrospinal fluid examination showed 150 leucocytes/µL, 50 erythrocytes/µL, a protein concentration of 92 mg/dL and a glucose concentration of 59 mg/dL.

The infant was started ampicillin, ceftriaxone, and acyclovir. Polymerase chain reaction for herpes simplex virus type 1, which was positive on day 1 of acyclovir therapy became negative after 21 days of treatment.

Learning Points/Discussion

This case of postnatal herpes simplex encephalitis is noteworthy for emphasizing the

- Essentialness of realizing any skin lesion that may be of utmost importance for the infant's diagnosis and treatment while keeping in mind that vesicles may be absent in up to 30-40% of newborns with central nervous system disease.

- Indispensability of a very early diagnosis and prompt treatment in order to prevent neurological sequalae.

- Standard acyclovir therapy duration of 21 days, after which, a repeat lumbar puncture should be done in order to make sure that cerebrospinal polymerase chain reaction for herpes simplex virus has become negative

ESP16-0093
06. CONGENITAL AND PERINATAL INFECTIONS

CONGENITAL CYTOMEGALOVIRUS AND INTESTINAL INVOLVEMENT IN A TERM IMMUNOCOMPETENT NEWBORN: A RARE CASE REPORT

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Title of Case(s)

Congenital Cytomegalovirus with early onset intestinal involvement in an immunocompetent newborn.

Background

Cytomegalovirus (CMV) is the most common cause of congenital viral infection, affecting 0.2% to 2.3% of all live births in developed countries. Gastrointestinal involvement is very rare in acquired CMV infections, but could be an important manifestation of postnatal infection in patients admitted to neonatal intensive care units. We describe a case report of a term newborn with congenital CMV and gastrointestinal involvement with onset in the first 24 hours of life.

Case Presentation Summary

Female, birth weight 2330 grams, 37 weeks of gestational age. During pregnancy, serologic conversion for CMV was documented in the third trimester. Due to a sudden important abdominal distension immediately after birth, blood and radiologic tests (abdomen ultrasound and X-ray) were performed and excluded a surgical cause. Oral feeding was started on the 3rd day of life, with good tolerance but persistence of liquid stools for the next two weeks, suggesting a colitis as cause of the symptoms. Urine and blood tested for CMV DNA through PCR resulted positive (1.296.341 copies/mL and 2.322 copies/mL). All the other examinations (ophthalmologic examination, brain ultrasound and magnetic resonance) were normal. The patient progressively improved until normalization of gastrointestinal symptoms, without any sequela caused by CMV infection.

Learning Points/Discussion

Gastrointestinal involvement during congenital and post-natal CMV infection is uncommon, in particular in immunocompetent and physiologic newborns. Particularly rare is the onset of this manifestation in the first 24 hours of life. Controversial is the utility of antiviral treatment to avoid possible sequelae (as stenotic intestinal lesions) and the use of intestinal biopsy to perform the diagnosis.

ESP16-0198
06. CONGENITAL AND PERINATAL INFECTIONS

ESCHERICHIA COLI AS MAIN CAUSE OF EARLY ONSET SEPSIS IN A SECONDARY LEVEL NEONATAL UNIT

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Title of Case(s)

Early onset sepsis in a secondary level neonatal unit.

Background

Neonatal sepsis is currently one of the most serious and feared problems affecting infants ≤ 28 days of life, due to its severity, morbidity and mortality both among term and preterm newborns. In a three year retrospective study we collected all the cases of early onset sepsis (EOS) admitted to our neonatal pathology ward with positive blood culture.

Case Presentation Summary

During the period 2013-2015, 4715 newborns were admitted to our neonatal unit (4469 terms, 242 pre-terms and 4 post-terms). Considering only newborns admitted for at least 3 days (4676), EOS with positive blood culture occurred with an incidence of 0.89‰ (4 patients, 1,33 each year). These patients (2 males, 2 females), were all born at term (37+5 to 41 weeks of gestational age). Three of them had blood culture positive to *Escherichia coli* (E. coli) and one to group B *Streptococcus agalactiae* (GBS). Two of these patients were diagnosed after developing significant signs/symptoms of early systemic infection (one with E. coli and one GBS); the other two (E. coli) did early blood tests to a anamnestic infectious risk factors, with a significant increase of C-reactive protein and positive blood culture, so were treated before developing clinical signs. All were treated for 11 (10-14) days, with complete recovery.

Learning Points/Discussion

Despite GBS is considered the most common agent of EOS worldwide, E. coli is a growing problem in neonatal units, both in premature and term newborns. An early recognition of signs and symptoms, in particular in patients at high risk of infection, is very important to start immediately an appropriate antibiotic treatment, to reduce mortality and possible severe sequelae.

ESP16-0881
06. CONGENITAL AND PERINATAL INFECTIONS

CONGENITAL RUBELLA SYNDROME SURVEILLANCE AT DR.SOETOMO HOSPITAL, INDONESIA

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Background

Congenital Rubella Syndrome (CRS) is one of vaccine-preventable morbidities, but Rubella vaccine is not yet in Indonesia National Immunization program. To convince the authority that mass vaccine is needed, surveillance of CRS burden in major hospital in Indonesia is needed. This study aimed to describe the surveillance outcome of suspected CRS cases at Dr.Sutomo hospital from January until June 2015.

Methods

This was a prospective cohort study as a part of the hospital-based national surveillance regarding CRS conducted in Soetomo General Hospital, Surabaya. Medical report of suspected CRS infants (fulfilled at least one criteria: eye defect, hearing impairment, any Congenital Heart Disease (CHD), or suspected maternal rubella) along with their parent's interview were evaluated and classified as confirmed CRS, and clinical CRS according to WHO CRS surveillance guideline.

Results

A total of 104 infants were included. Surveillance outcome confirmed 16 (15.4%) infants with confirmed CRS, and 17 (16.3%) clinical CRS. Seventy-one (66.3%) infants were discarded. Among 33 patients with clinical and confirmed CRS, 20 (60.1%) were male, 17 (51.5%) patients were born premature, and 19 (57.6%) patients had low birth weight. One (0.9%) patient had 3 major clinical symptoms, and 12 (11.5%) patients presented with 2 major clinical symptoms. In clinical CRS, common manifestation were CHD (48.5%), developmental delay (33.3%), and born at term (10/33, 30%) with low birth weight (9/33, 27.3%). Common clinical symptoms in confirmed CRS infants were CHD in 13/16 (81.3%) infants and born preterm, had low birth weight and congenital cataract each in 10/16 (62.5%) infants.

Conclusions

Amongsuspected CRS cases, confirmed and clinical CRS was found in 14.4% and 16.3% infants

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0694
06. CONGENITAL AND PERINATAL INFECTIONS

RECURRENT GROUPE B STREPTOCOCCUS DISEASE IN A NEWBORN - A CASE REPORT

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Title of Case(s)

Recurrent group B streptococcal disease in a newborn

Background

Group B streptococcus is the most common cause of severe bacterial infections during the neonatal period.Most infections occur during the first week of life, and the recurrent disease is very rare- with only 48 published cases.

Case Presentation Summary

We present a case of a recurrent GBS disease at a baby born at term, by vaginal delivery. There was history of early onset GBS disease and the baby had been treated by intravenous Ampicillin during 9 days. Since discharge, she was exclusively breastfed. Aged 22 days, she presents fever, refusal to feed and submandibular erythema.There was a full infectious screening at admission and she received empirical antibiotherapy of Ampicillin and Cefotaxime. GBS was isolated at the blood culture, the CSF culture resulted negative. The ultrasound showed a submandibular cellulitis. The clinical course after antimicrobial therapy was excellent. The immune-defficient disorders testing resulted negative. We performed maternal milk cultures where the same GBS was isolated and we suspected a horizontal GBS transmission.

Learning Points/Discussion

During the neonatal period a submandibular cellulitis might be one of the signs of a GBS infection.We suggest to test maternal milk in case of recurrent neonatal GBS disease, although data over horisontal transmission is controversial whether the origins of the infection lie on the infected milk or in a oropharyengeal contamination from the baby's mucosaes. Some cases reported that a course of rifampicine administrated at the mother would eradicate the carriage, permitting the continuation of the breastfeeding,but no consensus has been set so far.

ESP16-0701
06. CONGENITAL AND PERINATAL INFECTIONS

SUPPURATIVE MUSCULOSKELETAL INFECTIONS IN INFANTS – DIAGNOSTIC METHODS AND TREATMENT

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Title of Case(s)

Suppurative musculoskeletal infections in infants – diagnostic methods and treatment

Background

Suppurative infections in infants are mostly skin infections–pyoderma followed by septicemia. t is very rare that infection will take place at musculoskeletal organs and if it is not diagnosed at time, it can lead to severe deformity of the limb.Suspicion for suppurative infection is raised in case of painful livid swelling over the joint.Standard inflammatory markers are obtained (CBC, ESR, CRP).Puncture of the swelling is performed and material sent for bacteriology culture and sensitivity to antibiotics.Besides evacuation of the puss parenteral antibiotics are administered.Punctuations are repeatedly done at least 2 or 3 times till results are negative.

Case Presentation Summary

In a 10 year period, we have seen 3 cases.A 30 day old baby presented with swelling around clavicle and pain on palpation.Punctuation was made timely and operative procedure lead to total evacuation of the abscess.The causative organism was *Streptococcys pyoegenes*. The second case was 20 day old baby with knee swelling.Parenteral antibiotic therapy was administered after punctuation.In this case *Staphylococcus aureus* was isolated from the puss.The third infant who had swelling of the right thumb was hospitalized at the neonatology ward and was treated with antibiotic therapy after punctuation.In all these cases, infections were caused by gram positive bacteria.

Learning Points/Discussion

Infants with swelling of the joints, followed by high temperature or not should be considered very seriosly.Swelling can follow after skin lesions –wounds with pus, especially around arm and foot nails.Evacuation of the puss and appropriate parenteral antibiotic therapy can lead to complete cure.

ESP16-0275
06. CONGENITAL AND PERINATAL INFECTIONS

CONTROL AND MANAGEMENT OF CONGENITAL AND PAEDIATRIC CHAGAS DISEASE IN EUROPE AND OTHER NON-ENDEMIC COUNTRIES: AN OVERVIEW OF CURRENT POLICIES AND PRACTICES

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Background

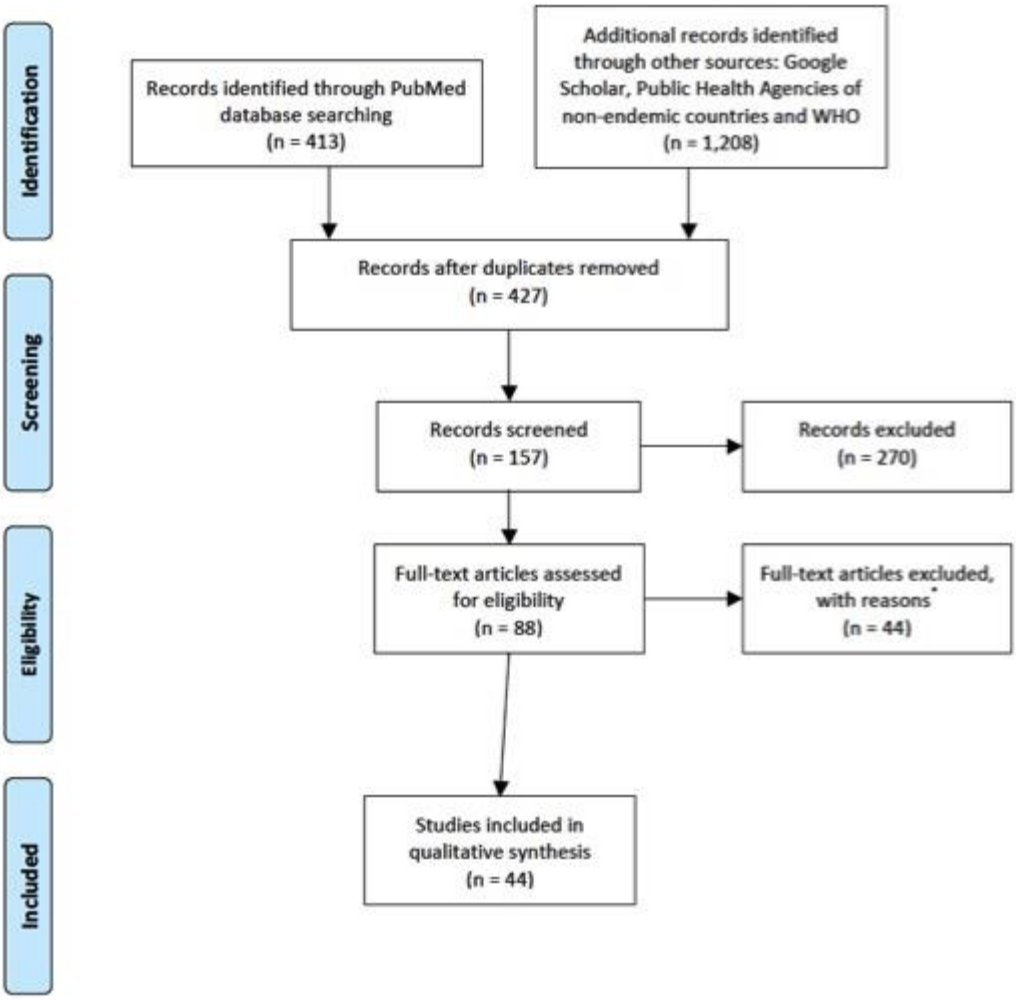
Identifying pregnant women infected with Trypanosoma cruzi represents one of the major challenges for preventing and controlling Chagas disease in non-endemic countries. The aim of this paper was to perform a policy evaluation of the current practices of congenital Chagas disease control in non-endemic countries and to propose specific targets for enhanced interventions to tackle this emerging health problem outside the endemic areas of Latin America.

Methods

We conducted a mixed method review of Congenital Chagas Disease policy strategies by searching the literature in the PubMed, Google Scholar and the World Health Organization (WHO) databases. The following key terms were used: "congenital Chagas disease", "pediatric Chagas disease" and "non-endemic countries"; as "free text" and combined as one phrase to increase the search sensitivity. Reviews, recommendations, guidelines, and control/surveillance program reports were included.

Results

A total of 427 Congenital Chagas Disease papers were identified in non-endemic countries. After close examination, 44 articles matched the inclusion criteria and were used in the final evaluation. Although local programs were launched in different countries with large numbers of Latin American immigrants, there were considerable disparities in terms of the programs' distribution, delivery, integration and appropriated Congenital Chagas Disease control strategies. Moreover, Catalonia, Spain was the only region/country with an established systematic monitoring of Congenital Chagas Disease in pregnant women from Latin American countries.



Conclusions

Given the worldwide dissemination of Chagas Disease, the nature of its vertical transmission, and the gaps of the current strategies in non-endemic countries, there is an urgent need to standardize, expand and reinforce the control measures against Congenital Chagas Disease transmission.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESP16-0475
06. CONGENITAL AND PERINATAL INFECTIONS

REFINING THE USE OF C REACTIVE PROTEIN IN THE DIAGNOSIS OF NEONATAL SEPSIS

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Background

C-Reactive Protein(CRP) is often overused in establishing the risk of neonatal sepsis. Our aim was to establish if there are situations in which CRP values are increased in the absence of sepsis and if the exclusion of these cases from the interpretation of the CRP could increase the sensitivity of this marker of possible infection.

Methods

Normal values for CRP at 24 hours of age were established in 1500 term neonates. There were differentiated neonates born by vaginal delivery, neonates with meconium stained amniotic fluid, birth asphyxia, cephalhematoma, birth weight>4000 grams. There were analyzed 95 cases of neonates with risk of sepsis based on risk factors: positive vaginal or urine cultures in the mother, suggestive clinical signs. Blood culture, complete blood count and CRP were noted for all the patients. There was also noted the presence of the above mentioned factors

Results

Mean CRP values were significantly increased in the case of the patients with vaginal deliveries(8 mg/dl), meconium stained fluid(21 mg/dl), birth asphyxia(11 mg/dl), birth weight>4000 grams(13.5 mg/dl). In the case of sepsis, CRP had a good negative predictive value(97.5%), but a poor sensitivity(67%). When eliminating from the sample the patients with conditions associated with increases in CRP, the sensitivity(91%) and negative predictive value(99.5%) increased. The best sensitivity was obtained by using a combination of risk factors, positive clinical sings and abnormalities of either CRP or complete blood count.

Conclusions

Interpretation of CRP values as a risk factor for neonatal sepsis should be refined by considering the situations in which CRP is increased in the absence of sepsis and not using CRP as a marker these cases. Clinical suspicion remains the gold standard in establishing the risk of sepsis in a neonate.

ESP16-0641
06. CONGENITAL AND PERINATAL INFECTIONS

NEONATAL GBS INFECTION IN CRETE: REGIONAL INCIDENCE AND LONG TERM OUTCOME

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Background

Group B streptococcus(GBS) sepsis and meningitis remains a leading cause of mortality and long term sequelae in neonates and young infants, however reported incidence rates greatly vary worldwide. We investigated the regional incidence of invasive GBS infection in infants in Crete over 21 years and the long term neurodevelopmental outcomes.

Methods

Cases ofculture-proven GBS invasive disease in infants less than 3 months old between 1995 and 2015 were reviewed and neurodevelopmental outcomes were evaluated based on parental interviews and hospital records.

Results

A total of 23 neonates and young infants were affected with invasive GBS infection, 8 of whom with meningitis. The incidence varied from 0.0 to 0.374 (average 0.16) per 1000 livebirths per year. Most cases were of early onset (14/23) presenting at the ages of 0-3 (median 1) days; among them four developed meningitis, two were born premature, and two had prolonged rupture of membranes (>18 hours). Nine cases presented with late onset infection at the age of 7-77 (median 18) days; four of them had meningitis and four a history of previous hospitalization. No death was reported in the EOS group and one death in the LOS group (4.3% overall case fatality rate). In the meningitis group, 6 out of 8 cases were further assessed for long term sequelae. One infant developed quadriplegia, one obstructive hydrocephalus with minor disability, and a further one speech delay without cognitive defects.

Conclusions

Our study demonstrates low incidence of GBS sepsis and meningitis in the study area and considerable rates of long-term disability among newborns with GBS meningitis.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0587
06. CONGENITAL AND PERINATAL INFECTIONS

OPTIMISED PATHWAY FOR THE DIAGNOSIS OF CONGENITAL CMV RELATED HEARING LOSS IN NEWBORNS

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Background

Congenital Cytomegalovirus (cCMV) is the most common congenital infection and causes up to 15% childhood sensori-neural hearing loss (SNHL). The majority of these newborn are otherwise asymptomatic. Valganciclovir improves the audiological outcome of children with cCMV when started within the first month of life. Although in the UK the national newborn hearing screening programme (NHSP) identifies newborns with SNHL within the first weeks of life there is no pathway to identify cCMV in this window.

Methods

In September 2013 we devised a pathway of care within our NHS trust aiming to optimize the diagnosis of cCMV related SNHL. This modified pathway recommended that newborns who did not pass their NHSP tests, were referred for audiological assessment within 3 weeks of life, and that if sensori-neural hearing loss (SNHL) was found they were directly referred to Paediatric Infectious Diseases (PID) for cCMV screening.

Retrospective case note review of newborns identified with SNHL who were screened for cCMV examining the feasibility of this approach.

Results

From September 2013 – December 2015 (28 months), 24 newborns <28 days old have been referred for cCMV screening after having SNHL confirmed at audiological testing after NHSP. 2 families declined cCMV testing. 100% returned a urine CMV PCR result within a month of life, and 5/22 (23%) were positive. All of these were treated with valganciclovir.

Conclusions

Our optimized pathway for audiological assessment after NHSP and timely referral for cCMV screening is effective and identifies neonates with cCMV related SNHL who might benefit from treatment with valganciclovir. This approach could be rolled out in other UK settings.

ESP16-0578
07. FUNGAL INFECTIONS

UNUSUAL CAUSE OF BLEEDING PER RECTUM IN IMMUNOCOMPETENT CHILDREN

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Title of Case(s)

Unusual Cause of Bleeding Per Rectum in Immunocompetent Children

Background

Basidiobolomycosis is a rare fungal infection caused by Basidiobolus ranarum which was first described in 1886.

Case Presentation Summary

We are presenting a previously healthy 3 year-old male child presented with history of fresh bleeding per rectum for three months duration. It was associated with supra pubic abdominal pain, intermittent fever and weight loss.

Examination showed a thin pale child with normal systemic examination except per rectal examination which revealed an anterior wall mass rounded smooth 3×4 cm with fresh blood and no anal fissure or external mass.

CBC showed WBC 16.8×10^3/mm, eosinophils 6%, HB 6.8g/dL, Platelets 599×10^3/mm and ESR 33 mm/hour. Immunological work-up was normal and negative HIV serology. Abdominal CT-scan showed ill identified mass involving the left anterior lateral aspect of the rectum.

Patient underwent surgical exploration, evacuation of pus collection and biopsy was taken. Vancomycin, tazocin and Liposomal Amphotericin B were given empirically. The gram stain and cultures were negative. Histopathology showed eosinophilic infiltration with microabscess formation and fungal hyphea surrounded by an eosinophilic inflammation characteristic for Basidiobolomycosis. Antifungal was changed to PO itraconazol which was given for 12 months. He showed remarkable improvement and follow up abdominal US confirmed complete resolution of the rectal mass**Learning Points/Discussion**

Bleeding per rectum secondary to basidiobolomycosis is extremely unusual and so far no reported cases in pediatrics. The aim of presenting the case is to increase awareness among health care professionals in areas of endemicity and appropriate specimen processing enhance case detection and reporting. The best outcome of this unusual fungal infection is achieved by combination of medical and surgical treatment .In our case the mass was unrespectable and patient was cured by medical therapy only.

ESP16-0793
07. FUNGAL INFECTIONS

CANDIDA LUSITANIAE OSTEOMYELITIS WITH A DENTAL ORIGIN IN AN IMMUNOCOMPETENT CHILD

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Title of Case(s)

***Candida Lusitaniae* Osteomyelitis with a Dental Origin in an Immunocompetent Child**

Background

Candida lusitaniae is a yeast that has emerged as a low frequency pathogen in a immunocompetent host. Early identification is important for patient morbidity. We report the isolation of *Candida lusitaniae* as an etiologic agent of an osteomyelitis in a immunocompetent child and in our knowledge it is second *Candida lusitaniae* osteomyelitis in the English literature.

Case Presentation Summary

A 11-year old boy presented with swelling and pain of the left side mandibular area. He had a three-day history of left jaw pain and decreased oral intake. He was afebrile. He had no significant past medical history. Examination findings included mild trismus and marked left submandibular swelling. Oral hygiene was very poor and 6th tooth was tender and decayed. His laboratory findings showed leukocytosis and high levels of acute phase reactants. Neck imaging (ultrasound and contrast enhanced magnetic resonance) were compatible with submandibular abscess and mandibular osteomyelitis. The abscess was drained and ceftriaxone was started empirically. *Candida lusitaniae* was identified from abscess drainage sample. The antibiotherapy was switched with intravenous fluconazole. Lymphocyte subset analysis, dihydrorhodamine 123 flow cytometry and the serum immunoglobulins levels were normal. The patient was clinically stable and acute phase reactants were decreased. Intravenous fluconazole was given for 14 days and the patient was discharged with oral voriconazole. Contrast enhanced mandibular MRI was normal at 6th month of antifungal therapy. Total antifungal treatment completed 6 months. Relapse did not determine during the one year follow-up.

Learning Points/Discussion

We want to highlight of rare osteomyelitis agent and importance of careful microbiological identification. We also want to emphasize physician’s attention toward the possibility of succesful treatment in fungal osteomyelitis.

ESP16-0964
07. FUNGAL INFECTIONS

CANDIDA ALBICANS ARTHRITIS IN AN INFANT AFTER COMPLETE TREATMENT FOR NEONATAL CANDIDEMIA

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Title of Case(s)

CANDIDA ALBICANS ARTHRITIS IN AN INFANT AFTER COMPLETE TREATMENT FOR NEONATAL CANDIDEMIA

Background

Severe disease by *Candida albicans* (*C. albicans*) mostly occur in immunocompromised patients, in those who have prolonged intravenous catheters, prolonged hyperalimentation or long term antibiotic therapy.

Fungal sepsis occurs in 10% of low-birth-weight infants frequently associated with central nervous system disease. Fungal arthritis originates hematogenously and requires prompt diagnosis and treatment to prevent sequelae.

Case Presentation Summary

We report a case of a 4 months old infant with right knee arthritis.
Candida albicans (*C. albicans*) was isolated from the knee aspirate. Blood and urine cultures were sterile. Complete recovery was achieved with 6 weeks of fluconazole treatment post-arthrotomy.

He was a premature male infant born at 30 weeks with a birth weight of 1540g, admitted at birth in a neonatal intensive care unit for parenteral nutrition. On day 10 he developed a *C. albicans* sepsis with meningoencephalitis, and was treated with intravenous amphotericin B for 45 days and a further 6 weeks course of fluconazole. He was discharged on D60 with neurologic sequelae (spastic tetraparesis).

The infant was HIV negative and no primary immunodeficiency was identified: lymphocyte immunophenotyping, lymphocyte function tests and oxidative burst were normal. On follow-up he did not present any other infections.

Learning Points/Discussion

Premature neonates and infants present a physiological immaturity of the immune system. In this case *C. albicans* arthritis was diagnosed 8 weeks after completing a 60 days course of antifungal therapy for a severe candida sepsis and no primary or acquired immunodeficiency

was found, which suggests the persistence of a latent focus. This complication is rarely described. Careful follow-up after neonatal candidemia is required to promptly detect recurrence.

ESP16-0530
07. FUNGAL INFECTIONS

FUNGEMIA DUE TO RHODOTORULA MUCILAGINOSA IN PEDIATRIC PATIENTS

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Title of Case(s)

FUNGEMIA DUE TO *RHODOTORULA MUCILAGINOSA* IN PEDIATRIC PATIENTS

Background

Rhodotorula species are commensal yeasts that have been recognized as emerging human pathogens, with *Rhodotorula mucilaginosa* being the commonest cause of *Rhodotorula* fungemia, mainly affecting immunocompromised patients with central venous catheters (CVCs). Few cases of *Rhodotorula* fungemia have been reported in children. We herein present two pediatric cases diagnosed over a 2-month period in our hospital.

Case Presentation Summary

Case1. A 16 year-old female in the Pediatric Oncology Department with metastatic Ewing sarcoma and a CVC inserted, developed febrile neutropenia (ANC<500/μL) after chemotherapy. *R. mucilaginosa* was isolated from blood collected at day 1 of neutropenia. The patient was empirically treated with voriconazole, replaced by fluconazole after 1 day due to visual disturbances. 5 days later fluconazole was substituted by liposomal amphotericin B, according to susceptibility data (resistant to azoles). The episode of fungemia was resolved 6 days after collection of the first positive culture, with neutropenia recovery and without catheter removal.

Case2. An 11 year-old girl with Gaucher disease type III and long term hospitalized in the PICU, had a febrile episode with concomitant CRP increase, while receiving broad-spectrum antibiotics. The patient had a CVC, tracheostomy and gastrostomy. During this episode she developed moderate neutropenia (ANC500-1000/μL) and died 3 days later of pulmonary hemorrhage. Blood culture from the CVC grew *R. mucilaginosa* 3 days after her death. She did not receive any antifungal therapy.

Learning Points/Discussion

These cases are added to 40 cases of *Rhodotorula* fungemia reported since 1960 and suggest that in immunosuppressed children with CVCs receiving broad-spectrum antibiotics and/or cytotoxic drugs, *Rhodotorula* spp. should be considered a potential pathogen causing bloodstream infections. Prompt treatment based on correct identification and susceptibility testing is of high importance.

ESP16-0602
07. FUNGAL INFECTIONS

PERSISTENT CANDIDA INFECTION DUE TO ITS BIOFILM IN EXTRACORPOREAL MEMBRANE OXYGENATION

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Title of Case(s)

A persistent Candida infection due to its biofilm in extracorporeal membrane oxygenation.

Background

Introduction: Extracorporeal membrane oxygenation (ECMO) implies the use of devices that can conduce to invasive fungal infection (IFI), Candida can develop a biofilm that perpetuates the infection.

Case Presentation Summary

Case report: female infant 20 months of age, admitted to the paediatric intensive care unit (PICU), secondary to necrotizing pneumonia by S. pneumoniae, with acute respiratory distress syndrome and septic shock. Antibiotic treatment was started with cefotaxime and vancomycin.

After day 10, she experimented a severe worsening, so piperacillin-tazobactam and amikacin was started, and ECMO was indicated due to multiorganic failure, with good response.

However, after 5 days from starting ECMO, the infant presented a bad general condition, with febricula and altered analytical parameters (leukocytosis 16000 l/mm3, C-reactive protein 148.7 mg/L and procalcitonin 1.5 ng/mL). Cultures of several patients' samples and from ECMO circuit were taken, and micafungin (4 mg/Kg/day) was initiated.

At 24 and 72 hours, sensible Candida tropicallis was found in all cultures from patient and circuit samples. Owing to improvement watchful waiting was decided, with negative consecutive cultures at day 5 and 7 post IFI. The patient evolution was favorably with ECMO removal at day 12.

Learning Points/Discussion

Commentaries: in particular cases of Candida infection, the use of highly anti-biofilm active drug such as micafungin, may avoid the ECMO circuit removal.

ESP16-0340
07. FUNGAL INFECTIONS

INVASIVE CANDIDIASIS IN A PEDIATRIC REFERENCE CENTRE: LESS CASES AND A BETTER OUTCOME

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Background

Recent studies show a global decline in the last years in the incidence of invasive candidiasis (IC) among children. Data is lacking in our media. Aim: to describe the epidemiological, clinical and therapeutic features of IC patients admitted in our hospital.

Methods

Retrospective study including all pediatric patients (<18 years of age) admitted with ≥1 episodes of IC (January 2010-December 2015). IC was defined as a positive culture to *Candida* spp. from any sterile site

Results

We included 82 episodes in 77 children (50 males); 35 newborn and 42 pediatric individuals (13.6 episodes/year) with a significant decrease (57%) along this period, mainly in the newborn group. The commonest isolated species were *C.albicans* (36) and *C. parapsilosis* (29). Principal risk factors for developing IC were: central venous catheter (81), total parenteral nutrition (59), and broad spectrum antibiotic (57), extremely immature preterm babies (26) and immunosuppression (25). Fluconazol was the commonest initial therapy (39) followed by liposomal amphotericin B (23). Four isolates were resistant to fluconazol (*C.tropicalis*, *C.guillermondii, C.glabrata and C.krusei* one each), and only one resistant to echinocandins (*C.parapsilosis*). Median therapy duration was 21 days (16-32.5). CVC was removed in 91% of cases (median delay of 2 days (1-4)). Disseminated candidiasis (DC) was present in 10 patients, meningitis (4), endocarditis (3), and peritonitis (2). Candidemia-related mortality was 13% and was greater in those patients in whom CVC was not removed (p=0.005) or presented with DC (p=0.001).

Conclusions

A significant decrease of IC was observed since 2010, mainly in newborn individuals. *C. albicans* remain the commonest isolated specie. Antifungal resistance was uncommon and restricted to non-*albicans* species. Early CVC removal is mandatory to improve outcome in IC.

ESP16-0252
07. FUNGAL INFECTIONS

VAGINAL CANDIDIASIS IN UNDERGRADUATE STUDENTS OF A NIGERIAN UNIVERSITY

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Background

Vaginal candidiasis has been a source of discomfort to many young girls despite the availability of many antifungal creams, passerines and tablets. No research has been conducted in tertiary institutions on candidiasis in Anambra State, South Eastern Nigeria. This study was aimed at ascertaining the incidence, knowledge, management and antibiogram of candidiasis among Unizik pharmacy undergraduate girls in Agulu campus

Methods

The studyduration was from April to June 2015. Structured questionnaires were distributed to 160 students who were recruited into the study after written informed consent. Candida species isolated from the study participants were subjected to speciation using standard yeast identification protocol and CHROMagar. Antifungal susceptibility testing was done by the disc diffusion method with Nystatin, Fluconazole, and Voriconazole.

Results

Based on our findings, greater percentage of the students are knowledgeable on candidiasis and majority of the study participants have a good management behaviour as they consult healthcare providers whenever they experience vaginal discomfort. Among the 160 students screened, 70 positive isolates were obtained, there were mixed species in 5 (7.6%), *C. albicans* 25 (33.3%), *C. tropicalis* 30 (40%), *C. krusei* 7 (9.3%), *C. glabrata* 5 (5.3%) and others 9 (13.6%). The percentage susceptibility was in the order: nystatin (41.4%) < fluconazole (48.6%) <Voriconazole (61.4%).

Conclusions

The incidence of non-*Candida albicans* was high among the university students and the isolates were resistant to the azole group of antifungals. Among the three antifungal drugs used in this study, Voriconazole appeared to be the drug of choice in the treatment of vaginal candidiasis in this locality.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0991
07. FUNGAL INFECTIONS

INVASIVE FUNGAL INFECTIONS IN HEMATOLOGY/ONCOLOGY CHILDREN: A TEN YEAR REVIEW

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Background

Invasive fungal infections (IFI) are a significant cause of morbidity and mortality in children with hematology-oncology conditions. Aim: to describe the epidemiology and outcome of IFIs in our hematology-oncology unit during a ten-year period.

Methods

Retrospective, descriptive study in patients younger than 18 year admitted to the hematology-oncology ward between 2006-2015 with an IFI. Clinical characteristics of mold and yeast infections, and their proportion over time were analyzed.

Results

Twenty two patients were included (59.1% males, median age 6.2 [2.3-10.8] years) in the study. Hematological malignancies were the most common baseline conditions (40.9%). Overall, 36.4% of patients had undergone HSCT (87.5% allogenic), and 45% of them were on antifungal prophylaxis (50% micafungin, 40% fluconazole). Regarding outcomes, 31.8% needed PICU admission and 18.2% died.

Molds were the most common cause of IFI (59.1%, all bronchopulmonary disease), including 2 confirmed *Aspergillus.* Yeasts infections included 44.4% fungemias and 44.4% urinary infections, and were mostly caused by *Candida albicans* and *Candida parapsilopsis*. Patients with mold infections were older (9.6 vs 3.8 years;p=0.010), had higher initial PCR (10.9 vs 4.7mg/dl;p=0.016), higher incidence of HSCT (61.5% vs 0%;p=0.003) and graft versus host disease (GVHD, 30.8% vs 0%;p=0.066), antifungal prophylaxis (76.9% vs 0%; p=<0.001), PICU admission (46.2% vs 11.1%,p=0.083) and mortality (30.8% vs 0%,p=0.066).

Comparing the first (2006-2010, 12/22 patients) and second period (2011-2015, 10/22 patients), the latter had an increased proportion of mold infections (33.3% vs 90%,p=0.007), which coincided with higher incidence of HSCT (25% vs 50%,p=0.225), GVHD (8% vs 30%,p=0.190), and antifungal prophylaxis (25% vs 70%,p=0.035).

Conclusions

An increasead proportion of mold infections and disease severity was observed between 2006-2015, probably secondary to an increased complexity of the hematology-oncology diseases during the last years.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0149
07. FUNGAL INFECTIONS

DRAMATIC RESPONSE TO POTASSIUM IODIDE IN SYSTEMIC BASIDIOBOLUS RANARUM

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Title of Case(s)

DRAMATIC RESPONSE TO POTASSIUM IODIDE IN SYSTEMIC BASIDIOBOLUS RANARUM

Background

Background: Gastrointestinal basidiobolomycosis (GIB) is a rare fungal infection caused by Basidiobolus ranarum (B. ranarum). Diagnosis of the infection is difficult because of the lack of specific clinical presentations and the lack of diagnostic tools. Treatment of gastrointestinal zygomycomycosis, includes both surgical resection and long term antifungal therapy.

Case Presentation Summary

Case Presentation: An immunocompetent 2.5 year old boy presented with abdominal pain, fever, diarrhea and a palpable abdominal mass in transverse colon diagnosed as basidiobolomycosis pathologically. Resection was done and treatment with itraconazol and amphotericin B started, but the infection spread to involve intestines, liver, ribs and lung and also abdominal wall after 6 months. Due to clinical unresponsiveness to antifungal drugs, Oral Potassium Iodide (KI) was added to the previous medications. The patient became afebrile after one week. During a three months follow up, the patient's condition improved as he showed complete resolution of the abdominal, chest and subcutaneous involvement.

Learning Points/Discussion

Learning Points/Discussion: Although KI is mostly used in the subcutaneous form, in our study (systemic) complete resolution was achieved over a short time. KI is an effective antifungal drug, given its availability and low cost, could be a therapeutic option for the treatment of systemic basidiobulomycosis.

ESP16-0753
07. FUNGAL INFECTIONS

ASPERGILLUS TERREUS SPONDYLODISCITIS IN AN IMMUNOCOMPROMISED CHILD

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Title of Case(s)

Spondylodiscitis caused by Aspergillus terreus

Background

Although invasive aspergillosis can occur in most organs in immunocompromised host, bone is rarely involved. In Aspergillus osteomyelitis (OM), the most common site is spine and the most common species is *A. fumigatus*. Vertebral OM caused by *A. tereus* has not been previously reported in children.

Case Presentation Summary

A 12-year-old boy was admitted in November 2015 with lower back pain of 1 month duration. He had received stem cell transplantation from Wiskott-Aldrich syndrome in February 2015. He had been treated with intravenous (IV) voriconazole (VCZ) under the impression of possible aspergillosis because of increased aspergillus galactomannan index (GMI). However, the primary site of infection had not been documented. Thereafter, oral VCZ has been continued in outpatient clinic. The patient has not been taking the medicine due to vomiting. At presentation, GMI was elevated as 4.56 from the previous level, 1.95. Spine magnetic resonance image (MRI) showed low signal intensity of L2-3 vertebral bodies and decreased L1/2, L3/4 intervertebral disc height. Culture of bone biopsy sample grew *A. terreus*. Following with a total of 4 weeks course of IV VCZ, the patient is currently taking VCZ orally. Serum trough levels of VCZ range between 6.1 and 10.0 ug/mL. Back pain and tenderness were improving and MRI revealed the improving state of spondylitis. GMI was decreased to 5.00 from the peak value of 7.36.

Learning Points/Discussion

To our knowledge, it is the first case of spondylodiscitis caused by *A. terreus* in immunocompromised child. It is important to document the primary infection site in a patient with high GMI despite prolonged VCZ therapy.

ESP16-0554
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

A RARE CAUSE OF MEDIASTINAL MASS IN A 5 MONTH-OLD BOY

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Title of Case(s)

A rare cause of mediastinal mass in a 5 month-old boy.

Background

Tuberculosis (TB) remains an important cause of morbidity and mortality worldwide especially in developing countries. Children represent one of the high-risk groups for this disease. Here, we present a case, which highlights the delayed diagnosis of a common disease due to an uncommon presentation.

Case Presentation Summary

A 5 month-old Pakistani boy, was admitted to the Hospital with the fever, cough and failure to gain weight. He was treated initially as pneumonia but found to have mediastinal mass.

His chest xray showed large ill-defined hilar and peri-hilar opacities in the right lung with mild pleural effusion (Figure 1). Magnetic resonance imaging (MRI) of the chest showed lobulated mediastinal mass mainly in the middle mediastinum, most likely representing lymphadenopathy (Figures).

Further investigated to identify the etiology of the mediastinal mass. He underwent chest mass core biopsy, which showed necrotizing granulomatous inflammation and but *acid*-fast bacilli Ziehl Neelsen stain was negative. He had positive tuberculin skin test and positive Quantiferon test. His early morning gastric aspirate yielded AFB on smear microscopy at three consecutive days. Mycobacterium TB Polymerase chain reaction (PCR) was positive . Cervical lymph node biopsy showed necrotizing granulomatous inflammation and AFB was positive on ZN stain.**Learning Points/Discussion**

We reported a case of TB in an infant who presented with mediastinal mass. It is very important to suspect TB in infants who are at high risk and who have pneumonia that is not responding to usual anti-microbial therapy. If tuberculosis is diagnosed in infancy period, family surveillance for tuberculosis must be performed.

ESP16-0161
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PERFORATION OF GASTROINTESTINAL TUBERCULOSIS DURING ANTI-TUBERCULOUS THERAPY

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Title of Case(s)

Perforation of Gastrointestinal Tuberculosis During Anti-tuberculous therapy

Background

Tuberculosis (TB) is still a serious public health problem throughout the world causing significant morbidity and mortality. Gastrointestinal (GIS) TB is a rare manifestation of extrapulmonary TB in children that is responsible for less than 1% of all tuberculosis cases. Pulmonary tuberculosis is present in only 15-20% percent of patients with GIS TB. Intestinal perforation is a relatively uncommon but a serious complication of gastrointestinal TB. Herein, we report a child who developed terminal ileal perforation 9 months after initiation of treatment for gastrointestinal TB.

Case Presentation Summary

A ten year old boy admitted with complains of abdominal pain, fever, vomiting and weight loss. On physical examination he had abdominal distention and a fixed, hard palpable mass of 2x2 centimetres in diameter in right abdominal region. Abdominal ultrasound revealed peritoneal thickening and computer tomography demonstrated lymphoproliferative infiltration around cecum and colon. With the suspicion of malignancy fine needle biopsy was performed which revealed necrotising granulomatous inflammation and Langerhans type mononuclear giant cells. Acid fast bacilli was seen by Erlich Ziehl Neelsen method. Chest radiography was normal. The tuberculin skin test and Quantiferon TB Gold test were negative. He was diagnosed as gastrointestinal TB, anti-tuberculous therapy and steroid were started. Nine months after initiation of treatment he presented with signs of peritonitis. X-ray revealed free intraperitoneal gas. An exploratory laparotomy was carried out, which demonstrated perforation over the terminal ileum. He had surgical resection of the affected bowel segment.

Learning Points/Discussion

This case demonstrates that gastrointestinal TB can develop in the absence of pulmonary TB and intestinal perforation can occur several months after the initiation of anti-tuberculous therapy.

ESP16-0835
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

CLINICAL CHARACTERISTICS OF HIV-TB CO-INFECTIONS AMONG PEDIATRIC PATIENTS

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Background

Tuberculosis (TB) is a common opportunistic infection among children with Human Immunodeficiency Virus (HIV) infection. This study aimed to determine the clinical characteristics of HIV-TB co-infected children and predictors for mortality among pediatric patients admitted to Soetomo Hospital Surabaya, Indonesia during 2009-2014.

Methods

We evaluated retrospectively medical records of children under 18 years old with TB-HIV co-infection in Dr. Soetomo Hospital Surabaya, Indonesia during 2009-2014. Tuberculosis was diagnosed using a TB score, HIV was categorised according to the WHO classification. Co-morbid diseases were recorded.

Results

During the study period, there were 54 children with HIV-TB co-infection. The median age was 28.5 (range 7-144) months, 9 (16.7%) children <12 years (16.7%), 25 (46.3%) between 12-35 months, 9 (16.7%) between 36-59 months, and 11 (20.4%) over 60 months; 55.6% were boys. The mean CD4+ was 15.7 (SD 10.9, range 2-37.7%) and 53.7% was categorized as severe immunodeficiency and 46.3% moderate deficiency. All had pulmonary tuberculosis. Tuberculin skin test was positive in 88.9% children. Both antiretroviral and anti-tuberculosis drugs were given in 34 (63%) HIV-TB cases, whereas 20 (37.0%) only received anti-tuberculosis drugs. The co-morbid diseases were PCP (25.9%), oral candidiasis (20.4%), chronic diarrhea (16.7%), and CMV infection (11.1%). The sign and symptom of tuberculosis improved after 2 months of anti-tuberculosis in 14 (25.9%) while 3/54 (5.6%) children died during treatment. There were no specific predictors for mortality among those children (P>0.05).

Conclusions

Chidren co-infected with HIV-TB had a median age of 28.5 months, CD4+ 15.7, 53.7% categorized as severe immunodeficiency and 46.3% moderate defiency. After a 2 month-antituberculous drugs 25.9% improved, 5.6% died during treatment. No co-morbid disease served as predictor for mortality.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1048
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

ABDOMINAL TUBERCULOSIS CAUSING MASSIVE GASTRIC BLEEDING IN AN ADOLESCENT GIRL

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Title of Case(s)

ABDOMINAL TUBERCULOSIS CAUSING MASSIVE GASTRIC BLEEDING IN AN ADOLESCENT GIRL

Background

Gastro-intestinal tuberculosis (TB) is a rare form of TB. We report an unusual case of an adolescent girl with a massive gastric bleeding caused by two gastric ulcers as the presenting symptom of gastro-intestinal TB.

Case Presentation Summary

A 14-year-old Sudan-born girl, presented to the emergency department with massive hematemesis after a bicycle-accident. Whole-body computed-tomography was normal except for a minor enlargement of lymph nodes along the internal thoracic artery. Esophagogastroduodenoscopy (EGD) revealed two gastric ulcers. Hemostasis was achieved by suprarenin injection and clipping of the ulcers. Biopsy showed no signs for *Helicobacter pylori* infection. Treatment with esomeprazole was initiated.

Repeated EGD after 27days of treatment with esomeprazole showed healing of the ulcers. Histopathology of a repeat-biopsy showed epitheloid granuloma without caseation.

Eight weeks after the initial presentation, the girl developed cough and dyspnea. Interferon gamma release assay (IGRA) was positive, HIV-testing was negative. Chest radiography showed pleural effusion. Multiple samples were analysed for *Mycobacterium tuberculosis* culture and PCR including sputum, gastric aspirates, urine, pleural and cerebrospinal fluid. One sputum sample was positive for *M. tuberculosis,* all other samples remained culture and PCR negative. Anti-TB-treatment with isoniazid, rifampicin, ethambutol and pyrazinamide was initiated and symptoms improved markedly within four weeks.

Learning Points/Discussion

Gastro-intestinal TB in children presenting with gastric ulceration is extremely rare. This form of TB usually presents with non-specific symptoms such as abdominal pain and weight-loss.

Concurrent pulmonary TB may be seen. In case of unclear etiology of gastric ulceration repeated biopsy may lead to the diagnosis. TB has to be considered in all patients at risk, particularly with immigrant background. Evaluation for TB with either IGRA or tuberculin skin test is recommended.

ESP16-0571
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

TUBERCULOSIS WITH PLEURAL EFFUSION AND PNEUMOTHORAX - STILL A MAJOR COMPLICATION

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Title of Case(s)

Tuberculosis with pleural effusion and pneumothorax - Still a major complication

Background

In Portugal, tuberculosis remains an important public health issue in endemic areas. Any patient with pneumonia, pleural effusion, a cavitary or mass lesion in the lung that does not improve with antibacterial therapy should be screened for tuberculosis.

Case Presentation Summary

A 16-year-old adolescent male was admitted with a two month history of high-grade fever (40ºC), cough, left chest pain, night sweat and weight loss. The lung auscultation revealed a left decreased vesicular murmur and crackles. He had anemia, normal white blood cell count (5900/mcL) and positive IGRA. Tuberculin skin testing was anergic. He also had elevated prothrombin time (20.6s), APTT (38.9s) and a mild factor VII deficiency (30%) was detected. The chest ultrasound revealed left pleural effusion (340 mL), bronchoscopy described grade II inflammation and the cytology of bronchoalveolar lavage was negative for AARB (PCR) and cultural examination positive for *Mycobacterium tuberculosis*. The chest computed tomography confirmed pleural effusion with characteristics of organizing empyema and left lower lobe atelectasis. Pleural biopsy and thoracic drainage was performed by thoracoscopy. The biopsy revealed caseatiing granulomatous inflammatory process and treatment with isoniazid, rifampicin, pyrazinamide and ethambutol was initiated. Due to persistent air leak and an incarcerated lung he underwent formal decortication by left thoracotomy after completing 1 month of treatment. The patient showed a progressive improvement of his clinical and radiologic condition, completed nine months of anti-bacillary therapy and was able to return to his normal life with minimal radiological sequelae.

Learning Points/Discussion

Tuberculosis is a potentially life threatening disease. The physician has to make the diagnosis and initiate treatment as soon as possible. Suspicion is of utmost importance especially in countries with a low prevalence.

ESP16-0816
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

TB OR NOT TB

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Title of Case(s)

TB OR NOT TB

Background

Unusual presentation of multiple gastrointestinal symptoms leading to delayed diagnosis and treatment

Case Presentation Summary

A 16 year old girl presented with 3/52 epigastric pain and loose stool. She was well and afebrile. Abdominal X-Ray showed mild faecal loading. She was discharged home. She represented 1/12 later with 1/52 history of intermittent RIF pain. Examination revealed RIF tenderness with guarding and pain on percussion. USS showed increased vascularity in the terminal ileal region. Clinical impression was appendicitis. She deteriorated over the next few hours developing fever and RUQ pain. Blood tests showed a neutrophilia 19.7 and CRP 211.4. IV antibiotics were commenced. USS showed free fluid adjacent to a poorly defined RIF mass. The following day, she had a palpable RIF mass. PID review revealed 1/52 of night sweats, 7/52 of weight loss but no cough. TB with or without HIV was considered. She was born in Zimbabwe with no known contact history. Mantoux test was 20mm. HIV test, blood cultures, blood film and LDH were negative. USS showed extensive para-aortic lymphadenopathy. CT scan showed terminal ileitis and lymphadenopathy. TB was diagnosed but tissue for culture required. With no superficial lymph nodes to biopsy, she was transferred to a Tertiary Centre for consideration of RIF mass or para-aortic LN biopsy. She started empirical quadruple TB therapy with good response. Two weeks later a supraclavicular lymph node appeared which was biopsied, showing necrotising granuloma but negative culture. She made a complete recovery.

Learning Points/Discussion

· Abdominal TB may present with non-specific sign and symptoms

· Abdominal TB should be considered with GI symptoms in children born in high TB prevalence areas.

· Patients with abdominal TB may have NO chest symptoms/signs

ESP16-0372
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

DISSEMINATED TUBERCULOSIS IN A CHILD WITH CROHN'S DISEASE RECEIVING ANTI-TNF-ALPHA MONOCLONAL ANTIBODY TREATMENT WITH ADALIMUMAB

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Title of Case(s)

Disseminated tuberculosis

Background

Patients with inflammatory bowel diseases (IBD) on immunosuppressants are predisposed to opportunistic infections, including tuberculosis (TB). Case reports in adults show that TB disease is often more severe in patients treated with monoclonal anti-TNF-alpha therapies. Our literature review identified only two published cases of TB in paediatric IBD patients treated with anti-TNF-alpha therapy (both during treatment with infliximab). To our knowledge this is the first report of TB in a paediatric IBD patient receiving adalimumab.

Case Presentation Summary

A 13-year-old Indian girl with a four-year history of Crohn's disease received adalimumab and azathioprine for 14 months, resulting in symptomatic remission. Prior to starting this regimen her interferon-gamma release assay (IGRA) result (QuantiFERON-TB Gold-in-Tube) was negative. She visited India for 6 weeks, with no history of TB contact. She presented 8 weeks later with a history of intermittent pyrexia, a dry cough and weight loss. Chest radiography showed fine nodular pulmonary opacities bilaterally highly suggestive of miliary TB, and abdominal ultrasound splenomegaly with disseminated lesions. At that point the IGRA result was indeterminate. Routine and mycobacterial cultures on sputum and bronchial lavage were negative. Adalimumab and azathioprine were stopped and quadruple TB therapy started empirically. Within five weeks of commencing treatment her symptoms resolved completely. A repeat IGRA four weeks after stopping adalimumab was positive, supporting the presumptive diagnosis.

Learning Points/Discussion

Several guidelines recommend IGRA for latent tuberculosis screening before initiation of anti-TNF-alpha therapy in children, despite substantial evidence suggesting that IGRA perform worse in children compared with adults. Although current data are limited, our case illustrates that IGRA are frequently not useful in the investigation of children on immunosuppressive treatment who present with features suggestive of active TB.

ESP16-0452
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PROFILE OF CHILDHOOD TUBERCULOSIS (TB) IN A PAEDIATRIC TERTIARY CARE CENTRE IN INDIA

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Background

AIM:

India has the highest tuberculosis burden but has very few studies on TB in children. This study aims at description of childhood TB with respect to types, clinical presentation, investigations and culture positivity in an Indian paediatric setting.

Methods

Clinical and laboratory data of 46 children in the age group of 0 – 18 yrs diagnosed to have TB according to the WHO guidelines were prospectively included during the study period October 2012 to November 2013. Main diagnostic tools included tuberculin skin test, chest X-ray, sputum/gastric aspirate culture with sensitivity testing, and direct microscopy for acid-fast bacilli on available samples. Clinical characteristics and outcomes of the patients were examined.

Results

Out of 40 children, 16 (34.8%) were diagnosed with pulmonary TB and 30 (65.2%) with extrapulmonary TB. Neurological TB constituted 15/30 (50%) of the extrapulmonary TB. 26 children had a positive BCG vaccine scar (65.2%) and 22/46 (47.8%) had a positive tuberculin skin test. An adult TB contact was identified in 10 (21.7%) cases. On direct microscopy, acid-fast bacilli were found in 11 (23.9%) patients. Specimens – gastric juice (3), bronchoaleolar lavage fluid(6) ,lymph node(1),pus(1).Positive culture for *Mycobacterium tuberculosis* was found in 7 (15.2%).CXR was abnormal in 93.7%(15/16) children with pulmonary TB but only 13.3%(4/30) in extrapulmonary TB . One patient with disseminated TB with underlying immunodeficiency died during follow-up.

Conclusions

Extrapulmonary TB was the commonest form of tuberculosis at our centre with neurological TB constituting the majority. Bronchoalveolar lavage contributed to increasing the smear positivity rates in our study

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0820
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

A CASE OF DISSEMINATED TUBERCULOSIS WITH RENAL LOCALIZATION COMPLICATED BY SEVERE HYPERTENSION

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Title of Case(s)

SEVERE HYPERTENSION IN DISSEMINATED TUBERCULOSIS WITH RENAL LOCALIZATION

Background

In developing countries genitourinary tuberculosis (TB) is the most common form of extrapulmonary localization of disease after pleural and lymphatic ones. Renal involvement usually occurs by hematologic dissemination of Mycobacterium Tuberculosis (MT) and pulmonary infection is the primary focus in most cases. Hypertension is an infrequent complication of renal TB.

Case Presentation Summary

A 8 months male infant was admitted to our emergency department for crying, refusing to feed, loss of weight, head and eyes laterodeviation to left since few days. Always afebrile.

At arrival the neurologic examination revealed deviation of the head and eyes to the left, axial hypertonia, reduced and afinalistic spontaneous motility. TC brain scan highlighted dilation of the supratentorial ventricular system, hypodensities in the left thalamic region and basal bilateral lenticular areas. Lumbar puncture showed clear CSF, normal pressure, increased WBC and proteins with very low glucose deposing for tuberculous etiology of the disease. Therapy with ethambutol, isoniazid, rifampin, pyrazinamide and metilprednisolone was started. Thorax Xray evinced pulmonary localization of disease with gastric aspirates positive for MT. At the same time, PCR on urine for MT was positive and abdominal ultrasound showed right renal, hepatic, splenic localizations, confirmed by TC scan. Since the first day of hospitalization the blood pressure was high so antihypertensive therapy was started (ramipril, amlopidine, enalapril).

After two months of TB treatment we observed neurological improvement as well as blood pressure therefore he is assuming only enalapril.

Learning Points/Discussion

In our case hypertension can be considered secondary to infection because of immediately identification after admission even if steroid treatment had probably worsened the pressure values. It is mandatory carefully monitoring blood pressure expecially in pazients with renal tubercular involvement.

ESP16-0546
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

TUBERCULIN SKIN TEST IN HIV-EXPOSED UNINFECTED (HEU) AND HIV-UNEXPOSED INFANTS WITH BCG IN THE FIRST MONTH OF LIFE

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Background

According to many guidelines, tuberculin skin test (TST) is still nowadays the preferred method to investigate tuberculosis infection in children under 5 years. However, bacille Calmette-Guerin vaccine (BCG) could interfere with TST result, especially in the first years after BCG administration. This study aims to assess TST in healthy infants aged less than 24 months not exposed to tuberculosis who had BCG vaccine administered during the first month of life.

Methods

Infants who fulfilled the above mentioned criteria were invited to participate. After written informed consent, 0.1 mL PPD RT-23 was administered by a qualified professional on the anterior forearm and measurement of induration was read after 72 hours with a millimeter ruler. The cut off levels applied for a positive TST were 5mm and 10mm. This study was approved by Ethics Committee of Federal University of Sao Paulo.

Results

Among the 52 children evaluated, 43 returned after 72h; 20/43 (46.5%) were male and mean age was 12.8 months (ranging from 7.9 to 19.4). TST had no induration in 37/43 (86%) infants and 6/43(14%) had an induration ranging from 3 to 8 mm. Six out of the 43 children were vertically HIV-exposed uninfected (HEU) and in all 6 (100%) TST had no induration. Among the 43 infants, there were 3 with positive TST if the cut off applied was 5 mm and no positive TST when it was 10 mm.

Conclusions

BCG vaccine does not seem to interfere with TST assessment when a 10 mm-cut off is employed. However, TST has still practical difficulties, the most important being the need to have the patient evaluated after 72h.

ESP16-0171
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MULTIFOCAL BONE TUBERCULOSIS IN AN INFANT

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Title of Case(s)

Multifocal bone tuberculosis in an infant: case report

Background

Multifocal bone involvement is uncommon. We report an infant who presented with mass over right shoulder and later over a period of few months over the chest wall appearing as lipoma, which bacterialogically and histopathologically, turned up to be tubercular in origin

Case Presentation Summary

We report an one and half year old girl who presented in outpatient department with complaints of gradually increasing swelling over right shoulder, low grade fever for two months, nodular swelling over chest wall since 2 weeks. There was no history of contact with tuberculosis. Mantoux test was positive (12 mm). Complete blood count was normal and ESR was high (62 mm) in first hour. Chest X-ray done was normal. Repeated course of oral antibiotics were given with no reduction in size. X-ray right shoulder revealed evidence of chronic osteomyelitis with soft tissue swelling. FNAC done from both sites revealed caseous material with presence of inflammatory cells and foamy macrophages. Scattered epitheloid cells were also present. Real time PCR done was also positive for mycobacterium tuberculosis complex. Patient was started anti tubercular treatment with Isoniazid, Rifampicin, Pyrazinamide and Ethambutol for initial two months and currently on maintenance therapy of Rifampicin and Isoniazid with reduction in size of swelling and fever.

Learning Points/Discussion

Tuberculosis should be the differential in any patient with persistent bone or skin lesions especially in endemic areas.

ESP16-0320
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

LATENT TUBERCULOSIS INFECTION SCREENING PROGRAM IN PEDIATRIC IMMIGRANT POPULATION IN THE AREA OF PARMA

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Background

Early diagnosis of Latent Tuberculosis infection (LTBI) is fundamental to prevent onset and diffusion of active disease. We report on a screening program in pediatric immigrant population in the area of Parma (north Italy).

Methods

From January to December 2015, 280 children (age from 1 to 17 years, mean 10.4 years) living in Parma area for less than 3 years and coming from, or having sojourned for more than 3 months, in tuberculosis endemic areas, were screened.
The screening was performed by Tuberculosis Skin Test (TST), read at 72 hours. Positive TST cases (> 10 mm) underwent Quantiferon TB-Gold (IGRA) test, associated with chest x-ray when TST > 15 mm. Patients with LTBI underwent 6 months prophylaxis with Isoniazid 5 mg/kg/die, prophylaxis undertaken independently of IGRA result in positive TST children under 5 years of age. Those who had had 2 positives TST in the previous years underwent IGRA only.

Results

277 patients had a TST, 51 were positives (18.4%), of which 26 > 15mm; IGRA was positive in 15 patients (29%). Chest x-ray performed were negatives. Eight patients were under 5 y of age, 1 with positive TST.

Conclusions

TST is the gold standard for the diagnosis of LTBI, also for its low cost, but it maybe affected by some bias as BCG vaccine, previous TST test and reader ability. In patients coming from endemic areas combining TST and IGRA may improve diagnostic sensitivity allowing early diagnosis of LTBI in children.

ESP16-0035
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

A CASE OF SEVERE OSTEOARTICULAR TUBERCULOSIS IN AN INFANT. A THERAPEUTIC CHALLENGE FOR CLINICIANS

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Title of Case(s)

A CASE OF SEVERE OSTEOARTICULAR TUBERCULOSIS IN AN INFANT.

Background

Skeletal tuberculosis is uncommon, representing 1-2% of all pediatric tuberculosis cases.

Case Presentation Summary

M.G.E., a Romanian 18-month-old girl, was admitted to our Pediatric Department on January 2015 for reddish cutaneous swellings on the right great trochanter and on the right gluteus, noted after removal of a plaster cast, previously placed in Romania for right traumatic hip dislocation. She presented in good condition, apyretic, but could not walk, her right leg was medially rotated, flexed and 2 cm shorter respect to left leg. Hip MRI showed a severe osteomyelitis of the right femoral metaphysis with bone abscess affecting also the acetabulum, the ischiopubic ramus, the omolateral gluteus, internal obturator and piriformis muscles, and fistula involving cortical bone, muscular and subcutaneous tissues. Blood examination revealed microcytic anemia (8.9 g/dl), mild increase of CRP and ESR. HIV negative. Mantoux reaction was markedly positive (>20 mm). Chest X-ray revealed a nodular radiopaque image in the middle-lower right lobe. Culture of abscesses' drainage material resulted positive for Mycobaterium tuberculosis, susceptible to common antitubercular drugs; bacterioscopic examination and M.tb complex PCR were positive, too. Examinations of gastric aspirates were negative, except for positive culture in one sample. Osteoarticular tuberculosis was diagnosed; treatment with isoniazid, rifampicin, pyrazinamide and ciprofloxacin was started and maintained for 4 months, then ciprofloxacin was suspended. During the follow-up the baby remained well, cutaneous abscesses nearly resolved in 4 months, repeated MRI imaging is showing a slow, but progressive improvement. Treatment is ongoing.

Learning Points/Discussion

Pediatric osteoarticular tuberculosis Guidelines differ, especially for treatment duration, and therapy management may be a challenge for clinicians in the most severe cases. A patient-centered approach is needed for optimizing therapy.

ESP16-0385
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MANTOUX SCREENING FOR TB INFECTION IN CHILDREN IN A LOW-RISK COUNTRY – DOES BCG VACCINATION MATTER?

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Background

The Mantoux test is used as a screening tool for tuberculosis (TB) in all children arriving to Malta from high risk countries and all Maltese children prior to BCG vaccination at twelve years of age. Our primary outcome was to assess whether a Mantoux test of 10 - <15 mm is also indicative of TB infection in children who had received BCG immunization.

Methods

All children identified as having a Mantoux reaction of ≥10 mm were assessed for TB by clinical examination, chest X-ray and interferon gamma release assay. BCG vaccination status was documented. The children were divided into two groups according to Mantoux size of 10 - <15 mm or ≥15 mm. Significant differences between the two groups were inferred from 95% confidence intervals.

Results

121 children under 16 years of age (mean 10.2 years) were recruited between May 2009 – June 2015. Of these, 60% were male and 66% were foreign. 74 patients had a Mantoux reaction between 10 - <15 mm, with 22 patients (30%) having latent tuberculosis. 16/22 patients had been immunized with BCG (72.7%; 95% CI: 54-92%). A Mantoux reading of ≥15mm was documented in 47 children, of whom 45% (n=21) had latent tuberculosis. 14/21 patients had evidence of BCG immunization (67%; 95% CI: 47-87%). There was no significant difference in the proportion of TB infection between BCG vaccinated children in the two groups.

Conclusions

Our results show that children with a Mantoux reaction between 10 - <15 mm and who have received BCG immunization should still be investigated for TB. Half of our patients with latent TB would have been missed had screening been limited to children with a Mantoux reaction ≥15 mm.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1092
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

RECURRENT TUBERCULOSIS AFFECTING THE CENTRAL NERVOUS SYSTEM: A CASE REPORT

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Title of Case(s)

Recurrent Tuberculosis affecting the central nervous system: a case report.

Background

Recurrent tuberculosis (TB) may result from exogenous re-infection or endogenous reactivation. The risk of recurrence depends on a combination of infection, treatment and host factors. We present a case of recurrent TB affecting the central nervous system (CNS).

Case Presentation Summary

A 15 year-old girl, born in Afghanistan, previously healthy, HIV negative and fully vaccinated, including uncomplicated BCG, presented with fever, headache, neck stiffness and leg weakness. Due to acute neurological deterioration she was admitted to the Paediatric Intensive Care. *Mycobacterium tuberculosis* (MT) was isolated from the cerebrospinal fluid(CSF) and respiratory samples by microscopy, PCR and culture. Brain and spinal MRI were consistent with a extensive spinal and meningeal tuberculosis. Treatment consisted of the recommended WHO 4-drug regime and dexamethasone for two months, followed by isoniazid and rifampicin. The treatment was prolonged for sixteen months in total.

Seven months after treatment completion, she represented with fever, headache and nausea. Her CSF showed 883 WBC (60% polymorphs). The viral PCR, 16sPCR, AAFB microscopy, MT-PCR and CSF cultures were negative. Nevertheless, the brain MRI showed images compatible with tuberculomas. She was restarted on tuberculosis treatment, with the addition of moxifloxacin to the standard recommended quadruple therapy. Vitamin D deficiency was corrected. Immunological investigations (immunoglobulins, response to vaccines, lymphocyte subsets, Nitro Blue Terazolium test and IL12/INF-gamma-pathway) were unremarkable. She showed both clinical and radiological improvement on therapy,continued for 18 months.

Learning Points/Discussion

Relapse seems to be the most likely cause of her second episode of TB meningitis in spite of a prolonged course of treatment. Further research is needed to establish the optimal treatment regimen, the length of treatment and the follow up for extensive TB-CNS disease.

ESP16-0366
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

CONGENITAL TUBERCULOSIS: A CASE SERIES REPORT

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Title of Case(s)

Congenital tuberculosis

Background

Congenital TB is rare, but fatal if untreated, and is difficult to diagnose in time to treat successfully without knowledge of a maternal history of TB. We report 4 cases of congenital tuberculosis diagnosed on basis of revised Cantewell criteria.

Case Presentation Summary

Four vaginally delivered term neonates (aged 16-42 days) presented with cough, repiratory distress, abdominal distension and fever. One neonate presented with severe sepsis with shock and required blood transfusion, ionotropes and mechanical ventilation support. They had nonspecific pulmonary infiltrates in Chest x ray and massive hepato-splenomegaly. Gastric aspirates were positive for Acid fast bacilli in 3 neonates while endotracheal aspirate was positive in 4th neonate. Mantoux test was positive in all four neonates. Ultrasonography and computerized tomography of abdomen and thorax in one neonate showed multiple hypoechoic lesions in liver along with regional lymphadenapthy, ascites and right pleural effusion. Other possible co-morbidities like malaria, TORCH infection, HIV and storage disease were ruled out thoroughly. Standard antitubercular therapy was started and all recovered well. The mothers of all four neonates were asymptomatic, but Mantoux test was positive. Histopathology for endometrial biopsies showed typical tubercular granulomas and PCR was positive for mycobacterial DNA. They all had good response with standard antitubercular treatment. Other contacts of neonates were healthy and had negative screening for tuberculosis.

Learning Points/Discussion

•Non-specific presentation of congenital tuberculosis should be familiar to clinicians because early identification and treatment can prevent devastating consequences of serious disease.
•Congenital tuberculosis should be considered in newborn with pneumonia not responding to antibiotic, if the mother is at risk for tuberculosis.
•As most of the women are asymptomatic, we recommend the screening of all possible pregnant women for tuberculosis.

ESP16-1082
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

NECROTISING CERVICAL LYMPHADENITIS: COULD THIS BE KIKUCHI DISEASE?

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Title of Case(s)

NECROTISING CERVICAL LYMPHADENITIS: COULD THIS BE KIKUCHI DISEASE?

Background

Cervical lymphadenopathy is common in childhood. Bacterial Acute Lymphadenitis can be defined as larger lymph nodes (>1cm) which are tender, fluctuant and usually associated with fever. The majority are straight forward and respond to antibiotics however, as we learnt from this patient that is not always the case.

Case Presentation Summary

We present a case of a 4 year old Somali boy who was admitted with a left sided acute lymphadenitis. He was initially treated with IV co-amoxiclav but also required incision and drainage. Despite a drain in situ and intravenous antibiotics he continued to spike temperatures. After 6 days of IV co-amoxiclav he was switched to IV Ceftriaxone and had an MRI. The MRI showed that there was some improvement in the collection compared with the preoperative CT. The blood cultures were negative and specimens sent for acid fast bacilli and mycobacterial culture were also negative.

As he continued to spike despite conventional antibiotics we started to look into the possibility of Tuberculosis. However, he had a Mantoux test which was normal and a quantiferon test was indeterminate. Interestingly, the biopsy came back showing a necrotic lymphadenopathy. This raised the possibility of Kikuchi disease. This is an uncommon, idiopathic, generally self-limiting cause of lymphadenitis. There have been various viruses identified as the triggers – CMV, EBV, parainfluenza and parvovirus. This rare disease is more typically found in Asian populations although cases have been reported in all races all over the world.

Learning Points/Discussion

We have learnt from this case that not all necrotising lymphadenitis are acute infection or mycobacterium and it is therefore important to think of causes such as Kikuchi or malignancy in our differential.

ESP16-0450
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

DIAGNOSTIC CHALLENGES OF TUBERCULOUS MENINGITIS (TBM) IN 16 YEAR OLD ADOLESCENT

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Title of Case(s)

DIAGNOSTIC CHALLENGES OF TUBERCULOUS MENINGITIS (TBM) IN 16 YEAR OLD ADOLESCENT

Background

Lithuania is TB endemic country, however TBM is very rare in children. We present unusual TBM case which brought many diagnostic challenges.

Case Presentation Summary

Previously healthy adolescent presented with febrile fever, nausea, vomiting, severe head and back pain. The *patient was in flexed position because of severe lumbalgia.* On examination he had hypestesia in lower limbs, painful palpation of paravertebral muscles, very brisk patellar and ankle jerk reflexes, pronounced plantar clonus on both sides, expressed hand and tongue tremor. CFS revealed very high protein (22.7g/l) and glucose (6.2mmol/l) level. Brain and spine MRI (3T) showed contrast enhancing pachimeningitis with non-caseous granuloma and spinal cord arachnoiditis with compressive myelopathy. *CSF Xpert*MTB/RIF, acid-fast bacilli and CSF culture was negative. No history of contact with tuberculosis. TST, QFT was positive. Differential diagnosis included fungus, lymphoma, sarcoidosis, malignancies. Primary TB focus wasn't found. Patient was diagnosed with tuberculous pachymeningitis and spinal cord arachnoiditis. Anti-TB treatment was started with high dose of steroids, severe pain was managed with opioid analgesics.
One month later patient's status has improved. Back pain was managed with ibuprofen. However findings in the CSF revealed no improvement. Repeated brain MRI showed persistent leptomeningeal and pachymeningeal contrast enchancement, focus in the quadrigeminal bodies revealed circular enhancement patter (caseous granuloma). Anti-TB treatment was continued. 3 months later patient had no complains of back pain, he was able to walk in upright position, neurological status improved significantly. Currently patient is still receiving anti-TB treatment.

Learning Points/Discussion

The diagnosis of TBM is very challenging as there are no specific clinical findings and diagnostic methods are not complete. Often the diagnosis ex-juvantibus may be the only evidence of TBM.

ESP16-0711
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PROFILES OF CHILDHOOD CONTACTS OF TUBERCULOSIS: WHO HAVE LATENT TUBERCULOSIS?

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Background

Tuberculosis is still a major morbidity in Korea and most childhood cases are from an adult or adolescent with infectious tuberculosis. We evaluated the profiles of children with the tuberculosis contact and the cases of latent tuberculosis.

Methods

We reviewed medical records of a total of 110 children tested for a contact history with infectious tuberculosis at Chonbuk National University Children's Hospital from January 2014 to December 2015. All contacts were managed in compliance with Korean Guidelines for Tuberculosis.

Results

All children had a documented history of BCG vaccination and/or a BCG scar. Most index cases were parents (N=62), followed by grandparents (N=27), siblings (N=6) and uncle/aunts (N=5). Among the 110 children, 25 latent tuberculosis cases (22.7%) were found with tuberculin skin test using 2TU PPD. Eleven cases (10.0%) showed an initial negative skin test result but a positive conversion through a serial tuberculin skin test, and 5 (45.4%) of them were under 2 years of age. None had active tuberculosis diseases. For all latent tuberculosis cases, the index contact were caregivers (13 were from parents, 10 from grandparents, 2 from uncles/aunts).

Conclusions

Most of childhood latent tuberculosis cases were infected from caregivers with infectious tuberculosis in this study. Thorough investigation with tuberculin skin tests is needed in children, especially of younger age.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0752
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

LATE-ONSET IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME: IN IMMUNOCOMPETANT INFANT WITH TUBERCULOSIS MENINGITIS

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Title of Case(s)

LATE-ONSET IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME: IN IMMUNOCOMPETANT INFANT WITH TUBERCULOSIS MENINGITIS

Background

immune reconstitution inflammatory syndrome (IRIS) is usually seen during central nervous system (CNS) tuberculosis coinfected with Human Immunodeficiency Virus-1 (HIV-1). But also in the settings of immunosuppression or immunodeficiency IRIS can be result of CNS tuberculosis. Here in we present a case about late-onset IRIS associated with pulmonary and CNS tuberculosis in a fourteen-month immunocompetant girl.

Case Presentation Summary

A 5-month-old girl admitted to hospital with fever and prolonged cough. In her physical examination at the admission revealed that rhonchus and rales on chest oscultation. On the 7th day of hospitalization noticed that she didn't follow the object and threw her head back. Cranial computerized tomography (CT) showed hydrocephalous. Five days after surgery she had generalise tonic-clonic convulsion. Abdominal distension occurred and peritonitis developed. Cerebrospinal fluid (CSF) polymerase chain reaction (PCR) analysis for *M. tuberculosis* was positive. IGRA (Interferon-gamma release assays) test was positive. Anti-tuberculosis and corticosteroid treatment were started immediately. Thorax CT revealed that cavitary lesions in right upper lobe posterior segment, right middle lobe middle segment and left lower lobe superior segment and consistent with pulmonary tuberculosis. Corticosteroid treatment was given eight weeks. At the nine months of anti-tuberculosis treatment cranial magnetic resonance imaging (MRI) revealed that 1.5x0.8x1.1 cm lobule lesion with contrast enchantment in bulbus, inferior cerebellar peduncle. It was consistent with IRIS. Corticosteroid treatment started again and after two months therapy the lesions were regressed.

Learning Points/Discussion

As a conclusion IRIS is being recognized in cases without HIV. It is a significant cause of morbidity and mortality and requires exclusion of differential diagnosis

ESP16-0674
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

COMPARISON OF COMBINATION OF ISONIAZID AND RIFAMPIN WITH ISONIAZID IN THE TREATMENT OF TUBERCULOSIS INFECTION IN CHILDREN

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Background

Tuberculosis (TB) is an important cause of morbidity and mortality worldwide. In order to control and eliminate tuberculosis (TB), the management of latent TB infection (LTBI) as well as active TB is inevitable. This study compared result of treatment and toxicity of short-course therapy with isoniazid plus rifampin for 3 months vs only isoniazid treatment for LTBI in children.

Methods

We retrospectively studied the files of 282 children to visit for LTBI. Among them, 82 children(29.1%) was treated with only isoniazid, 199 children(70.6%) was treated with combination treatment.

Results

There was no case of TB disease in children treated with only isoniazid or combination regimen. Only 5 children in combination treatment showed toxicity within 3 months after start of treatment. Three children showed transient skin rash and 2 children showed elevations of liver enzymes, one of whom had to discontinue the treatment due to severe liver toxicity. Comparing our results with recent Cochrane review, The 95%CI for relative risk and odds rates of hepatotoxicity in the treatment with isoniazid and rifampin was 0.0894 to 1.4796 and 0.396 to 2.175 respectively.

Conclusions

Short-course therapy with rifampin plus isoniazid was equivalent and tolerable to standard therapy with isoniazid in efficacy and the proportion of side effect, but the further monitoring and evaluation are necessary because the severe case to discontinuation of treatment occurred in combination group.

ESP16-0986
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

BCG-TRIGGERED ENCEPHALOMENINGITIS IN A 9-MONTH-OLD INFANT WITHOUT CELLULAR AND HUMORAL IMMUNITY DEFECT

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Title of Case(s)

BCG-triggered encephalomeningitis in a 9-month-old infant

Background

The BCG vaccine has the longest history of use. In spite of the fact that over 4 billion people have been vaccinated its use is still controversial. Additionally, infant immunization may place children with cellular immunodeficiency at increased risk.

Case Presentation Summary

The disease developed in the girl without any perinatal risk, born at term in the family without TBC, immunized according to the mandatory schedule (BCG at birth), growing normally until the first symptoms at the age of 8 months. Acute hydrocephalus at the age of 9 months was preceded by subfebrilestates for 3 weeks, alternating somnolence and anxiety, sporadic vomiting, mild hemiparesis. Analysis of spinal fluid revealed inflammatory changes: pleocytosis 740 mm^3, increased protein level and decreased glucose concentration. Ventriculoperitoneal shunt was performed to treat hydrocephalus. Apart from routine microbiological tests for meningitis we decided to search for tuberculosis (genetic probe followed by positive culture). TB strain genotyping confirmed bovine tuberculosis caused by Mycobacterium bovis BCG.

Examination of the humoral and cellular immunity parameters revealed no abnormalities. Serum concentrations of C3 and C4 complement components as well as the reactive oxygen species production by neutrophils were normal. We found the proper expression of IFN-γ receptor on lymphocytes. Stimulated blood mononuclear cells were able to produce IFN-γ.

Learning Points/Discussion

Mendelian susceptibility to mycobacterial disease (MSMD) is a rare condition characterized by predisposition to clinical disease caused by weakly virulent mycobacteria, such as BCG vaccines and environmental mycobacteria. Specific molecular testing in our case are in progress.

Acute hydrocephalus developing in an infant without clear-cut cause should prompt exclusion of CNS infection due to BCG in countries where the vaccination is widely used.

ESP16-0975
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

COMPARISON OF THE EFFECTIVENESS OF THERAPY OF PULMONARY TUBERCULOSIS IN CHILDREN FROM CONTACT WITH MDR-TB

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Background

Drug resistance of M. tuberculosis may be one of the reasons for reducing the effectiveness of TB treatment in children, primarily from contact with MDR / XDR TB.

Methods

36 children 3-14 years old with pulmonary TB from TB contact were examined and treated during 2014-2015. Diagnostic complex included: computed tomography,tuberculin skin test,Diaskintest(DST),microbiology methods,real time PCR. All patients were divided in 2 groups:I(17) - from TB contact with preserved sensitivity of M. tuberculosis, II(19) - from TB contact with MDR/XDR TB. They were examined before therapy,after 2 and 6 month of therapy.Effectiveness of therapy(H+Z+R+E) was analyzed.

Results

In I group all children diagnosed TB of intrathoracic lymph nodes, 64.7% (11) – with complications. Results of microscopy and culture for M. tuberculosis were negative at all patients, while 11.8%(2)-positive by PCR. In II group TB of intrathoracic lymph nodes diagnosed only in 63.2%(12), in 3 children diagnosed primary TB complex and in 4 cases - secondary forms of tuberculosis.Complicated course of the disease occurred in II group - 94.7%(18). M.tuberculosis was revealed by cultural methods in 21.1%(4),PCR was positive in 31.6%(6).

There were not significant differences of clinical and radiological dynamics between groups after 2 months of therapy, in I group positive dynamics was in 12 (70.6%), in II group - 11 (57.9%) ($\chi^2 = 0.626, p > 0.1$). During examination after 6 months of therapy was detected a positive dynamics (disappearance of the symptoms of intoxication, positive radiologic dynamics, reduced activity TB based on the results of DST) in I group (64.7%) vs. 26.3% in II group ($\chi^2 = 5.355, p < 0.05$).

Conclusions

Using standard regimens in therapy children from MDR/XDR TB contact is not effective, this is confirmed by the absence of positive dynamics in 73.7% of cases.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0999
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

DETECTION OF LATENT TUBERCULOSIS INFECTION IN CHILDREN WITH DIFFERENT RESULTS OF TUBERCULIN SKIN TEST

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Background

Children with latent tuberculosis infection (LTBI) have the high risk of developing tuberculosis.

Objectives. The aim of this study is significance of immunological tests in children with different results of tuberculin skin test (TST).

Methods

97 children from 1 to 15 years old with positive results of tuberculin skin test were examined during 2013-2015 at children`s phthisiopulmonology department. Diagnostic complex included: Tuberculin skin test (TST),QuantiFERON®-TB Gold(QFT), Diaskintest(DST) and computed tomography(CT). After examination tuberculosis was excluded at all children. All patients were divided by results TST in 3 groups: I group(14) –patients with low results, II group(68) – with medium results, III group(15) - with high results.

Results

LTBI was diagnosed in all groups in the same percentage of cases. However, in children with high results of TST positive immunological tests (DST and QFT) were twice as likely than children with low results of TST. In I group positive results of DST were registed in 21.4% (3) and QFT - in 21.4%(3), II group - 32.3% (22) and 35.3%(24) respectively, III group-40.0%(6) and 33.3% (5).

Conclusions

LTBI in children does not influence the results of TST. LTBI was diagnosed in children with low and high results of TST with the same frequency. Results of DST and QFT are comparable.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1018
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

THE EFFECTIVENESS OF THERAPY OF LATENT TUBERCULOSIS INFECTION IN CHILDREN

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Background

Effective treatment of latent tuberculosis infection (LTBI) is an important component in the fight against tuberculosis in children.The aim of this study is determine the effectiveness preventive treatment of latent tuberculosis infection in children.

Methods

209 children from 3 to 14 years old with positive results of tuberculin skin test were examined during 2014-2015 at children`s phthisiopulmonology department (St.-Petersburg Institute of Phthisiopulmonology). Diagnostic complex included: QuantiFERON®-TB Gold (QFT), Diaskintest ® (DST) and computed tomography (CT). After examination 80 children had diagnosis LTBI, 54 children - tuberculosis, 75 – healthy children. Patients with LTBI (80) were followed for 12 months. All children were divided on two groups: I group – 32 children (37.3%) who received preventive therapy (two anti-tuberculosis drugs for 3 months: isoniazid at a dose of 10 mg / kg and pyrazinamide at a dose of 25 mg / kg). II group – 48 children (62.7%) who did not get preventive therapy because their parents refused.

Results

After control examination in 12 month 52 children (65%) had tuberculosis and 28 children (35%) – LTBI. When comparing the incidence of active tuberculosis in children found that those who received preventive therapy, became ill in 59.4% (19) of cases, and children who didn’t receive– in 68.8% (33), which is not statistically significant (p> 0,1).

Conclusions

The risk of developing TB in children with LTBI is quite high (65%). Carrying out preventive therapy for children with LTBI for 3 months was not significantly reduced the number of cases of tuberculosis.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0662
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

TUBERCULOSIS AMONG IMMIGRANT WORKERS FROM HIGHLY ENDEMIC COUNTRIES FOLLOWING PRE-ENTRY SCREENING IN TAIWAN, 2011-2014

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Background

To estimate the tuberculosis (TB) burden among new-entry immigrant workers from highly endemic countries following pre-entry screening combined partial repatriating during 2011-2014 and to assess the effectiveness of conducting post-entry (follow-up) mandatory TB screenings for these entry cohorts.

Methods

1.The TB prevalence based on post-entry screening was calculated from the Taiwan TB archive database, which was linked with a foreign worker physical exam screening database.
2.Odds ratio about several clinical and demographic characteristics for cases finding by active screenings vs. passively identification illness was assessed.

Results

In 2011-2014, 2080 TB-positive immigrant workers were identified among 1,91,1966 immigrant workers from Southeast Asia following their pre-entry screening and partial repatriating. In total, the respective gender-, age (20-49)- specific TB incidence rate of 65.8-175.6 per 100 000/year were 2.1-5.5 fold higher than those of the corresponding age Taiwanese. These cases were encompassed 14.2% (298/2080) smear-positive TB of high infectivity, 74.3% (1544/2080) smear- negative TB of less infectivity and 7.8% (163/2080) extra-pulmonary TB. It shown that immigrant workers with TB was 58% passively identified vs. 41% actively detected via post-entry screenings paralleled with a higher proportion of smear-positive (189/1223 vs. 108/857; OR 1.56, 95% confidence interval (CI): 1.2-2.0). In terms of effectiveness, the TB yield of the mandatory screening at the post entry 6^{th}- 30^{th} month among immigrant workers from highly endemic countries, was 61.1- 180.5 per 100,000 screenings, in Taiwan.

Conclusions

The post-entry screening following pre-entry screening combined partial repatriating is subsequently contributed to finding 41.2% TB cases encompassed 87.4% smear- negative pulmonary TB of less infectivity in an early pathogenesis for reducing TB burden among immigrant workers from highly endemic countries.

Systematic Review Registration (Please input N/A if not registered)

I have no potential conflict of interest to disclose

ESP16-0676
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

TRENDS IN ETIOLOGY OF PERICARDIAL EFFUSION

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Background

Tuberculosis has been attributed to be a major cause of pericardial effusion (PE) in Afro Asian countries as compared to developed nations. After implementation of Revised National TB Control programme in India, prevalence of all forms of TB has been brought down from 338 (1990) to 249 per 100,000 population (2009).We planned to study the impact of the control programme on pericardial tuberculosis in pediatric age group.

Aim: To ascertain the etiological diagnosis of pericardial effusion

Methods

Retrospectively data of 51 pericardial effusion patients was analyzed from 2010 to 2015 admitted to a tertiary level teaching hospital in capital of India.

Results

19 cases were tubercular, 23 were pyogenic, 4 were viral, 1 was fungal, 1 autoimmune, 1 malignant and 2 idiopathic. From 2010–12, 13 cases of tubercular were noted as compared to 6 cases during 2013-15 (p value **0.0044*).**

43 patients were discharged, 4 expired, and 1 patient with malignant pericardial effusion was referred. 3 cases quit treatment in-between. The median duration of stay was 15 ± 10.72 days. 2 patients had recurrent PE.

Table 1 Year wise distribution : Aetiological pattern

Year	Cases	Tubercular	Pyogenic	Viral	Idiopathic	Others
2010	6	***5***	0	1	0	0
2011	5	***3***	1	1	0	0
2012	11	***5***	4	1	2	0
2013	10	2	***6***	0	0	1(malignant)
2014	6	1	***4***	0	0	1(fungal)
2015	13	3	***8***	1	0	1(SLE)

Conclusions

Our study shows an evolving etiological pattern towards western countries where tubercular PE is uncommon; effectiveness of RNTCP in Indian subcontinent substantiated.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0663
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PREVALENCE AND RISK FACTORS OF ANEMIA IN PEDIATRIC LEPROSY DURING MULTI DRUG THERAPY (MDT)

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Background

Ten percent from new detected cases of leprosy in Indonesia is leprosy in children. Despite the process of chronic infection, Dapsone one of the component of MDT is known to cause haemolytic anemia especially in Multibacillary patiens before 6 months or at first 3 months of therapy. The objective is to obtain prevalence and risk factors of anemia in leprosy children during MDT therapy.

Methods

A cross sectional study with consecutive sampling was carried out from April to December 2013 at Kusta Sitanala Hospital, district of Tangerang. Subjects were leprosy children aged less than 18yo. Inclusion criterias were all children with MDT therapy and signed the informed consent. Children who received other leprosy drugs, or drop out from MDT over 6 months, or in leprosy reaction were excluded. The analysis was determined by Chi Square and Fisher Exact test.

Results

We enrolled 70 leprosy cases in this study of which half of them were boys. 40 (57.1%) of them were confirmed anemia. Mean of erythrocyte index showed the normocytic normochromic anemia. Significant risk factor of anemia was duration of therapy ≥ 3 months (OR: 2.716; CI:1.019 – 7.232). Age, sex, and nutritional status as external factors were not significantly considered as risk factors of anemia

Conclusions

Anemia was found in 57.1% of leprosy children receiving MDT. Duration of therapy ≥ 3 months was the significant risk factor of anemia during MDT therapy.

ESP16-0079
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

BCG ARTHRITIS

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Title of Case(s)

A boy with Mycobacterial arthritis following a bacille Calmette-Guérin vaccination

Background

Tuberculosis remains a health issue worldwide and BCG vaccination is widely used to prevent tuberculosis. BCG-related arthritis and osteomyelitis is a rare but severe complication

Case Presentation Summary

A 20-month-old fully vaccinated afebrile boy living in northern Taiwan presented with swelling of the right knee for 5 days. No other respiratory or gastrointestinal symptoms were associated, and a bacille Calmette-Guérin (BCG) vaccination was performed as scheduled. The knee magnetic resonance imaging (MRI) showed abscess formation in the right suprapatellar bursa (**Figure**). Surgical debridement was performed, and histological examination revealed granulomatous inflammation with caseation necrosis. The pus culture yielded *Mycobacterium bovis*. The patient was immune-competent and was administered with isoniazid and rifampicin. He recovered without complications.

Learning Points/Discussion

1. Tuberculosis remains an important health threat and the live attenuated BCG vaccine was used to prevent childhood tuberculosis.

2. BCG-related arthritis and osteitis is a rare but severe complication.

3. Pediatricians should remain alert for mycobacterial infections in children with BCG vaccination, and ensure early diagnosis and correct treatment.

ESP16-0970
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

CONGENITAL TUBERCULOSIS DUE TO MYCOBACTERIUM BOVIS SSP. CAPRAE

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Title of Case(s)

Congenital tuberculosis due to *Mycobacterium bovis* ssp. *Caprae*

Background

Congenital tuberculosis (CTB) is an uncommon disease (<400 cases reported) characterized by non-specific clinical signs and high mortality rates. Transmission occurs hematogenous (from infected placenta) or via aspiration/ingestion of amniotic fluid. We report the 1st case of CTB by *Mycobacterium bovis* ssp*. Caprae.*

Case Presentation Summary

An 8-week-old female baby was admitted into hospital with fever, respiratory distress and pulmonary infiltrates and high acute phase reactants (CRP 270mg/l, leukocytosis 24.930/mm3). Despite broad-spectrum antibiotic treatment initially with cefotaxime, subsequently with Piperacillin/Tazobactam and Trimethoprim-Sulfamethoxazole, she deteriorated needing ventilatory and hemodynamic support; CT scan showed numerous pulmonary infiltrates and pleural effusion. Abdominal, cerebral ultrasound and echocardiography were normal. Blood and urine cultures, serology for syphilis, PCR-CMV/*Pneumocystis*/*Bordetella*/HIV and respiratory virus were negative. *Candida albicans* was isolated in BAL culture. Mantoux 0 mm. Anamnesis of the mother revealed an 11-year history of suspected tuberculosis peritonitis (culture medium Lowenstein-Jensen negative) for which she received 1st line treatment (HRZ 2m/HR 7) with good clinical response.
CTB was suspected and treatment with a four-drug-regimen (HRZAmikacin) was initiated. *Mycobacterium bovis* ssp*. Caprae* was identified from bronchial lavage by molecular genetic assay for differentiation of the *M.tuberculosis* complex (Genotype®MTBC Hain Lifescience©). First line drug testing using BD BACTEC™ MGIT™ 960-SIRE Kit showed no resistance. Subsequently criteria for haemophagocytic lymphohistiocytosis (HLH) were fulfilled and treatment with low-dose corticosteroids was added, however she died due to cardiorespiratory failure.

Learning Points/Discussion

A high index of suspicion of CTB in infants born to mothers from endemic areas for TB including accurate maternal anamnesis is essential to establish early diagnosis, prompt treatment initiation and improve clinical outcome of this fatal disease.

An ongoing survey of the ptbnet group (http://www.tb-net.org) is currently addressing this important issue.

ESP16-0500
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

CONCOMITANT MULTIDRUG-RESISTANT AND SUSCEPTIBLE PULMONARY TUBERCULOSIS STRAINS IN A 3-YEARS OLD CHILD

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Title of Case(s)

Concomitant Multidrug-resistant and susceptible pulmonary Tuberculosis strains in a 3-years old child.

Background

Co-infection by two different *M tuberculosis* strains has been described in literature but it is very uncommon in children. Management of these cases is difficult, magnified by the longer duration and major adverse effects of MDR-tuberculosis scheme compared with susceptible-tuberculosis therapy.

Case Presentation Summary

A HIV-negative 3-year old boy was hospitalised on May 2015 with a parapneumonic pleural effusion. Successful drainage was done and Intravenous penicillin was given with poor clinical response. TST was positive and Thoracic CT scan showed pulmonary and splenic enlarged lymph nodes. Genomic amplification–based assay (Xpert MTB/RIF®), performed on gastric aspirate, detected RIF-resistant Mycobacterium tuberculosis genome. InhA mutation confirmed MDR-TB strain. Source case was not identified. Immunity studies were normal. Treatment for MDR-TB was initiated with initial good response. Two months later, he presented with cough, asthenia and loss of weight; chest X-ray showed collapsed upper and middle right lobes. Bronchoscopy evidenced bronchial obstruction by the presence of an endobronchial granuloma that was removed. Steroid-therapy was started with clinical and radiological improvement. RIF-susceptible M. tuberculosis was detected in broncho-alveolar samples. However, we decided to maintain second-line drugs for MDR-TB. No other complications were observed during the 5-months follow-up.

Learning Points/Discussion

This is a challenging case with two different TB strains. We thought that deterioration in this MDR-TB child was due to a mechanical effect of paradoxical reaction, which was confirmed by good response to surgical and steroid treatment. This child never received tuberculosis treatment; so it was necessarily a new infection from two sources or from a double-strain source. Despite of adverse effects of MDR tuberculosis therapy, we think treatment must be adjusted to the more resistant strain.

ESP16-0630
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

EXTRA-PULMONARY TUBERCULOSIS DISEASE IN CHILDREN

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Background

Introduction: Children with*Mycobacterium tuberculosis* infection develop disease quickly and have a higher probability of having a severe disease or extrapulmonary subtype. Portugal reports 20:100,000 cases/year but with high TB incidence bags in certain regions. This study will review cases of an hospital that serves a population with immigrants from tuberculosis endemic countries.

Objective: To evaluate extra-pulmonary tuberculosis cases among children admitted in a level II hospital with about 60% of african immigrants.

Methods

Material and methods: Retrospective analysis from January 2004 to December 2015 (11years). Epidemiological, clinical, radiological, microbiological and treatment data was analysed.

Results

Results: We found 30 cases (60% of tuberculosis cases). The population mean age was 11,14 years ± 5,19 SD and 92% had african origin. There were 1-5 cases/year (max. 2009 and 2012) with a similar distribution along the years. 96% had received BCG (confirmed with scar or bulletin card). Tuberculin skin test was positive in 21/30 and IGRA in 5/30. There was one case of co-infection with chronic hepatitis B but none with HIV co-infection. The diagnostics were pleural (12), ganglionic (11), miliar (7) osteoarticular (1) and ocular (1) tuberculosis. Diagnosis was made by PCR (4) and culture (17). In all was held 1st line therapy. None of the patients died but 4 of them remained with sequelae (bronchiectasis and limited joint mobility). The index case was identified in 9/30 cases.

Conclusions

Comments: In countries with low incidence of tuberculosis the prompt diagnosis and treatment of adult source cases, effective contact investigations and treatment of latent infection, giving special attention to immigrants or travellers from tuberculosis endemic countries, are necessary to reduce morbidity in the paediatric population.

ESP16-0619
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PERIPHERAL LYMPHADENITIS CAUSED BY NON-TUBERCULOUS MYCOBACTERIA IN SPAIN: A MULTICENTER STUDY

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Background

In previously healthy children non-tuberculous mycobacteria (NTM) predominately cause cervico-facial lymphadenitis. The diagnosis of NTM infections can be challenging, and the optimal management remains uncertain.

Methods

Ongoing retrospective and prospective, multi-center observational study among Red Española de Tuberculosis Pediátrica (pTBred, Spain) centers/investigators. Patients aged 0-18 years with a microbiologically-confirmed diagnosis (culture and/or PCR-positive) peripheral NTM lymphadenitis are eligible. Epidemiological, clinical and treatment data are collected using Redcap software.

Results

118 patients (48.3% males; mean[SD] age, 32.5[17.3] months) were included. The majority were non-BCG-vaccinated (94.9%) and without known risk factors for tuberculosis (94.9%). Most patients had unilateral (92.4%) single-site (69.5%) localised lymphadenitis (submandibular, 69.5%; cervical, 27.1%). At diagnosis, median (IQR) duration of symptoms was 3(2-5) weeks and clinical stages were 1 (painless and firm), 2 (fluctuant), 3 (skin

changes) and 4 (fistula) in 47.0%, 8.5%, 38.9% and 5.6%, respectively. *Mycobacterium lentiflavum* (39.1%) and *M.avium* (35.7%) were the most commonly identified causative species. TST results were positive (≥5mm induration) in 58.8%. IGRAs were performed in 39 (33.6%) cases, with the following results: negative (n=34;87.2%), indeterminate (n=2;5.1%) and positive (n=3;7.7%: *M.lentiflavum*, *M.avium* and *M.szulgai* infection, one patient each). Most patients with a negative IGRA result (29/34;85.3%) showed some TST induration. Of 63 patients with clinical stages 1-2 at diagnosis, 40 initially underwent surgery and 23 did not, without difference in outcome with regards to lack of long-term sequelae between those groups (47.5% vs. 52.6%;p=0.71).

Conclusions

In previously healthy children presenting with long-standing unilateral cervico-facial lymphadenitis, the combination of a negative IGRA result together with some induration on TST testing is highly suggestive of NTM infection. *M.lentiflavum* was the most common causative species, contrasting with the predominance of *M.avium* in most previous studies.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0538
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

BCG INDUCED LUPUS VULGARIS: AN UNEXPECTED ADVERSE EVENT

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Title of Case(s)

BCG induced lupus vulgaris: an unexpected adverse event

Background

BCG lupus vulgaris is a rare complication of BCG vaccination, with an estimated incidence of 5 per million vaccinations. Due to the pauci-bacillary nature of the infection, staining or culture of biopsy specimens as well as molecular analysis may be unrevealing. We present a case of BCG induced lupus vulgaris.

Case Presentation Summary

A 12-year-old boy presented with a slowly enlarging, painless, purplish plaque over his left arm which reached 10cm in diameter 14 months after administration of the BCG vaccine (Statens Serum Institute, Danish strain 1331). His Mantoux reaction was 14mm and interferon-gamma release assay was negative. Skin biopsy revealed non-caseating dermal granulomata composed of epitheloid histiocytes and Langhans-type multinucleated giant cells. No acid fast bacilli were seen and PCR for *Mycobacterium tuberculosis* complex (includes *M. bovis*) was negative. A clinical diagnosis of BCG lupus vulgaris was made and in view of negative cultures and the possibility of isoniazid resistance in some of the BCG strains, he was treated with isoniazid, rifampicin and ethambutol for 6 months. Investigation of his Interferon-ɣ (IFN-ɣ) and Interleukin-12 (IL-12) axis showed a reduced IFN-ɣ response to PHA stimulation, diminished IL-12 and suboptimal down-regulation of IL-10 in response to IFN-ɣ, possibly compatible with a partial IFN-ɣ receptor deficiency. Mutational analysis of the IFNGR1 and IFNGR2 genes was unrevealing. The lesion healed with extensive scarring. No recurrence was documented up to 3 years after treatment completion.

Learning Points/Discussion

In the absence of positive cultures and PCR, diagnosis of BCG induced lupus vulgaris would rely on the clinical picture and a suggestive histopathological appearance. Defects in the IFN-ɣ and IL-12 axis should be sought to identify children with Mendelian susceptibility to mycobacterial infections.

ESP16-0561
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PYRAZINAMIDE INDUCED HEPATOTOXICITY IN 3 CLINICAL CASES

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Title of Case(s)

PYRAZINAMIDE INDUCED HEPATOTOXICITY IN 3 CLINICAL CASES

Background

Drug induced hepatotoxicity is the most common adverse drug reaction leading to interruption of antituberculosis treatment. Published data and guidelines of liver function monitoring during TB treatment are often contradictory and are not directly relevant to the pediatric population. We present first 3 clinical cases of anti-TB drug induced hepatotoxicity at Children's Hospital² during the last decade.

Case Presentation Summary

In total 3 patients who developed hepatotoxicity were treated by daily course therapy comprising Pyrazinamide (28.5 ± 4.7 mg/kg), Isoniazid (6.75 ± 1.7 mg/kg), Rifampicin (10.37 ± 3.0 mg/kg), Etambutol (22.45 ± 5.7 mg/kg) at Children's Hospital² during 6 month period in 2014. Clinical status of patients were checked by daily basis. Liver enzyme testing (ALT, AST) was performed several times during the treatment course.

In all 3 cases treatment was discontinued after 8±1 days, due to gastrointestinal symptoms (weakness, nausea, vomiting) and findings of liver damage (ALT and AST elevation more than fifty times the upper normal limit). In all cases liver enzyme values returned to normal in about 3 weeks after discontinuation of medication.

TB treatment was introduced gradually at the same regimen (except of pyrazinamide) and the same daily doses. Liver enzyme values and clinical status of patients remained under control during all treatment course after stopping pyrazinamide.

Learning Points/Discussion

Anti-TB drug induced hepatotoxicity was rare at Children's Hospital². However these cases indicated that intensive monitoring of hepatotoxicity should be performed for children receiving pyrazinamide as part of anti-TB treatment. Pyrazinamide may not be re-introduced because of the risk of recurrence and the poor prognosis of pyrazinamide-induced hepatitis.

ESP16-0581
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PEDIATRIC SKELETAL TUBERCULOSIS

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Background

To describe the characteristics of skeletal tuberculosis (TB).

Methods

Retrospective study of children diagnosed with skeletal TB in the last 20 years.

Results

During the study period, 11 patients (5.2%) out of a total of 213 children with TB had osteoarticular involvement (3rd most frequent clinical form after pulmonary and lymphadenitis). Four children were diagnosed with spinal TB, 5 with osteoarticular TB (2 knee, one hip, one ankle and one hip, knee and shoulder); and 2 with isolated osteomyelitis (one femur, one mastoid bone). Five patients had pulmonary involvement.

The average age at diagnosis was 5.3±3.6 years, with a median time between symptom onset and diagnosis of 12 months (range 2 weeks-3 years). All were immunocompetent. Two patients (18.2%) were immigrants and 7 (63.6%) immigrants' children. The index case was identified in 4 patients (36.4%) . The most frequent clinical sign was functional impairment (64%), accompanied by pain in 45% and fever in 36%.

All had positive tuberculin skin test. *Mycobacterium tuberculosis* was isolated in 82%: 2/11 joint fluid culture; 5/11 gastric aspirate, 6/11 synovial or bone biopsy. The most frequent radiological findings were bone destruction (82%), cold abscesses (36%) and synovial hypertrophy (27%). There was only one multidrug-resistant isolate. Surgery was required in 45% (3 drainage of the lesion, 2 joint stabilization). Five patients (43%) developed long-term sequelae: 3 kyphosis, one leg length discrepancy and one limited joint mobility.

Conclusions

Skeletal TB is the third most common presentation of pediatric TB in our environment. Early diagnosis is critical, as many children require surgery and have long-term sequelae. It should be suspected in patients with prolonged pain and/or disability, even in the absence of fever, especially in immigrants's children.

ESP16-0067
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MOTHER'S KNOWLEDGE ABOUT CHILDHOOD TB IN BANGLADESH AND RELEVANT HEALTH-SEEKING BEHAVIOR

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Background

Childhood TB is an important public health problem worldwide, especially in the 22 high burden and low and middle-income countries including Bangladesh. In Bangladesh the prevalence of child TB is as low as 3% which is an underestimation. Inadequate knowledge and poor health-seeking behavior of the mothers as first caregiver may impair effective control of child TB.
Objective: To elicit level of knowledge and health seeking behavior towards child-TB among mothers of patients with child-TB in urban areas of Bangladesh.

Methods

This cross sectional study interviewed 257 mothers of child-TB patients (under 15 years) who were enrolled in BRAC supported TB programme in the urban areas during first quarter of 2013, using a pre-tested semi-structured questionnaire. BRAC an NGO, provides community based TB services with largest population coverage in collaboration with National Tuberculosis Control Programme.

Results

Although 84% of the mothers were informed about child-TB, "weight-loss" and "failure to thrive" as symptom, were mentioned by only 20% and 3.5%, respectively. However, low grade fever and cough as main symptom were mentioned by 79.8% and 73.2% of the mothers, respectively. Awareness on BCG and Isoniazid therapy as preventive measures, were mentioned by only 6.6 % and 40.1 %, respectively. Although majority (67.3%) were informed about sputum testing as diagnostic method, followed by X-ray (63%), awareness on tuberculin test was relatively low (26.8%). Median treatment delay for children was 60 days. Diagnosis at private sector was reported by 30 % of the mothers.

Conclusions

Although some level of general awareness on TB was present, childhood TB related information such as symptom, preventive measures and diagnosis, were not adequate. Specific IEC intervention on childhood TB is needed to improve care seeking.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0690
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

CEREBROSPINAL FLUID ARACHIDONATE-5-LIPOXEGENASE LEVELS FOR THE DIAGNOSIS OF TUBERCULAR MENINGITIS IN CHILDREN

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Background

BACKGROUND and AIM:

Early and rapid diagnosis of TBM poses a great challenge. Arachidonate-5-Lipoxygenase is an enzyme involved in the synthesis of bioactive leukotrienes from arachidonic acid. We measured and compared the levels of Arachidonate-5-lipoxygenase in the cerebrospinal fluid of children with tuberculous meningitis in respect to pyogenic meningitis and controls.

Methods

METHODS: 3 groups were made for the purpose of this study comprising of pediatric patients of tuberculous meningitis, pyogenic meningitis and controls, using predefined accepted criteria. Arachidonate-5-lipoxygenase was estimated in the cerebrospinal fluid of these patients using ELISA technique by Evolis-Twin plus Bio-Rad machine. Statistical analysis was done using SPSS software for windows.

Results

RESULTS: The mean **±** S.D value of CSF Arachidonate-5-lipoxygenase in the tuberculous meningitis, pyogenic meningitis and control groups was 1.09 ± 0.363 ng/ml, 0.747 ±0.306 ng/ml and 0.493 ±0.216 ng/ml respectively. CSF Arachidonate-5-lipoxygenase in tuberculous meningitis group was significantly higher than pyogenic meningitis group ($p=0.001$) and control group ($p<0.001$).

Conclusions

CONCLUSION: Cerebrospinal fluid Arachidonate-5-lipoxygenase may be a useful marker in the early diagnosis of tuberculous meningitis.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0885
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

ELISPOT CONTRIBUTION TO DIAGNOSIS OF ACTIVE AND LATENT M.TUBERCULOSIS INFECTION IN IMMUNOCOMPETENT AND IMMUNOCOMPROMISED CHILDREN AND ADOLESCENTS

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Background

This survey evaluated the contribution of ELISpot to diagnosis of *Mycobacterium tuberculosis* infection in children and adolescents.

Methods

This retrospective cohort study took place at Pediatric Units of Federal University of São Paulo. T-SPOT.TB was performed in patients who were on investigation of latent or active tuberculosis along with other diagnostic tests like Tuberculin Skin Test (TST) and microbiological tests. Patients were classified in two groups according to presence or absence of an immunodeficient condition. We evaluated the performance of ELISpot, concordance between tests and its contribution to diagnosis. The study was approved by the Ethics Committee of Federal University of São Paulo.

Results

Median age of 86 patients was 9.8y (range,0.1-24.1); 55% were female. Forty-one (48%) immunocompetent children (IC) and 45 (52%) with some immunodeficiency condition (ID) (14 HIV infection, 13 oncologic disease, 11 autoimmune disease, 7 other immunodeficiency conditions) were evaluated. All patients were submitted to ELISPOT that was indeterminate in 13 (15%) patients (4 IC and 9 ID; Chi-squared,p=0.306). In 63 patients both ELISpot and TST were performed; tests were concordant in 50 (79.4%), 22/31 (71.0%) in IC and 28/32 (87.5%) in ID (Chi-squared,p=0.190). Tuberculosis infection (latent or active disease) was diagnosed in 33 (38.4%) children (19 IC and 14 ID) and excluded in 53 (61.6%)(22 IC and 3 ID;Chi-squared between groups, p=0.219). ELISPOT contributed to diagnosis in 17/86 patients (19.8%) (12/41 IC and 5/45 ID) and did not add to other tests or was not considered for clinical management in 29 IC and 40 ID (Chi-squared, p=0.066).

Conclusions

ELISpot and TST had a high concordance in both groups of patients. A higher rate of ELISpot contribution among immunocompetent patients was observed although not statistically significant.

ESP16-1080
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MULTI-FOCAL BONE TUBERCULOSIS PRESENTING IN NEW IMMIGRANTS TO THE UK

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Title of Case(s)

MULTI-FOCAL BONE TUBERCULOSIS PRESENTING IN NEW IMMIGRANTS TO THE UK.

Background

Skeletal tuberculosis (TB) accounts for up to 35% of cases of extra-pulmonary tuberculosis. Multi-focal bone disease is less common. The presentation of multi-focal bone TB is often delayed due to the lack of systemic symptoms. The diagnosis may be further delayed due to initial investigations prioritising the exclusion of malignant disease. We present two cases of multi-focal skeletal TB.

Case Presentation Summary

Case 1

An 11 year old boy from Bangladesh, living in the UK for 6 months, complained of a 2 month history of fever and night sweats and a longer history of shoulder and back pain. On examination, he had an obvious shoulder deformity and clear X-ray changes of the scapula and clavicle. A bone scan revealed parietal skull and sacral lesions. He responded to 12 months of anti-tuberculous therapy, which was extended due to concerns of dural involvement.

Case 2

An 8 year old boy from Indonesia, living in the UK for 4 years, presented with a 4 week history of elbow pain. The X-ray showed a lytic lesion of the humerus, initially felt to be malignant. He also had obvious skull and mastoid swellings. The focus of investigation was therefore to exclude malignant disease. The biopsy identified granulomas and a positive culture later confirmed the diagnosis of TB. He remains on anti-tuberculous therapy and shows signs of an excellent clinical response.

Learning Points/Discussion

Both children were immigrants from TB endemic areas who had not undergone TB screening. Access to screening may have lead to earlier identification of tuberculous disease.

In both cases, basic immune function tests were normal. However, there may be unidentified host factors which predispose certain individuals to this indolent presentation.

ESP16-0281
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MESANGIO-CAPILLARY GLOMERULONEPHRITIS COMPLICATING PULMONARY TUBERCULOSIS

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Title of Case(s)

Mesangio-capillary glomerulonephritis complicating pulmonary tuberculosis

Background

The European influx of migrants originating from sub-Saharan Africa is a controversial and current issue. All such migrants arriving in Malta are screened for infectious diseases, including mycobacterial infection. We present a case where screening in a minor travelling alone reveals active pulmonary tuberculosis, later complicated by mesangiocapillary glomerulonephritis, a rare complication of this infection.

Case Presentation Summary

A 15-year old Somali migrant was screened routinely for tuberculosis on arrival to Malta. His Chest X-ray showed changes suggestive of pulmonary tuberculosis, and his interferon-gamma release assay was positive. Computed chest tomography showed left upper lobe scarring and calcification and a left basal consolidation with effusion. His HIV antibody test was negative. Sputum samples obtained by sputum induction were smear negative. He was started empirically on rifampicin, isoniazid, pyrazinamide and ethambutol.

Four days following treatment initiation, he developed lower limb and sacral oedema, with mild ascites. The combination of heavy microscopic haematuria, an urinary protein of up to 5g/day, hypercholesterolaemia and severe hypo-albuminaemia was in-keeping with a mixed nephrotic/nephritic picture. An US-guided renal biopsy, revealed mesangiocapillary glomerulonephritis, possibly induced by his tuberculosis. Treatment-induced nephrotoxicity was thought to be unlikely due to the type of renal pathology, normal renal function, rapidity of manifestation of the renal disease and clinical resolution of oedema despite continuation of the anti-TB agents.

Learning Points/Discussion

In this case what is initially uncomplicated pulmonary tuberculosis, revealed an accompanying nephrotic syndrome with nephritic features. This patient's cultural background, together with the clinical scenario, presented unique diagnostic, medico-legal and therapeutic challenges to the authors. The case also highlights the importance of screening of irregular migrants.

ESP16-1041
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

OSTEOMYELITIS OF THE HAND ASSOCIATED WITH BACILLE CALMETTE-GUE´RIN VACCINATION

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Title of Case(s)

Osteomyelitis of the hand associated with Bacille Calmette-Gue´rin vaccination

Background

Skeletal tuberculosis (TB) with involvements of the metacarpals and phalanges of the hand are infrequent. Here we report osteomyelitis due to *Mycobacterium bovis* in an otherwise healthy infant.

Case Presentation Summary

A 2 year old male patient presented with a painful swelling over the dorsum of left hand. He had a minor trauma 2 months ago and the swelling was recognized 1 month before. He was born at 36 weeks gestation and his family history was unremarkable except his aunt having TB 7 years ago. On admission he had no fever. Physical examination revealed a swelling of 1 cm diameter over the second metacarp of the left hand. The C-reactive protein level was 0.11 mg/l, and the leukocyte count was 3700 /mm3 (lymphocytes 980 /mm3). Magnetic resonance imaging (MRI) disclosed an expansive lesion affecting second metacarpophalangeal diaphysis, expanding to metaphysis. A diagnosis of Ewing sarcoma or osteomyelitis was estimated. On surgical exploration a greyish colored soft tissue was excised. *Moraxella catarrhalis* growth led us to start antibiotic therapy. The pathology revealed necrotizing granulomatous inflammation. His chest X- ray was normal. Tuberculin skin test resulted in 15 mm induration. IFN-γ-inducible protein 10 (IP-10) result was indiscriminate. He was re operated for surgical debridement. *Mycobacterium tuberculosis complex* growth was detected at bone culture. Molecular studies indicated *Mycobacterium bovis*. Anti-tuberculous therapy with isoniazid, rifampicin, and ethambutol were initiated. His lymphocyte sub group analysis and serum immunoglobulins were normal. Neutrophil function tests showed slight abnormality.

Learning Points/Discussion

Osteomyelitis is a very rare complication of BCG vaccine. Immunologic disorders affecting IL-12/IL-23Rb1 and IFN-gR should be investigated if BCG complications occur as a result of dissemination.

ESP16-0398
08. TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

USEFULNESS OF INTERFERON-GAMMA RELEASE ASSAY FOR THE DIAGNOSIS OF LATENT TUBERCULOSIS INFECTION IN YOUNG CHILDREN

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Background

Latent tuberculosis infection (LTBI) in young children may progress to severe active tuberculosis (TB) disease and serve as a reservoir for future transmission of TB disease. There are limited data on interferon-γ release assay (IGRA) performance in young children. We investigated the usefulness of IGRA for children younger than 5 years old.

Methods

We performed tuberculin skin test (TST) and IGRA in children under 18 years old admitted to the Chung-Ang University Hospital between May 2011 and June 2015. Blood samples for IGRA were collected, processed, and interpreted according to manufacturer's recommendations.

Results

Among 149 children, 31 (20.8%) and 10 (6.7%) were diagnosed as LTBI and active pulmonary TB, respectively. In the subjects without contact history with active TB patients, TST and IGRA were positive in 41.4% (29/70) and 12.9% (9/70), respectively. The agreement (kappa) of the two tests was 0.123. In the control group, which was consisted of non-TB infected subjects, age was not correlated with changes in the concentrations of interferon-γ after stimulation with nil antigen, TB-specific antigen, and mitogen in IGRA (*P*=0.384, 0.176, and 0.077, respectively). In serial IGRA tests, interferon-γ response to TB antigen was increased in IGRA-positive LTBI subject, but was not considerably changed in IGRA-negative LTBI subjects or subjects in control group.

Conclusions

Interferon-γ response was not decreased in young children. Usefulness of IGRA should be re-evaluated in children younger than 5 years old, especially for those with no history of contact with active TB patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0545
09. S - HIV/AIDS

HIV IN CHILDREN, FAR BEYOND THE VIRAL SUPPRESSION ...

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Background

Perinatal HIV infection carries a significant cardiovascular risk burden. We aimed at characterizing cardiovascular risk markers in a pediatric HIV positive population.

Methods

Observational cross-sectional descriptive study including 23 HIV infected children on antiretroviral therapy(ART) followed at our Cardiovascular Risk Clinic. Two treatment groups were included, one receiving protease inhibitors(PI) (n = 15), and the other not (n = 8). The results were considered statistically significant if $p \leq 0.05$ (SPSS 22).

Results

The average age was 11.4 years, 70% male. A third had hypercholesterolemia and 38% hypertriglyceridemia. There were no significant differences between total cholesterol (TC), HDL-C, LDL-C and triglycerides (TG) levels for the different treatment groups.

The high-sensitivity C-reactive protein(hs-CRP) correlated directly with the clinical stage at diagnosis ($\rho=0.741$), the HOMA-IR with the ART therapeutic period ($\rho=0.516$) and Lipoprotein(a) with current viral load ($r=0.912$). We found an inverse correlation between the CD4/8 ratio, TC ($\rho=-0.467$), LDL-C ($\rho=-0.527$,) and TG ($\rho=-0.465$). Intima-Media carotid thickness (IMTc) was >95th percentile in 77.7%. Cardiac dimensions, function and the pulmonary artery systolic pressure were within normal limits and without statistical difference between both groups.

Conclusions

We observed a direct relationship between current hs-CRP levels and the clinical stage at diagnosis, implying that the inflammatory process in HIV infection is related to disease severity at diagnosis. As hs-CRP is considered a cardiovascular risk factor marker, it is of clinical interest in the follow-up of this population, so much so that we found changes suggestive of early onset atherosclerosis, namely an increase in IMTc, compounded by an adverse lipid profile. Based on our findings, cardiovascular risk prevention ought to be implemented in this population group. Broader studies are needed to better characterize this metabolic deregulation and the underlying mechanisms.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0637
09. S - HIV/AIDS

THERAPEUTIC CAMPS IN HIV INFECTED ADOLESCENTS

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Background

Human Immunodeficiency Virus (VIH) infection in adolescence is a challenging chronic disorder, and as any disease in this age faces obstacles like the acceptance of the disease, adherence to therapy and society integration. The search for adequate interventions is constant, and the therapeutic camps emerge as a promising field. The authors describe the methodology of a therapeutic camp for HIV infected adolescents, along with the results of the evaluation performed by the adolescents.

Methods

Therapeutic camps were performed once a year, in 2013 and 2014 with HIV infected adolescents.

Results

Two camps were performed for a period of three days, organized by a multidisciplinary team (physicians, nurses, psychologists, kindergarten teachers, social workers and volunteers). Eighteen and 19 adolescents participated, in 2013 and 2014 respectively, ages ranged from 12 to 18 years. In the camps, workshops are performed on issues related to HIV infection (adherence to therapy, legal issues, sexuality and affectivity) with encouragement of interaction and sharing experiences. In addition outdoor and recreational activities are performed to encourage relationships between peers. The camps were evaluated in a strongly positive manner by adolescents, and the main positive were the possibility of new friendships and learning more about HIV infection.

Conclusions

Previous studies demonstrated that therapeutic camps are effective interventions in adolescents with HIV infection, with improvement in autonomy, acceptance and responsibility when facing the disease.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1050
09. S - HIV/AIDS

PERINATAL EXPOSURE TO ANTIRETROVIRAL THERAPY IN HIV UNINFECTED CHILDREN

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Background

Mother-to-child HIV transmission hugely decreased in the last 20 years, with an increase in the number of uninfected children perinatally exposed to antiretrovirals(ARV). Although some adverse effects are well described, the long term effects of exposure remain unknown. The aim of this study was to evaluate the adverse effects of perinatal exposure to ARV therapy in uninfected children.

Methods

Prospective reevaluation of HIV uninfected children exposed to ARV therapy in our unit, between 2001 and 2011.

Results

One-hundred thirty five children were identified and follow-up was possible in 30 (22%), 67% of which male. Ages ranged from three to 13 years (mean of 6,8 years). Mean maternal age at birth was 29,1 years, 29 infected with HIV type 1. The pregnancy was monitored in 82%, and 53% initiated antiretrovirals in the first trimester, 7% in the second trimester, 10% in the third trimester and in 30% the timing of initiation was unknown. At birth three had cardiac defects and one a single kidney. Four had low intelligence quotient(IQ) and seven children were diagnosed with ADHD. Nine performed MRI(normal in eigth, one with groove enlargement). One child had anemia and measurement of lactate was normal in 15.

Conclusions

As mentioned in other studies contact and reevaluation of the HIV uninfected children exposed to antiretrovirals was difficult. In the evaluation performed no significant alterations were found so far. Low IQ and ADHD appeared to be more prevalent than in general population.Long-term follow-up of these children is important for a better knowledge of ARV safety.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0889
09. S - HIV/AIDS

LYMPHOADENOPATHY IN HIV-POSITIVE CHILDREN: IS IT FIRST CLINICAL STAGE OF HIV OR....?

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Title of Case(s)

Lymphoadenopathy in HIV-positive children: is it first clinical stage of HIV or ….?

Background

The lymph nodes enlargement is non-specific signs of HIV- infection in children and characterized the first clinical stage of HIV. However, this "simple" symptom can masks more severe co-morbidity, such as tuberculosis, oncology.

The 4 clinical cases of "atypical" enlargement of lymph nodes in HIV positive children are presented below.

Case Presentation Summary

1. 16 years old female with fever, pain and enlargement of lymph node in left axilla. HIV diagnosed in 16 years old. The blood count showed **anemia, leukopenia** and ESR -75 mm/h. CRP- 42 mg/l and CD 4 cells-– 11%- 76 cells.

2. 9 years old male with fever, hepatosplenomegaly and cervical and axillaries lymphadenopathy. HAART was started at 7 years old. The blood test showed: leukopenia, ESR -70 mm/h .CD4: 50%- 687 cells/ml.

3. 9 years old female with lymph nodes enlargement on both side of neck. The HIV status was diagnosed in 9 year, without signs of immunosupression. The blood test was normal.

4. 11 year old female hospitalized with enlargement of left-sides lymph nodes of neck. CD 4 : 46%-1117 cell/ml. The blood test was normal, CRP – 13 mg/l.

Ultrasound of lymph nodes,CT of neck, chest, abdomen and biopsy of lymph nodes were performed.
The histological conclusion were: cases 1 and 3 -tuberculosis , case 2 – non- Hodgkin's lymphoma , case-3 – TB /cervical cysts of neck.

Learning Points/Discussion

These cases illustrated that lymphoadenopathy in HIV –positive children could masked other co-morbidity.

The next symptoms: enlargement of lymph nodes more than 2 cm, asymmetrical localization, round form and heterogeneous structure required additional examinations.

Biopsy of lymph node with histological analysis are clue to verification of diagnosis.

ESP16-0683
09. S - HIV/AIDS

CRYPTOCOCCAL MENINGITIS IN HIV POISTIVE CHILDREN IN UKRAINE

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Background

Cryptoccocal meningitis is rare infections caused *Cryptococcus neoformans or Cryptococcus gattii.* The incidence of Cryptococal meningitis decreased dramatically in the era HAAART, but still occur in patient with HIV who have deep immunosuppression (CD4 cells less than 50/ml). We present 3 cases of HIV positive children with Cryptococcal meningitis, who were observed in the Center of Infectious Diseases "Clinic for treatment Children with HIV/AIDS" National Specialized Children's Hospital "OKHMATDYT", Kyiv, Ukraine during the period between February 2008 and February 2015.

Methods

We reviewed the patient's files and collected data of the 3 HIV positive patients who had submitted Cryptococcal meningitis during the chosen period of time.

Results

The incidence of Cryptococcal meningitis among HIV-positive children in our hospital is 0.1%. The average age of patients was 11 years old; 1 female and 2 male. Average absolute CD4 count was 5 cells/ml. The leading symptom was headache: severe in 67% and moderate on the peak of fever in 33%. Seizure was presented in 67 %. Clear meningeal symptoms were positive only in 1 patient. The mortality rate was 100%.

Conclusions

- Cryptoccocal meningitis meet in HIV-positive children mainly older age and with dramatically low CD 4 cells(less than 10 cells) and is characterized by high mortality

- Clinical manifestation is not specific, but severe headache with fever in HIV- positive patients with CD 4cells less than 50 cells/ml should be considered as an indication for lumbar punction (LP) with microscopy and fungal culture of cerebrospinal fluid (CSF)

- The main prophylaxis of Cryptococcal infections is early start of HAART.

Systematic Review Registration (Please input N/A if not registered)

ESP16-0721
09. S - HIV/AIDS

IMPORTANCE OF ASSESSING CD4/CD8 CELL COUNT RATIO IN HIV SERO-POSITIVE PATIENTS WITH OROPHARYNGEAL CANDIDIASIS

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Background

The acquired immunodeficiency syndrome (AIDS) is characterized by the gradual loss of immune system functions. The hallmark of this process is a marked depression in cellular immune response and often leads to several opportunistic infections including fungal infections. The most common manifestations of candidal infections in HIV-infected person are oropharyngeal candidiasis, an invasive life threatening disease ranges from 12% to 93% of cases and showing parallel decline in CD4 cell count and hence the CD4/CD8 ratio. The present work was done to determinecorrelation between oropharyngeal candidiasis and CD4/ CD8 ratio.

Methods

18 HIV positive patients at their different stages of HIV infection and 10 HIV negative healthy individuals were enrolled at VCTC center KGMU, Lucknow. Oropharyngeal scraping swab specimen was collected from each individual, Direct KOH mount preparation, Gram staining and culture was done on SDA medium. Identification of isolate was done by standard methods. CD4/CD8 T cell estimation of each individual was measured by FACS machine.

Results

Oropharyngeal candidiasis due to *Candida albicans* was present at all stages of HIV infection even at CD4 counts > 500 cells/mm^3 in all patients.Thus, It is not the CD4 but CD4/CD8 ratio is more important to assess the oropharyngeal candidiasis in HIV positive patients.

Conclusions

Assessment of CD4/CD8 ratio is important than CD4 only for the better management in HIV positive individuals with secondary opportunistic infections particularly in oropharyngeal candidiasis.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0758
09. S - HIV/AIDS

HERPES SIMPLEX VIRUS-2 IGM ANTIBODY IN HUMAN IMMUNODEFICIENCY VIRUS POSITIVE INDIVIDUALS

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Background

HSV-2 is generally associated with genital infections and also infections of newborns. Primary infection with HSV is sub-clinical and unrecognized in the majority of cases, but it can determine generalized and fatal disease in the newborn or in immunocompromised patients. The present study was aimed to know the sero-incidence of HSV-2 in HIV positive versus HIV negative individuals and also to look for the association of HSV-2 infection with HIV.

Methods

The study was carried out at VCTC of King George's Medical University, Lucknow. The informed consent was taken from study as well as healthy individuals. 2 ml of blood was collected at VCTC for HIV testing, same blood sample was used for the present study. HSV-2 IgM antibody was detected by ELISA kit.

Results

A total of 70 sera (30 from HIV positive individuals; 40 from HIV negative individuals) were screened for HSV-2 IgM antibody by "HSV-2 IgM EIA, kit", Out of 30 HIV positive individuals sera, 14 (47%) sera were positive for HSV-2 IgM, whereas, only 3 (7.5%) individuals sera were positive in 40 HIV negative individuals.

Conclusions

The incidence of HSV-2 among HIV positive was so high that it cannot be attributed to chance finding; it could be either due to social behavior as a common source of infection or due to HSV predisposing person or increased risk of HIV infection.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0473
09. S - HIV/AIDS

IMPACT OF HIV-1 INFECTION AND ANTIRETROVIRAL THERAPY ON BONE HOMEOSTASIS AND MINERAL DENSITY IN VERTICALLY INDÌFECTED PATIENTS

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Background

Antiretroviral drugs and immune-activation lead to important side effects particularly evident in HIV vertically-infected patients. One of the most important side-effect is bone homeostasis impairment and reduction of bone mineral density.

Methods

Single-center prospective study. 67 patients with HIV-1 vertically transmitted (6-31 years) were enrolled. Bone turnover markers were analized (procollagen type 1 N-terminal propeptide – P1NP and C-terminal telopeptide – Ctx); 47 patients underwent lumbar spine and femoral dual energy X-ray absorption (DXA). Personal and anthropometric data and informations related to HIV-infection severity and HAART were collected.

Results

At lumbar spine DXA, osteopenia was recorded in 34% of patients while osteoporosis in 2%; at femoral DXA, osteopenia was recorded in 22% of patients, 4% of osteoporosis. BMD values recorded by DXA showed a significant correlation with age, race, BMI, physical activity and antiretroviral therapy duration. P1NP was higher than normal values in 43% of patients, while CTx in 61% of them. P1NP alteration was related to age, race, BMI, physical activity, therapy duration and ever use of protease inhibitors and nucleotide reverse transcriptase inhibitors.

Conclusions

Prevalence of low bone mineral density observed in our population is comparable to that of other studies analyzing vertically infected patients. Of particular value is the relationship between antiretroviral therapy and alterations of bone mineral density, since vertically-infected patients undergo life-long exposure to antiretroviral drugs. The relationship between an increased P1NP value and duration of antiretroviral therapy confirms the hypothesis that HIV infection causes a prevalence of bone resorption over bone formation; homeostasis is rebalanced only by antiretroviral therapy.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0335
09. S - HIV/AIDS

HEALTH OUTCOMES OF HIV-EXPOSED UNINFECTED INFANTS: A LITERATURE REVIEW

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Background and Objective

In developing countries, coverage of interventions to prevent mother to child transmission of HIV are increasing faster than maternal HIV prevalence is declining, resulting in a growing population of HIV-exposed uninfected (HEU) infants. Despite avoiding HIV infection, an emerging body of evidence suggests that HEU infants are at increased risk of infection compared to HIV-unexposed infants. We aimed to review this epidemiological evidence, and reflect upon the causes of such findings.

Methods

We searched PubMed using the terms (HIV or human immunodeficiency virus[MeSH Terms]) AND (expos* or uninfected or maternal or affect*[MeSH Terms]) AND (child* or infant* or fetus or fetal or foet* or neonat*[MeSH Terms]) for English language papers between January 1983 and December 2015.

Learning Points Discussion

(1) Increased infectious morbidity and mortality in HEU infants has been demonstrated in several sub-Saharan African cohorts. In the current era of suppressive maternal antiretroviral therapy in Europe, HEU children remain at risk of infectious morbidity, both in the neonatal period and throughout infancy. Infections with opportunistic organisms, including *Pneumocystis jirovecii* pneumonia, have been described in developed and developing countries, suggestive of immunological dysfunction.

(2) HEU infants have higher baseline levels of systemic inflammation and immune activation than HIV-unexposed infants. These findings of immune dysfunction may contribute to infection susceptibility. Transplacental transfer of antibody is lower in HIV-affected pregnancies, but HEU infants make good vaccine responses, often surpassing the responses of HIV-unexposed children, highlighting the importance of timely and complete vaccination in this population.

(3) In areas where formula feeding is unsafe, breastfeeding saves lives. This remains true of HEU infants, despite the risks of postnatal HIV transmission. Maternal antiretroviral therapy reduces postnatal HIV transmission, and exclusive breastfeeding promotion should therefore be prioritised.

ESP16-0527
09. S - HIV/AIDS

ANTIRETROVIRAL THERAPY REGIMEN SWITCH IN HIV-INFECTED CHILDREN WITH SUSTAINED VIROLOGIC SUPPRESSION - A RETROSPECTIVE STUDY OF THE SPANISH COHORT

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Background

In high-incomes countries, simplification is, after ARV treatment failure, the 2nd most common cause of switching an antiretroviral (ARV) treatment regimen. Simplification strategies in HIV controlled children/adolescents aim to reduce pill burden and dosing frequency, to improve adherence and decrease short- and/or long-term toxicity, whilst maintaining viral suppression.

Methods

Retrospective cohort study, analysing ARV switching regimen in HIV-infected children/adolescents with sustained virological suppression from the Cohort of the Spanish Pediatric HIV Network, (CoRISpe) between 01/2013 and 12/2014. Data were extracted from the CoRISpe database.

Results

A total of 97.2% (379/390) of children received cART. During the study period cART in 70/379 (18.5%) patients with sustained virological suppression were switched using 80 regimens including 90 ARVs (Table 1). Median of age at switch was 14.0 years (IQR 11.7-17.4). Substitution of zidovudine 6/90 (6.7%) and didanosine 7/90 (7.8%) and switching emtricitabine, abacavir simple agents to lamivudine/abacavir 6/90 (6.7%) combined regimens were the most frequent changes in the nucleoside reverse transcriptase inhibitors (NRTIs).

In the nonNRTIs class efavirenz was replaced by rilpivirine in 6/90 (6.7%) patients; lopinavir/ritonavir in the protease inhibitor (PIs) class was the most commonly replaced agent 32/90 (35.6%). Efavirenz and rilpivirine substituted PIs in 10/90 (11,1%) and 9/90 (10%) regiments, respectively. Rilpivirine (not licensed <18 years) was used in 16/90 (17.8%). After ARV switches all 70 patients were on a once-daily cART regimen; 58/70 (82.9%) children received a combined ARV pill and 28/70 (40%) an off-label single tablet regimen. Causes of

switch were simplification 58/80 (72.5%) and toxicity in 17/80 (21.3%) patients.

	ARV used prior to switch					ARV used after switch				ARV Changes
	Switch from	Switch to	n	% of total switches		Switch to	Switch from	n	% of total switches	Differences(%)
NRTI class 32/90 (35.6%)	**AZT**	ABC 3TC TDF ETV	2 1 2 1	**6.7 %**		**AZT**	ABC	1	1.1%	**-5,6%**
	ddI	3TC TDF	5 2	**7.8 %**		**ddI**			0%	**-7,8%**
						3TC	ddI AZT	5 1	6.7 %	+6.7%
	ABC	AZT	1	1.1 %		**ABC**	AZT	2	2.2 %	+1.1%
						TDF	AZT ddI	2 2	4.4 %	+4.4%
	FTC, ABC	3TC/ABC	6	**6.7 %**						-6,7%
	3TC/ABC	FTC/TDF	8	8.9 %		**3TC/ABC**	FTC/ABC FTC/TDF	6 3	10.0 %	+1.1%
	FTC/TDF	3TC/ABC RAL	3 1	4.4 %		**FTC/TDF**	3TC/ABC	8	8.9 %	+4,5%
NNRTI class 16/90 (17.8 %)	**EFV**	**RPV** ETV ATV'r DRV'r LPV'r	6 1 1 1 1	11.1 %		**EFV**	NVP LPV'r ATV'r	5 8 2	16.7 %	+5.6%
	NVP	EFV	5	5.5 %		**NVP**	LPV'r	1	1.1%	-4,4%
	ETV	RPV	1	1.1 %		**ETV**	EFV AZT/ABC	1 1	2.2 %	+1,1%
						RPV	EFV ETV LPV'r ATV'r DRV'r	6 1 4 3 2	17.8 %	**+17.8%**
PI class 41/90 (45.5 %)	**LPV'r**	ATV'r **DRV'r** EFV NVP RPV RAL	5 13 8 1 4 1	**35.6 %**		**LPV'r**	ATV'r EFV	1 1	2.2 %	**-33,4%**
	ATV'r	LPV'r DRV'r EFV RPV	1 1 2 3	7.8 %		**ATV'r**	LPV'r EFV	5 1	6.7 %	-1,1%
	DRV'r	RPV	2	2,2 %		**DRV'r**	LPV'r EFV ATV'r	13 1 1	16.7 %	**+14,5%**
INSTI class 1/90 (1.1%)	**RAL**	DTG	1	1.1%		**RAL**	FTC/TDF LPV'r	1 1	2.2 %	+1,1%
						DTG	RAL	1	1.1%	+1.1%

NRTI: nucleoside/nucleotide reverse transcriptase inhibitor, NNRTI: non-nucleoside reverse transcriptase inhibitor, PI: protease inhibitor, INSTI: integrase strand transfer inhibitor.

Conclusions

In this study, switching ART regimens, in patients with sustained virological suppression, commonly included off-label ARV, and resulted in reduction of pill burden and dosing frequency.

ESP16-0264
09. S - HIV/AIDS

EARLY DIAGNOSIS OF HIV INFECTION IN PEDIATRIC PATIENTS: STILL A CHALLENGE IN MALABO, EQUATORIAL GUINEA

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Background

This study describes the HIV infected pediatric population at diagnosis in Malabo (Equatorial Guinea), investigates the existence of early diagnosis improvement, and analyzes the correlation between clinical aspects and advanced disease.

Methods

A retrospective cross-sectional study was carried out using Hospital Regional de Malabo's 2006 to 2015 registered data of HIV infected children under 15 years. Two cohorts were compared, before and after exclusive pediatric HIV consultation establishment.

Results

127 children were registered. Male: female ratio was 1.35:1, median age was 74 months (IQR: 26-114). About 72.7% presented with advanced clinical stages (III or IV WHO stages), 28.1% were severely immunosuppressed and 42.3% malnourished. The most common symptoms were lymphadenopathy (75.6%) and diarrhea (71.1%). Among children with available data, the most frequent mode of transmission was mother-to-child (90.9%), whereas through blood transfusion happened in 9.1%.

The comparison between the two cohorts showed that more children were diagnosed in outpatient clinics (16.7% vs 33.3%; p=0.031) and more nutritional data were registered (27.7% vs 49.4%; p=0.024) in the second period. Nevertheless, there were no significant changes in the age, advanced disease or malnutrition prevalence at diagnosis.

Analyzing the correlation between clinical aspects and advanced disease we noticed that there was a significant association with diarrhea (p=0.003) but not with lymphadenopathy, besides all malnourished children presented with advanced disease (p<0.001). 19.4% of children were both severely immunosuppressed and malnourished whereas 69.6% were neither (p=0.043).

Conclusions

Pediatric HIV diagnosis is still behind-the-time in Malabo, as a high percentage of children are diagnosed with advanced disease. Moreover, this situation has not improved over time. Concurrently, we observed a strong association between nutritional status and both severe immunosuppression (p=0.043) and advanced disease (p<0.001), fact consistent with findings in literature.

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Clinical Trial Registration (Please input N/A if not registered)

ESP16-0217
09. S - HIV/AIDS

SCHOOLING ON CHILDREN INFECTED WITH HIV
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Title of Case(s)

Schooling on children infected with HIV

Background

Introduction.

Human immunodeficiency virus (HIV) can be acquired through vertical transmission. In Uruguay, due to the improvement of high efficiency treatments it has declined since 1990 to today. However, it has become a chronic disease affecting the schooling of individuals with an impact on the development of capacities.

Objective.

To describe the educational level of patients, to make a diagnosis of the problem and to develop strategies to improve it.

Case Presentation Summary

Methodology

Descriptive cross-sectional study with patients 4 to 17 years that received medical assistance at the National Reference Pediatric Center for HIV-AIDS. The study excluded patients with mental retardation. The data source was the review of medical records. Patients verbal consents were obtained. The variables studied: age, sex, origin, presence of orphans, education, repetition of years, school abandonment and probable causes, and adherence to treatment. They were used medians and percentages**Learning Points/Discussion**

Results

The cases included : 80 patients; median age 12 years; 40 were orphans of which 24 live with at least a family relative, 9 were adopted and 7 institutionalized. The educational level was adequate in 34 (42.5%). Of the remaining 46, 34 repeated one or more years, 11 abandoned and 1 was not enrolled. The most common cause of repeated underperformance was multifactorial absenteeism. Of the total, 54 (67.5%) had good adherence to treatment but did not provide adequate schooling association with the same. Instead, maternal orphanhood was associated with poor schooling .

Conclusions

The situation is alarming. More than half of the children have education problems although the disease control is appropriate. The presence of the mother helps children to maintain good schooling. Measurements to support families should be implemented

ESP16-1046
09. S - HIV/AIDS

DOLUTEGRAVIR IN BREASTMILK AND MATERNAL AND INFANT PLASMA DURING BREASTFEEDING

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Background

In the developing world WHO recommends exclusive breastfeeding for infants of HIV positive mothers, because formula feeding is associated with high infant mortality. Clinical trials demonstrated efficacy of combination antiretroviral therapy (cART) during pregnancy to reduce the rate of mother-to-child-transmission (MTCT). Drug transfer via breastmilk appears to be quantitatively important. Dolutegravir (DTG) in combination with a variable backbone is becoming the first-line antiretroviral but safety and PK data in lactating women and breastfed infants are not available.

Methods

We measured DTG levels in plasma and breastmilk of a 35 year old HIV-positive mother (HIV1-subtype CRF01_AE, CDC A1, CD4+ nadir 432/µl), treated with darunavir/ritonavir plus TDF/FTC during pregnancy, who switched to single-tablet DTG/ABC/3TC after delivery and continued breastfeeding against all medical expert advice. We also quantified plasma samples of her healthy baby girl at different time points. Furthermore, free and cell-bound HIV-DNA and proviral-DNA in breastmilk samples were analyzed.

Results

The DTG plasma concentration of the mother 10.75 hours after dosing was 4.48 mg/L which was rather high compared to available adult PK data. Corresponding DTG concentration in breastmilk was 0.10 mg/L. DTG plasma concentration of the breastfed infant appeared to be constantly low around the proposed target trough concentration in treatment naive patients (0.10 mg/L). HIV-DNA in plasma was below detection limit in the mother and infant until today. Free and proviral DNA in breastmilk demonstrated ongoing risk of infection.

Conclusions

DTG was transfered via breastmilk into the infant and reached low plasma levels. More safety, PK and resistance data of DTG during pregnany must be analyzed in the years to come.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0769
09. S - HIV/AIDS

FUNCTIONAL STATUS OF CHILDREN WITH HIV ENCEPHALOPATHY AND BILATERAL LOWER LIMB SPASTICITY

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Background

HIV encephalopathy (HIVE) is the most common neurological manifestation of HIV in children and diagnosis may include bilateral lower limb (BLL) spasticity. Little is known about functional limitations in this population. Therefore, the first aim of the study was to describe gross motor function in children with BLL spasticity due to HIVE. The second aim was to investigate the association between the child's age, CD4% and viral load (VL) at antiretroviral therapy (ART) initiation and current gross motor function.

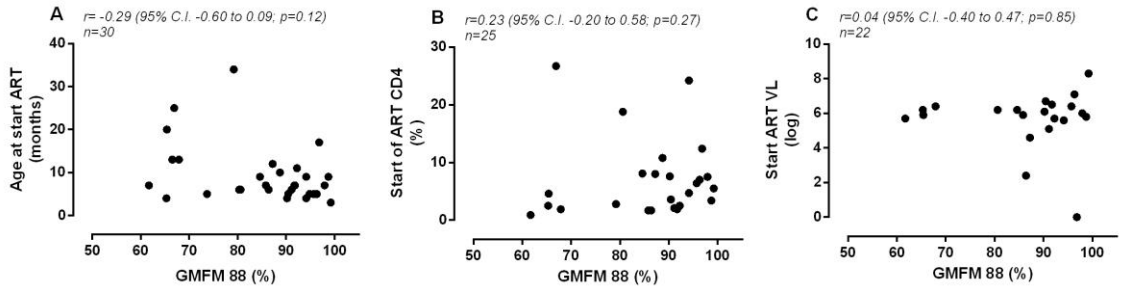
Methods

Thirty ambulant children with HIVE and BLL spasticity, between 5 and 12 years old, were recruited from HIV and Neurology services in Cape Town, South Africa. Demographic and clinical information was obtained from medical records. Gross motor function was assessed using the 88-item Gross Motor Function Measure (GMFM). Associations between start of ART- and GMFM- outcomes were investigated using Spearman's correlations.

Results

Fourteen boys and 16 girls (mean age [SD]: 8y8mo [2y2mo]) participated in the study. ART was initiated at a median age of 7 months [IQR 5 to 11 months] with a median CD4% of 4.7% [IQR 2.3-8.0%] and VL of log 6.0 [IQR 5.6-6.4]. There was substantial variation in total GMFM scores (Figure 1), which arose primarily from variation in the "Standing" domain (26-97%) and "Walking, Running and Jumping" domain (8-99%). There was no significant association

between start of ART- age, CD4% or VL and total GMFM score in this cohort (Figure 1).



Conclusions

Limitations in gross motor function in children with HIVE and BLL spasticity range from mild to severe. In this cohort, the current functional status did not appear to be related to age, CD4% or VL at the start of ART.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0765
09. S - HIV/AIDS

RALTEGRAVIR IN HIV-INFECTED WOMEN DURING PREGNANCY: SAFETY AND EFFECTIVENESS

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Background

Raltegravir (RAL)-containing cART might be important when a rapid decline of HIV RNA is needed or as a salvage strategy. We describe the use of RAL in HIV-infected pregnant women.

Methods

Cross-sectional study within the Madrid Cohort of HIV-infected pregnant women that included women on RAL during gestation (2007-March 2015). The safety and efficacy of RAL during pregnancy was estimated.

Results

Since RAL became available in 2007, 24/1234(1,9%) women registered in the Madrid Cohort were on treatment with RAL-containing cART. Four women were already on RAL before pregnancy: one due to suboptimal VL suppression (SO) and one due to an allergic reaction to the previous therapy, both continued with RAL throughout the entire pregnancy; for the other two patients, the indication for RAL was ART intensification (INT), which was discontinued during the second and third trimester of pregnancy. Among women who initiated RAL during pregnancy, the indications were late presentation in pregnancy (<14 weeks before delivery) with high viremia (n=11), SO(n=2) and INT(n=7), being the median gestational age at initiation 34[22-36] weeks. The overall median exposure duration to RAL during gestation was 44[18-169] days and 6 women received RAL for<2weeks. Tolerance to RAL was good and no side effects were reported. At the time of delivery, 17/20 women presented HIV-RNA<1000cop/mL, 9 of which were HIV-RNA suppressed(<40cop/mL). C-section was performed in 16(66.7%) women and 3 deliveries were preterm. Post exposure prophylaxis based on triple therapy was prescribed to 13 newborns. There were no cases of HIV vertical transmission.

Conclusions

RAL was well tolerated during pregnancy in our cohort. RAL-containing cART may be considered in pregnant women in a high risk situation for the prevention of mother-to-child transmission.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0854
09. S - HIV/AIDS

CHARACTERISTICS OF HIV-INFECTED CHILDREN BORN ABROAD THAT HAVE ARRIVED TO SPAIN FROM 2004 TO 2013

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Background

In recent years, HIV-infected children and adolescents from abroad have had clinical visits in Spain. Our aim was to describe the characteristics among patients that have arrived to our country (2004-2013).

Methods

The study included patients registered in the National Cohort of HIV-infected Children (CoRISpe) that were born abroad and settled in Spain (2004-2013). Patients could have been diagnosed with HIV in Spain (ND) or in their home country (PD). Epidemiological, clinical and HIV-related characteristics were analysed in their first and last registered (December 2014) clinical visits.

Results

During the 2004-2013 period, 280 patients were registered in CoRISpe, 136(48.6%) were foreign (86 (63.2%) ND and 50 (36.8%) PD). ND patients were mainly from sub-Saharan Africa (70,9%) while PD patients came from Central and South America (42%). Among PD patients, perinatal acquired HIV infection was more frequent (88% *vs.* 70%). During the first clinical visit, ND patients were younger: 3.6[2.1-6.8] vs. 7.4[4.3-10.9] years of age, had a worse clinical condition (28.3% vs. 15.9% were on stage C) and lower %CD4: 18[9-24.8] vs. 28[21-36]. Within the ND patients, pulmonary tuberculosis was observed in 7 children and 3 were diagnosed with extra pulmonary tuberculosis. Lost to follow up was more frequent in the ND group (32.6% *vs.* 12%). During the last registered clinical visit, most patients in care that were receiving antiretroviral treatment had supressed viremia: 79% within the ND group and 94.6% PD patients and all had a good immunological condition.

Conclusions

Nearly half of the patients registered in CoRISpe (2004-2013) were foreign. Although during the first clinical visit ND patients had a worse clinical and immunological condition, nowadays both groups of patients present a good control of the HIV infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0865
09. S - HIV/AIDS

CLINICAL, IMMUNOLOGICAL AND SOCIAL FEATURES OF A COHORT OF ADOLESCENTS AND YOUNG ADULTS WITH HIV INFECTION

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Background

Some adolescents and young adults with HIV infection acquired during childhood, are followed up by paediatricians in some hospitals. Our main objective is to study the clinical, immunological and social features of adolescents and young adults followed up by paediatricians.

Methods

Retrospective cross-sectional study that includes young people with HIV infection, whose age is between 16 and 25 and that were followed up by the Paediatrics Department in a tertiary Hospital until November 2015. Data collection obtained from medical records and last clinical control.

Results

28 patients were included, 17 of them were women (61%). The median age was 22.3 years (IQR18.6-23.6). 86% were Caucasian (14% were from South America). 93% of them had been infected through vertical transmission (19% have HIV encephalopathy). Last medical consultation: CD4 average count: 620/mm3 (IQR 439-771.7), having 64% of them a viral load <50cop/ml. 96% of the patients were on antiretroviral therapy: 80% once daily and 52% in single tablet combination, being RPV/TDF/FTC the most frequent combination (54%): 68% have good adherence. Side effects: 21% lipodistrophy, 28% hyperlipidaemia. Employment status: 46%-studying, 29%-working and 21%-unemployed. Those who are studying: 54% continues studying after the compulsory phase and 11% studies in an adult school. 25% have left school without graduating**.** Half of them are in a relationship and one of the patients is pregnant.

Conclusions

The number of patients with detectable viral load is still high and the main predisposing factor is the bad adherence. In addition, a significant percentage have HIV encephalopathy. The social status of these patients is very worrying because there is a large number without the school graduate that, coupled with the lack of employment, represents a risk in their final passage to adulthood.

ESP16-0075
09. S - HIV/AIDS

TRENDS IN HOSPITAL ADMISSIONS IN PATIENTS WITH ANY LISTED DIAGNOSIS OF HIV IN IRISH HOSPITALS: 2010 TO 2014

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Background

The number of HIV notifications in Ireland increased in 2014 to 8.2 per 100,000 population having previously been stable at 7-7.5 per 100,000 from 2010 to 2013. This study aims to evaluate trends in Irish hospital admissions in adult and paediatric patients with any listed diagnosis of HIV from 2010-2014.

Methods

The Hospital Inpatient Enquiry System was evaluated from 57 Irish hospitals from 2010-2014 for patients admitted with any listed diagnosis of HIV. Data recorded included diagnosis, age distribution, and discharge outcome. Trends were examined using logistic regression analysis.

Results

From 2010-2014 there were 3901 admissions with a discharge diagnosis of HIV. This did not increase significantly from 2010 to 2014 ($r2= 0.05$, $p=0.69$). Of the total admissions 2857 (73.2%) were inpatient admissions and 1044 (26.8%) were day case. The number of inpatient admissions significantly decreased from 2010-2014 from 658 to 493 ($r2=0.9$, $p=0.008$). Day case admissions increased numerically from 69 to 229 however this was not found to be statistically significant ($r2= 0.3$, $p=0.2$). There were 50 admissions in the <15 year age group with an average of 10/year. This represents 1.2% of all admissions and did not significantly increase from 2010-2014 ($r2=0.3$, $p=0.3$). The most common diagnosis at discharge was HIV followed by dialysis and infectious disease.

Conclusions

The number of admissions among HIV affected patients has not significantly increased in Ireland from 2010-2014. The paediatric population represents just 1.2% of all HIV associated hospital admissions. The relative contribution of inpatient admissions to total admissions from 2010-2014 has decreased as day case admissions have numerically increased. Trends in discharge diagnosis reflect European trends in that HIV related illnesses, renal, infectious and respiratory disease are among the most common discharge diagnoses.

ESP16-0323
09. S - HIV/AIDS

METABOLIC SYNDROME IN CHILDREN AND ADOLESCENTS LIVING WITH HIV

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Background

Metabolic syndrome (MetS) is considered an independent risk factor for developing cardiovascular disease. It is well-known that the prevalence of metabolic disorders have increased in pediatric HIV-infected children.

Methods

A cross-sectional multicenter study in 152 patients from the pediatric cohort of the Spanish AIDS Research Network (CoRISpe) was performed. MetS was defined according to the new International Diabetes Federation (IDF) diagnostic criteria and the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria. Measurements included anthropometry, waist circumference, blood pressure, fasting lipids, glucose and insulin, and lipodystrophy assessment. Demographic, clinical, immunological, virological, and antiretroviral therapy data were obtained from the Network database.

Results

An abnormally low HDL-cholesterol level was the most prevalent disturbance (21.05%) found. Three patients met IDF criteria for MetS (1.97%), and MetS was significantly associated with lipohypertrophy (p=0.029) in the analysis. When the modified NCEP-ATP III criteria were used, the prevalence of MetS was 5.92% (9 patients), and MetS was significantly associated with Tanner stage ≥2 (p=0.041), lipohypertrophy (p=0.001), and higher *z*-scores for weight and body mass index (p=0.002 and p<0.001). Insulin resistance was observed in 17 patients

(11.18%) and was associated with MetS (as per the modified NCEP-ATP III criteria) (p=0.03) and lower HDL-cholesterol values (p=0.036).

Conclusions

The prevalence of MetS in our cohort was 1.97% (IDF) or 5.92% (NCEP-ATP III), depending on the diagnostic criteria used. MetS should be actively assessed, particularly in children or adolescents who show lipohypertrophy.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0608
09. S - HIV/AIDS

A MOVIE AGAINST QUACKS, TOGO

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Background

Located in Anèho, “ASSISTANCE CONSEIL” and “UNIS POUR LE DEVELOPPEMENT” caution HIV/AIDS infected people on the dangers that psychic healers, charlatans, imposters or the pseudo-religious, without scruples, represent. The association urges PLWHA to be wary of the doubtful practices of the pseudo-healers who in addition to swindling them to the last penny wreck much more their health state than they really give it any treatment. A newly-tracked down seropositive without exception, is vulnerable to false promises of healing from charlatans and quacks. This vulnerability doesn’t depend on the social or the intellectual levels. Their motivation lies in the search for instantaneous healing.

Methods

These associations produced a film that relates the story of an HIV positive young woman, who, soon after being informed about her seropositivity, threw herself into a frantic, restless and expensive race for miraculous remedies, lured by the false promises of gurus in the money-hunt.

Sixty-five sketches on this movie entitled “LES PROPHETES ET LE SIDA”, which translates in English as “THE PROPHETS AND AIDS”, has been staged throughout the country. The distribution video-cds is assured by the association, ASSISTANCE CONSEIL.

Results

This film has helped a great deal PLWHA to adjust and to turn to HIV/AIDS care-giving associations. The seropositive persons now rely on care-giving associations.

Conclusions

We are calling on national and international outfits to encourage good and right actions that can help PLWHA to come back to the right track as far as their health-care is concerned.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESP16-0589
09. S - HIV/AIDS

SOLUBLE FAS RECEPTOR (CD95) IN HIV-INFECTED CHILDREN WITH IMMUNOSUPPRESSION

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Background

Soluble Fas receptor (sFas) competes with membrane-bound Fas receptor for binding to Fas ligand (FasL), thereby downregulating FasL-mediated cell apoptosis.

Aim was to evaluate serum levels of sFas in HIV-infected children with different immune status.

Methods

22 HIV-infected children (8 female, 14 male, median age 7 (3.5-9) years) and 61 adults non-adherent to antiretroviral therapy with CD4<25% (<500 cells/mL for those >6 years old) were observed in Gomel Regional Infectious Diseases Hospital, Belarus, during 2010-2012.

We assessed serum levels of sFas by ELISA in-house test by determining the optical density (OD). OD ≥0.2 units was considered as 'high level of sFas' based on results of testing of 46 healthy donors.

Results

High levels of sFas were detected only in patients with advanced and severe immunodeficiency (by WHO classification, in CD4<20% or <350 cells/mL). Rates of detection of high levels of sFas did not differ in children and adults (54.5% vs. 50.8%, p=0.458) and did not dependent on sex in both groups (p>0.05).

High levels of sFas correlate with lower CD4 lymphocytes levels (Spearman R= -0.47, p<0.001) and with higher clinical stage of HIV-infection (Spearman R=0.38, p=0.005).

Conclusions

High levels of sFas were detected in advanced and severe immunodeficiency, and correlate with CD4 lymphocytes levels and clinical stage of HIV-infection. We can suggest that high levels of sFas in HIV-infected children protect CD4 lymphocytes from apoptosis in case of significant reducing of their number in disease progression, and made possible for a child to respond to pathogens with clinical symptoms of infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0048
09. S - HIV/AIDS

HERBAL MEDICINE TODAY: CLINICAL AND RESEARCH ISSUES

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Title of Case(s)

Herbal Medicine Today: Clinical and Research Issues

M

Author Name : **Dr Mohammed Taqee Ansari**

Background

Demonstrate our indigenous medicines that are made by 1000 years old Herbal & Ayurvedic medicines practicing field in the spectrum of finding remedies for Asthma, Tuberculosis, Cancer and various other ailments.

Allopathic practitioners in India are outnumbered by practitioners of traditional Indian medicine and homeopathy (TIMH), which is used by up to two-thirds of its population to help meet primary health care needs, particularly in rural areas. India has an estimated 2.5 million HIV infected persons. However, little is known about TIMH use, safety or efficacy in HIV/AIDS management in India, which has one of the largest indigenous medical systems in the world.**Case Presentation Summary**

The purpose of this review was to assess the quality of peer-reviewed, published literature on TIMH for HIV/AIDS care and treatment. Of 206 original articles reviewed, 21 laboratory studies, 17 clinical studies, and 6 previous reviews of the literature were identified that covered at least one system of TIMH, which

includes Ayurveda, Unani medicine, Siddha medicine, homeopathy, yoga and naturopathy. Most studies examined either Ayurvedic or homeopathic treatments. Only 4 of these studies were randomized controlled trials, and only 10 were published in MEDLINE-indexed journals.

Learning Points/Discussion

Overall, the studies reported positive effects and even "cure" and reversal of HIV infection, but frequent methodological flaws call into question their internal and external validity. Common reasons for poor quality included small sample sizes, high drop-out rates, design flaws such as selection of inappropriate or weak outcome measures, flaws in statistical analysis, and reporting flaws such as lack of details on products and their standardization, poor or no description of randomization, and incomplete reporting of study results.

ESP16-0207
09. S - HIV/AIDS

INSIDE INTO HIV-1 ACQUISITION THROUGH MOTHER TO CHILD TRANSMISSION: CASE OF TWINS

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Background

Mother to child transmission of HIV is still fueling pediatric HIV infection. Previous studies have identified some factors that may explain susceptibility or resistance of HIV infection in children; like the order of delivery in twins, the sex of the baby…

Methods

We analyzed the association between mother-to-child transmission (MTCT) of human immunodeficiency virus type 1 (HIV-1) and type of twin sets, to test the hypothesis that transmission varies according to the type of twins' sets. A retrospective study was carried out on 161 twins sets registered for early infant diagnosis of HIV programme.

These 161 sets of twins were further grouped according to the sex of the babies in the twin sets as follow: female-female (63), male-male (45) and male-female (53). The rate of positivity was calculated according to the type of twins' sets.

Results

Baby born first or second in a twin set have equal chance of been infected by HIV-1, $p = 1$.

According to the type of twins' sets, there were more HIV infected children in the male-female couples compared to the other two types of couples; $P = 0.037$.

Also, we found out that girls were more infected in the male-female pairs than in the couples of female-female, $p = 0.043$; meanwhile the infectivity of boys did not depend on the type of twins' sets $p = 0.103$. But in the male-female twins' sets, girls and boys have the same chance of been infected, $p = 0.696$.

Mechanisms underlying these associations of type of twins' sets with MTCT should be further investigated.

Conclusions

Interventions to decrease MTCT of HIV through family planning and regular pre natal consultation should be re-enforced, especially for twin pregnancy.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0627
09. S - HIV/AIDS

ADAPTATIVE STRATEGIES IN HIV CLINIC ORGANIZED BY A SPANISH NGO IN LAMU (KENYA)

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Background

Since 2008 an HIV clinic is running in Pablo Horstman Anidan Hospital. The loss of patients and poor adherence called for restructuring.

Logistics, government health policies, language and a religious cultural and economical gaps are issues which make adherence and follow-up hard to manage.

Our main objective is to analyze impact in number of patients being followed up after adaptive strategies were implemented in 2013 in our HIV clinic.

Methods

Our strategies are based on making local people part of their own health care project:

- Training and updating of local staff on pediatric HIV.
- Individual and group Psychological counseling focused destigmatizing HIV.
- Outreach visits to remote areas with HIV tests as an active search of new diagnosis.
- Adaptation of International HIV Guidelines to the National ones.
- Mother-Child follow up.
- Supportive family services by Social Worker follow up.

Results

Progressive increase in the number of new diagnosis and patients being followed up. (Graph1 and 2)

- 2013: Total patients 37; 10 exposed babies and 27 infected.

- 2014: Total 41;, 8 exposed y 33 infected.

- 2015: Total 53.

o 10 exposed babies

o 43 infected

§ 26 pediatric patients: Mean 8.6 years, [2 – 17]

o 17 adults

§ 9 caretakers: Mean de 30 years, [17 – 40 years].

· 50% followed from 2014

· 40% from 2015

Conclusions

The increase of new diagnosis and follow ups is consequence of the strategies implemented, being that no significant changes in HIV prevalence have been registered that may justify our results.

Having well trained Local staff, active search of new cases, health education and psychological and social support are key issues.

ESP16-1036
09. S - HIV/AIDS

TRANSITIONING ADOLESCENTS WITH VERTICALLY ACQUIRED HIV-1 INFECTION TO ADULT CARE IN SPAIN (FARO PROJECT): CHARACTERISTICS AND PERFORMANCE OF PEDIATRICIANS AND ADULT CARE PHYSICIANS

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Background

Transitioning adolescents with vertically acquired HIV-1 infection to adult care poses significant challenges. As part of the FARO project, we describe the characteristics and clinical performance of the involved pediatricians and adult care physicians who participate in the Cohort of the Spanish Paediatric HIV Network (CoRISpe).

Methods

An online questionnaire based on common recommendations for a successful transition was sent to the 20 pediatricians (21 items) and 36 adult care physicians (19 items) participating in the CoRISpe.

Results

Pediatricians (response rate: 80%) transferred a median of 15.5 [4-20] HIV-1 patients. Clinical appointments were set every 3.5 [3-4] months. 50% worked in general pediatrics, 50% in infectious diseases units. 43.8% worked within adequate multidisciplinary teams. 81.3% established individualized transition plans. Their assessment of nonclinical needs ranged from 75% to 37.5%. 6.3% prepared transition with at least two years in advance. 6.3% evaluated the process. Pediatricians' average overall performance was 51.8%. A relationship between a broader experience and a better performance was found ($p = 0.03$).

Adult care physicians (response rate: 62.8%) received a median of 6 [3-10] HIV-1 patients. Clinical appointments were set every 6 [4-6] months. 9.1% worked in internal medicine, 90.9% in infectious diseases or HIV units. 18.2% worked within adequate multidisciplinary teams. 63.6% used an individualized transition plan. Half met the patient in the pediatric unit. Their assessment of nonclinical needs ranged from 68.2% to 45.5%. 4.5% evaluated the process. Their average overall performance was 48.8%. The relationship between a broader experience and better performance was no significant ($p = 0.07$).

Conclusions

Professional performance during transition varies widely both among pediatricians and adult care physicians. There are relevant areas for improvement in both cases.

ESP16-0745
09. S - HIV/AIDS

INTERNATIONAL COOPERATION FOR TRAINING IN PEDIATRIC INFECTIOUS DISEASES IN RESOURCE LIMITED SETTINGS: THE ESTHER-SPAIN PROJECT

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Background

The ESTHER- Spain project was launched in 2007 as a collaborative initiative between the Spanish Ministry of Health and the Spanish Society for Pediatric Infectious Diseases (SEIP), integrated into the European ESTHER initiative. The main objective was to offer training in management of pediatric HIV infection to pediatricians in resource-limited-settings.

Methods

The ESTHER- Spain project allowed to launch seven training teams, all of them including a Specialist in Paediatric Infectious Diseases, who travelled to different countries in Latin America in order to offer theoretical and practical training in secondary and tertiary care hospitals. Trainees would then complete their formation during a stay at the participating Spanish Hospitals. Simultaneously, an online Master degree was started and offered for free for all professionals, in collaboration with Rey Juan Carlos I University.

Results

To date, three editions of onsite training courses have taken place in each of the seven participating countries between 2007-2011. In 2011, 461 professionals attended the onsite courses, and 18 completed the trainer of trainers course. From 2009, the Master degree for distance learning is ongoing, with 1800 teaching hours including theory lessons, case rounds and a Research Project and Masters dissertation, with a mean of 180 students per year. On top of improving clinical management, the ESTHER initiative has generated a network of local trainers, has launched the creation of National Cohorts of HIV-infected children in many countries, and has pushed forward the implementation of PMTCT and National Guidelines.

Conclusions

The ESTHER- Spain collaborative project has significantly improved the training of pediatricians in Latin America, decreasing MTCT and improving the management of ART and opportunistic infections. Training strategies in resource-limited-settings should be a priority for medical societies and European Institutions.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0631
09. S - HIV/AIDS

EFFECT OF A NUTRITIONAL INTERVENTION ON THE INTESTINAL MICROBIOTA OF VERTICALLY HIV-INFECTED CHILDREN

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Background

Recent studies have confirmed a microbial gut dysbiosis in HIV adults on antiretroviral therapy (ART) that correlates with chronic bacterial translocation and systemic inflammation. Changes in microbial communities in vertically HIV-infected children, whose immune system has developed in the presence of the virus and bacterial products from the impaired gut, remain unexplored. We aim to characterize the intestinal microbiota of HIV-infected children compared to healthy children, and to modulate it using a nutritional supplement.

Methods

Pilot, double blind, randomized placebo-controlled study including HIV-infected children receiving a pre/probiotic supplement. DNA was extracted at baseline and after a 4-week intervention from stool samples and 16S rRNA gene amplicons were pyrosequenced. The sequences were analyzed using the Qiime pipeline. Bacterial biomarkers were identified using the LEfSe Biomarker discovery tool. Uninfected siblings were recruited as controls.

Results

22 HIV-infected children completed the follow-up, and were compared to 11 controls. Mean age was 11.4±3.4, 8 (32%) were male. All were on ART and had VL<50/ml. Their microbiota showed reduced alpha diversity compared to controls (P=0.042) and distinct composition at the genus level (Adonis P=0.042). Patients showed decreased abundance of commensals Faecalibacterium and Lachnospira and increase of the pathogenic Fusobacterium but not imbalance of Prevotella trade-off, as observed in adults. After the intervention, changes between the microbiota of cases and controls were non-significant and an increase of the butyrate producers Faecalibacterium and Butyricicoccus was documented.

Conclusions

VerticalHIV infection is characterized by intestinal dysbiosis despite ART, but the abnormalities at the compositional level are distinct to the ones observed in adults. Although not fully effective to restore the microbiota, a short intervention with pre/probiotics attenuated

bacterial dysbiosis, increasing butyrate producing bacteria, which may play an anti-inflammatory role.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0190
09. S - HIV/AIDS

PREDICTORS OF EXCLUSIVE BREASTFEEDING FOR INITIAL THREE MONTHS IN HIV EXPOSED TANZANIA INFANTS, 2004-2007

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Background

HIV prevalence is 5.7 % in Tanzania and yearly about 84,000 pregnant women are diagnosed with HIV infection hence significant population of HIV exposed infants yearly.

Objective: To determine the socio-demographic and biological predictors of exclusive breastfeeding in HIV exposed Tanzanian infants.

Methods

Subjects included in this analysis were 2387 in number and were part of a clinical trail. The socio-demographic factors, biological factors and feeding practices for the infants for the first six months of life were accessed and made used of in the analysis.

P values for comparison of children and mother baseline characteristics for those who completed at least three months of exclusive breastfeeding to those who did not were obtained from chi square for categorical variables and Wilcoxon rank sum test for continuous variables.

All analyses were performed using SAS software version 9.2 (SAS Institute, Cary, NC).

Results

The mothers who were more likely to exclusively breastfeed their children for at least the first three months of life were those who were younger, with higher CD4 counts or not receiving ARVS during pregnancy, and women who had babies with better nutritional status at randomization or HIV positive at baseline were more likely to be breastfeed exclusively for the initial three months of life. These were statistically significant with p value less than 0.05.

Conclusions

The children who were more likely not exclusively breastfeed in the initial three months were those who were of poor nutritional status at randomization and those whose mothers were older and symptomatic of HIV infection, hence this group needs more counseling and follow up care to attain the optimal recommended infant feeding practice in the initial three months of life.

Clinical Trial Registration (Please input N/A if not registered)

NCT 00197730

ESP16-0099
09. S - HIV/AIDS

IDENTIFICATION OF NAÏVE AND MEMORY T CELL SUBSETS IN ANTIRETROVIRAL-TREATED HIV-INFECTED CHILDREN BEFORE AND AFTER IMMUNIZATION

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Background

Patients with human immunodeficiency virus (HIV) infection are generally observed with a decrease of CD4 and an increase of CD8 counts. Most patients are then treated with antiretroviral therapy (ART) and some are given vaccination; however, the influence of the immunization on T cell subsets' distribution remains ambiguous. This study, therefore, focuses on (i) an alteration of naïve, effector, and memory T cell subpopulations from both CD4+ and CD8+ T cells in ART-treated HIV-infected children before and after immunization with influenza A H1N1 2009 vaccine, and (ii) a relationship between the classical CD4 and CD8 counts with each T-cell subset's number.

Methods

Fifty HIV-infected children receiving ART were recruited and injected intramuscularly with influenza A H1N1 2009 vaccine on the day of enrollment (Day 1) and Day 29. Blood samples were collected twice, before and after vaccination. Flow cytometry technique was used to analyze T cell phenotypes.

Results

Only effector CD8+ T cells were significantly reduced after vaccination and other T cell subsets from both CD4+ and CD8+ had no change. Numbers of all T cell subsets in the subjects with controllable viral loads (<40 copies/mL) remained almost the same in those with virologic failure. A good relationship of absolute CD4 count with naïve CD4+ and CD8+ T cells was also found.

Conclusions

It is suggested that viral replication has little impact on dynamic changes of naïve, effector, and memory T-cell subsets in ART-treated HIV-infected children after receiving vaccines. The measurement of CD4 count is useful to predict naïve T-cell level in patients responding to ART.

Clinical Trial Registration (Please input N/A if not registered)

Approval by Institution Review Board (IRB) at the Faculty of Medicine Siriraj Hospital (675/2552(EC2)).

ESP16-0144
09. S - HIV/AIDS

VIROLOGICAL AND IMMUNOLOGICAL OUTCOME OF HIV-1 INFECTED CHILDREN TREATED BEFORE ONE YEAR AND AFTER TWO YEARS OF AGE IN A RESOURCE-LIMITED SETTING OF SOUTH AFRICA

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Background

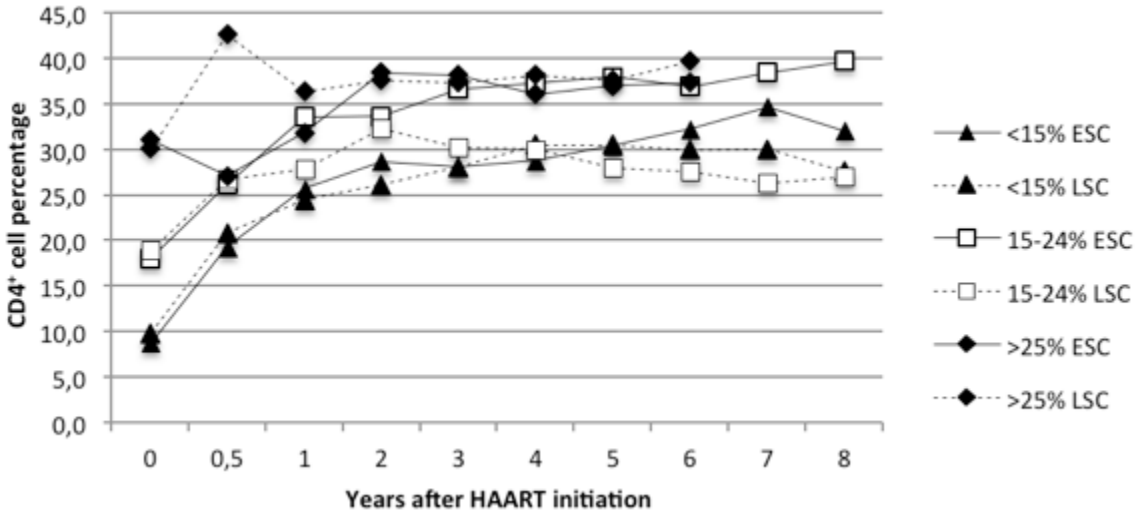
Benefits of early Highly Active AntiRetroviral Therapy (HAART) to reduce infant mortality have been demonstrated in resource-limited and rich settings. However, long-term virological and immunological data collected in Sub-Saharan Africa are scarce. This retrospective study describes the long-term outcome of children who started HAART before 1 year of age (Early Starters Cohort or ESC) and compare their immunological and virological outcomes to children who started their therapy after 2 years of age (Late Starters Cohort or LSC) in KwaZulu-Natal, South Africa.

Methods

Fifty-five children were included in the ESC (mean follow-up period 7.9 years) and 96 children were included in the LSC (mean follow-up period 6.3 years) during their routine visit. Children from the ESC and the LSC were subdivided into three subgroups according to $CD4^+$% at HAART initiation (<15%, between 15-24% and ≥25%).

Results

Disregarding mean $CD4^+$% at HAART initiation, the ESC reached a better immunological outcome six years after treatment initiation. Children with <15% and ≥25% $CD4^+$% at HAART initiation had the same immunological outcome in the ESC and the LSC. Children in the ESC with $CD4^+$% between 15 and 24% at HAART initiation, reached higher $CD4^+$% three years after treatment initiation (picture 1). ESC had a lower proportion of virological failure six years after HAART initiation (p=0.006) and persistent undetectable viral load was more frequent (p=0.008).



Picture 1: Immunological outcome in the three subgroups (<15%, 15-24%, ≥25%) from the both cohorts (ESC, LSC)

Conclusions

HAART appeared highly effective in terms of immunological and virological long-term outcome both in ESC and LSC. However, early starters seemed to have a better immunological outcome when they had intermediate immunosuppression at HAART initiation; they had less virological failures and more sustained virological suppression.

Clinical Trial Registration (Please input N/A if not registered)

B403201215585

ESP16-1023
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

IMPORTED MALARIA: AN 11 YEAR REVIEW

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Background

Malaria it's an endemic disease in most tropical countries. Portugal, a country historically bound to Africa, imports malaria.

Objective: Characterize the cases of malaria in hospitalized patients of a level II hospital in Portugal.

Methods

Retrospectiverevision of all the cases of malaria hospitalized between 2004 and 2015 (11 years). Descriptive analysis using SPSS® version 22.

Results

A total of 30 patients, median age was 8,9 years (max-16y; min-1y) from Angola (12), Guinea Bissau (7), Guiné-Conacri (5), São Tomé e Príncipe (3), Nigeria (1) Senegal (1) and Gâmbia (1). 43,3% were living in Portugal but traveled to endemic regions in the last year. It was a mean of 10,9 days (max-30d; min-2d) from their arrival to Portugal until they came to the emergency. Only one completed chemoprophylaxis. Main symptoms were fever (29), vomiting (19) and headache (13). Most had thrombocytopenia (80%) and anemia (70%). *P. falciparum* was the most identified specie (96,7%), with only one case of *P. malariae.* Mean parasitaemia was 2,6% (max-15%; min-0,1%). 7/30 (23,3%) cases had comorbidities: H1N1 infection, *Salmonella typhi* enteritis, hepatitis B, *Giardiasis,* sickle cell disease, rheumatic cardiopathy, epilepsy and impetigo. 18/30 (60%) children had complications: dehydration (16), altered consciousness (2), severe hypoglycemia (1), hemorrhagic discrasia (1), hyperparasitaemia >10% (2). Seven cases needed intensive care and four had severe malaria (WHO criteria). No patient died. Quinine was used in simple access and quinine with clindamycin/doxycycline in severe malaria. A mean of 5,5 days hospitalized.

Conclusions

The existence of co morbidities should not exclude malaria diagnosis in a patient that returned from an endemic region. The broad clinical presentation of malaria complicates a prompt diagnosis.

ESP16-0920
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

THE PREVALENCES OF PNEUMONIA, MALARIA AND DIARRHOEAL DISEASE IN CHILDREN AGED 0-59 MONTHS IN MANGOCHI, MALAWI

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Background

Reduction of childhood mortality is a millennium development goal. In developing countries, infectious diseases cause most childhood mortality. Malawi has childhood mortality of 67/1000. There is no data on infectious diseases in the community in Malawi. This study aimed to determine the annual prevalence of pneumonia, malaria and diarrhoea and the relationship of these diseases to malnutrition in children aged 0-59 months in Mangochi, Malawi. This work is part of the Mortality Reduction after Oral Azithromycin (MORDOR) study.

Methods

This was a cross-sectional study. 8 villages were randomly selected. Each household in selected villages was visited twice. All children aged 0-59 months that were residents of the villages (registered on a pre-study census) were included. Health passports were examined for pneumonia, malaria or diarrhoea diagnoses in the preceding 12 months. Children were physically examined for malnutrition (following Integrated Management of Childhood Illness guidelines) or current clinical pneumonia.

Results

828 children participated: the median (IQR) age was 27 (13-49) months. The annual prevalence of pneumonia was 32.6% (95% CI 29.3-36.0%), malaria was 70.4% (95% CI 67.0-73.7%) and diarrhoea was 68.1% (95% CI 65.1-71.4%). Acute malnutrition affected 5.3% (95% CI 3.8-6.8%) of children, 32.6% (95% CI 29.5-35.9%) were chronically malnourished and 16.0% (95% CI 13.2-18%) had acute-on-chronic malnutrition. Acute malnutrition (OR 3.06, P=0.02) and acute-on-chronic malnutrition (OR 1.69, P=0.01) were associated with pneumonia. Acute-on-chronic malnutrition (OR 0.96, P=0.03) was protective against malaria. Acute-on-chronic malnutrition (OR 1.94, P=0.04) and chronic malnutrition (OR 1.70, P=0.00) were associated with diarrhoea.

Conclusions

Infectious diseases present a significant burden of disease to healthcare services in Mangochi. Improved prevention of infectious disease is required in this population.

Longitudinal research is needed to confirm the association between malnutrition and infectious diseases.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0386
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

ACUTE CHOLECYSTITIS AS MALARIA PRESENTATION

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Title of Case(s)

ACUTE CHOLECYSTITIS AS MALARIA PRESENTATION

Background

While rare, acute cholecystitis is being increasingly described as an unusual and potentially severe condition associated with malaria, requiring a high clinical suspicion for a early and correct diagnosis and treatment.

Case Presentation Summary

Herein, we present a 4 years-old boy, previously healthy, born in Angola but resident in Portugal since the age of 12 months. He was admitted following five days of high fever, abdominal pain, diarrhea and jaundice. Three weeks prior to the admission, he had been in Luanda (Angola) for a few days. The physical exam revealed pallor, an enlarged spleen and liver, jaundice and tenderness in the upper-right abdominal quadrant. Laboratories studies disclosed anemia (8.4 g/dL), leukocytosis (21 000 /uL), increased inflammatory parameters (CRP 261.9 mg/L), thrombocytopenia (36 000 /uL), and conjugated hyperbilirubinemia (direct bilirubin: 2.06 mg/dL). Abdominal ultrasound confirmed hepatosplenomegaly and showed significant gallbladder wall thickening with biliary sludge content. Considering the recent trip to Angola (a malaria endemic country), a peripheral blood smear was requested and was positive to the presence of *Plasmodium spp* (later confirmed as *P. falciparum*) with a parasitaemia rate of 15-20%. Stool cultures were negative. Presuming the diagnosis of cholecystitis in relation with malaria, antibiotics (ampicillin, gentamicin and metronidazole) and antimalarials (quinine and doxycycline) were started. During the first 24 hours the anemia and thrombocytopenia worsened (6,3 g/dL and 30 000 / uL, respectively) requiring blood and platelet transfusion. Clinical and ultrasound improvement was progressively achieved in the following days.

Learning Points/Discussion

An approach to a patient has to take into account the current context of globalization. In this way, endemic diseases of tropical countries should be considered in the differential diagnosis in European countries.

ESP16-0062
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

COMMON CLINICAL FEATURES IN CHILDREN WITH DENGUE SHOCK SYNDROME IN MYANMAR: A CASE SERIES.

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Title of Case(s)

Common clinical features in children with dengue shock syndrome in Myanmar: a case series

Background

Dengue fever is a relatively common infection in children in the tropics and subtropics. In 2015 there was a significant outbreak of dengue in Myanmar. The aim of this case series is to identify common clinical features in children presenting with dengue shock syndrome (DSS) in Myanmar.

Case Presentation Summary

The medical notes of 26 children presenting with DSS to Mandalay Children's Hospital in Myanmar during September 2015 were reviewed. The mean age was 6 years (range 9 months - 12 years).

The majority of children presented to hospital after 4-5 days of fever and developed DSS after 5 days of fever. Haemorrhagic symptoms included: haematemesis (42%), malaena (35%), petechiae (12%), gum bleeding (8%), epistaxis (4%), haematuria (4%) and bruising (4%).

Other symptoms included: cold clammy extremities (42%), abdominal pain (39%), abdominal distension (27%), respiratory distress (31%), vomiting (19%), loss of appetite (19%), convulsions (19%), irritability (15%), facial puffiness (12%) and restlessness (12%).

Typical laboratory investigation findings included lymphocytosis, thrombocytopenia and a microcytic anaemia.

Medical treatment included the use of paracetamol, ranitidine, phytonadione, oral rehydration solution, normal-saline, dextrose-saline, gelofusine, fresh whole blood, platelets and furosemide.

4 (15%) of the children died from fluid overload, disseminated intravascular coagulation, gastrointestinal haemorrhage and encephalopathy. The mean duration of shock for the surviving 22 children was 6 hours with several having 2-3 recurring episodes of shock before making a full recovery.

Learning Points/Discussion

DSS remains a significant cause of morbidity and mortality in children. Common symptoms included cold clammy extremities, haemorrhage, gastrointestinal symptoms, dyspnoea, and convulsions. Early recognition of dengue warning signs and symptoms with intensive care monitoring and fluid management is key to improving outcome in DSS.

ESP16-0594
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

INCIDENTALLY DIAGNOSED ASYMPTOMATIC PRIMARY HYDATID CYST OF BRAIN

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Title of Case(s)

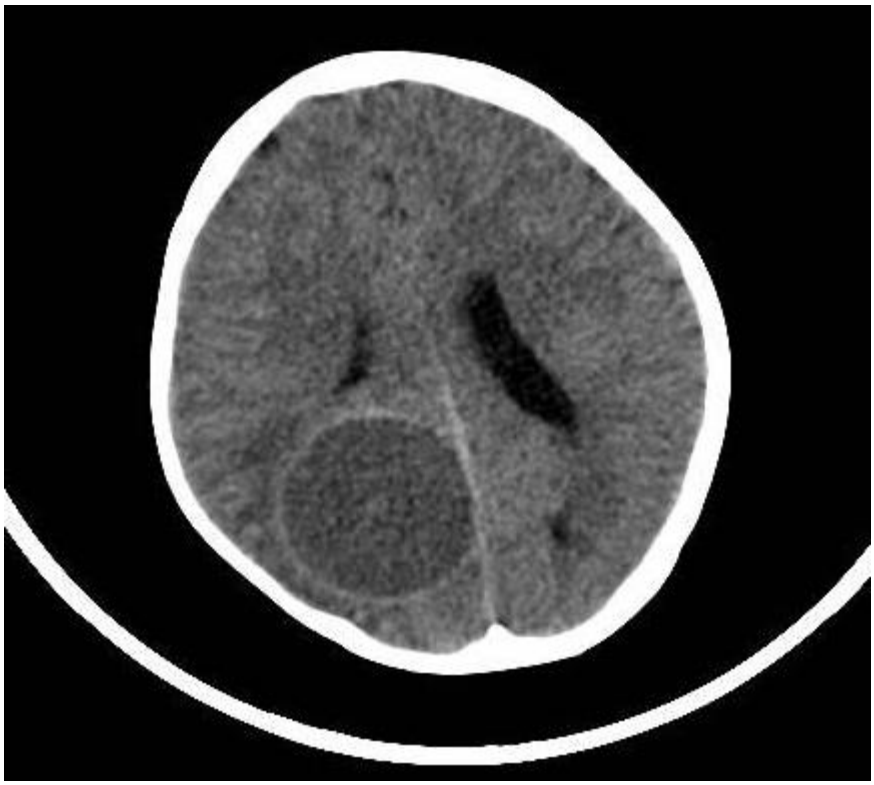
INCIDENTALLY DIAGNOSED ASYMPTOMATIC PRIMARY HYDATID CYST OF BRAIN

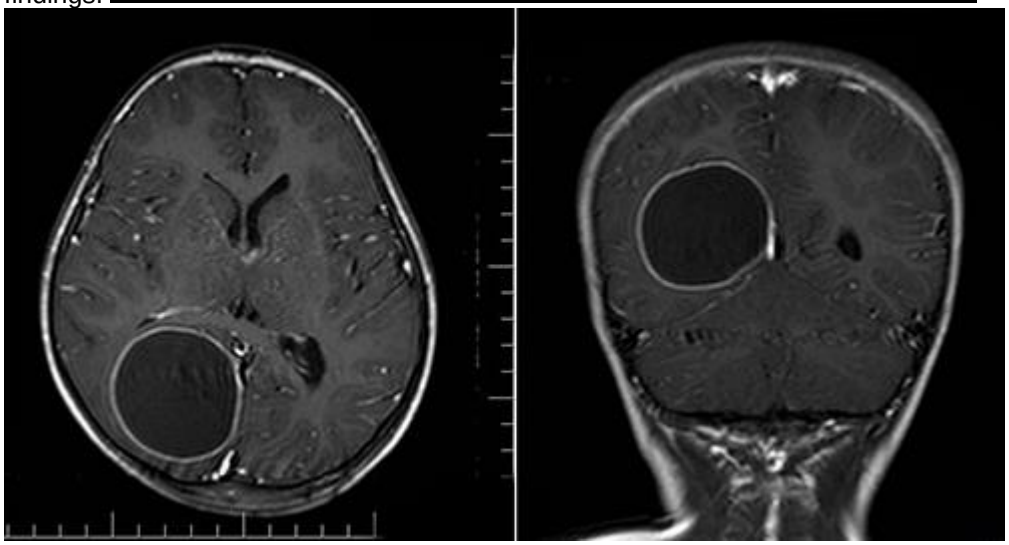
Background

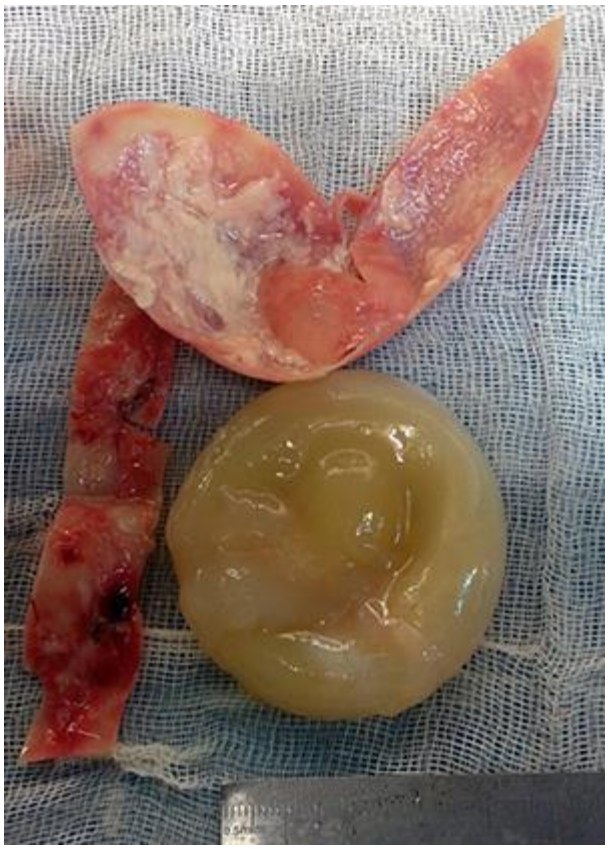
Turkey is an endemic country to hydatid disease. The definite hosts of *echinococcus* are various carnivores, the common being the dog. Neurohydatosis is a rare presentation and primary cerebral involvement is even rarer. Intracranial cases become symptomatic depending on location, size and growth rate of the cyst. This is an interesting case of asymptomatic primary hydatid cyst diagnosed after a traffic accident.

Case Presentation Summary

An 8 year-old boy who was living in countryside, was brought to ER because of vomiting due to head trauma. His neurological examination was normal. CT scan revealed a cystic lesion in right parieto-occipital region with approx. 5 cm diameter **(Image 1).** By cranial MRI large cystic lesion with periferal enhancement was detected **(Image 2**). Indirect hemagglutination was negative. Before surgery, 15 mg/kg/d albendasole treatment was administrated. Further examinations revealed no other involvement in body. Right parieto-occipital craniotomy performed and lesion was totally excised**.** Post-operative recovery was uneventful. In pathological examination, fibrous wall was excised and smooth semi-trasparent hydatid cyst was seen (**Image 3)**. Albendasole treatment was continued. Cranial MRI at the post-op 2nd month revealed no pathological

findings. 





Learning Points/Discussion

Albendasole is the first choice in hydatid disease but the primary treatment of intracranial hydatid cysts is surgery. In endemic countries hydatid cyst presentations may be more various then usual. Primary cerebral hydatid cyst rarely occur in pediatric population and we could not find any reported pediatric asymptomatic primary cerebral case in the literature.

ESP16-0653
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

PEDIATRIC CHAGAS DISEASE AND SCREENING DURING PREGNANCY IN MADRID

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Title of Case(s)

PEDIATRIC CHAGAS DISEASE AND SCREENING DURING PREGNANCY IN MADRID.

Background

Several recommendations for the diagnosis and treatment of pregnant woman-child pairs with Chagas disease (CD) have been published. However, systematic screening is not performed in all the countries which receive people who come from endemic areas. Our aim was to describe the clinical and epidemiological situation of children with CD in Madrid from 2007 to 2014.

Case Presentation Summary

Retrospective multicenter study. We reviewed the medical files of all children (<18 years) with the diagnoses of CD at 8 hospitals in Madrid.

Thirty cases were identified. All mothers came from Latin American, mainly Bolivia (96%). 28% of mothers were diagnosed of CD thank to the screening during pregnancy; 7% had been diagnosed before pregnancy without receiving specific treatment. Seventeen children (57%) were born in Spain. Children at diagnosis were aged from 1 month to 17 years (median: 96 months); 33% of them were less than one year of age. Only a child was symptomatic (*hydrops fetalis*). In 23 children treatment was started but in 2 cases (8%) treatment had to be definitively stopped. The rate of lost to follow up was 47%. Five patient (17%) were considered cured. Vertical transmission was the route of infection for 43%. In the rest of the patients, the type of acquisition was unclear due to the fact that they had lived in endemic areas.

Learning Points/Discussion

Following the screening recommendation, an important number of children were diagnosed under the 1st year of age. In most cases, treatment was well tolerated. It is important to highlight the high percentage of patients lost to follow up and the lost opportunities of planning treatment before pregnancy in mothers who were diagnosed previously.

ESP16-0610
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

THE TOPIC:VISCERAL LEISHMANIASIS IN ALBANIAN CHILDREN ADMITTED IN UNIVERSITY HOSPITAL CENTER OF TIRANA

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Background

The aims of the study: was to show epidemiological data, clinical signs, laboratory features and complications of visceral leishmaniasis in children admitted to University Hospital Center of Tirana from January 2011 to September 2015.

Methods

This was a retrospective study.A total of 1079 children were admitted in this period in our services, of whom 151 or 1.41% were diagnosed with visceral leishmaniasis. The diagnosis was based on bone-marrow microscopy in 126 children or 83, 44% of cases and in 25 cases or 16.56%(where bone marrow microscopy was negative),the diagnose was confirmed by serological test. We analyzed these data: age, gender, geographical and seasonal spread, clinical signs laboratory data and coplications.

Results

All patients were in the age range 0-14 years with a median of 4 years. 90 patients or 61, 6% of them came from urbanized area and the most of them 53(35, 8%) were admitted in the spring. 89 cases or 59% were male and 62 or 41% were female. Fever,pallor and hepatosplenomegalia were present in 100% of cases, weight loss in 98%, vomiting in 14.7%, and diarrhea 35,4%. Laboratory findings were: anemia in 95.4%, neutropenia 100% of cases hypergamaglobulinemia in 70% and thrombocytopenia in 72.18%.Bacterial infections were present in 40% of case as bronchopneumonia ,diarrhea, urinary tract infections and sepsis. 35 % of patients were treated with meglumine antimoniate and 65% of them with liposomal amfotericine B.In 3 cases treated with meglumine antimonate we observed relapses. Mortality was 0

Conclusions

Visceral Leishmanioza in pediatric age is present in a consideration number in Albania.In our country an active surveillance system is necessary, especially as regards diagnosis and fighting of parasitic hosts

ESP16-0237
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

NASAL EXPULSION OF TAENIA SAGINATA IN A 4-YEAR-OLD-BOY

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Title of Case(s)

Nasal Expulsion of *Taenia Saginata* in a 4-Year-Old-Boy

Background

Taenia saginata occurs worldwide, however it emerges mostly in Europe and some parts of Asia. Humans are the only exact hosts for *T. saginata* and carriersare mostly asymptomatic. Sometimes, *T.saginata* proglottids can be detected in the stool which helps to diagnose of the disease and the patients sense these movement pieces.

Case Presentation Summary

A 4-year-old-boy admitted to the hospital with a six-month history of expulsion of moving 4-5 cm length white colored pieces. He was treated with albendazole for few times in different hospitals in history however the symptoms continued. The patient was a routine uncooked sausage eater. At the admission, he weighed 14.5 kg (10-25 percentile) and was 100 cm long (10-25 percentile). The laboratory results showed a white blood cell (WBC) count of 7100/mm^3, hemoglobin level of 11.1 g/dl, platelet count of 320000/mm^3 and eosinophil count of 500/ mm^3. During the investigation, moving pieces were observed, because of the sharp shaped of one pole, we suspect as ascariasis. We transferred the pieces to microbiology department and the pieces were defined as *T.saginata* proglottids. The patient was given a single dose of 1 gr niclosomide. After the antimicrobial therapy, at the same day four tapeworms were passed through intestine which the longest one was nearly 1 meter. The patient recovered and had no repeating symptoms.

Learning Points/Discussion

This kind of nasal expulsion is very rare and because of the sharp shaped of one pole as seen in our patient, it can be interfered as ascariasis. For this reason, microbiological definition is very important in patients whom complaints continues with antimicrobial therapy.

ESP16-0166
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

EVALUATION OF PARASITE DENSITY COUNT FOR MALARIA DIAGNOSIS IN BLOOD FILM EXAMINATION

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Background

Parasite density count for asexual stage of malaria is important for follow up patients after treatment. However, inefficient or unstandardized examination of blood film leads to false negative result and underreport. This study aims to assess parasite density count from thick and thin blood film.

Methods

This study collected 11 thick and 15 thin blood films from PhopPhra Hospital, Tak Province, Thailand during 2015. Venous blood samples were collected at the time of admission to the hospital. Examination of malaria was performed at 100X (oil immersion lens). Thick blood films were count malaria per (WBC) 50, 100, 200, 300, 400, and 500 cells. Thin blood films were count per (RBC) 500, 1,000, 2,000, 3,000, 4,000, and 5,000 cells. The examination was count by 2 Medical Technologists independently and calculates average. For analysis, ratio of malaria per WBC/RBC was compared for each blood count.

Results

The results showed that thin blood films at malaria per RBC 5000 cells was a highest parasite found (ratio 0.78) following by per RBC 500 (ratio 0.62), 1,000(ratio 0.68), 2,000(ratio 0.77), 3,000(ratio 0.74), and 4,000(ratio 0.72) cells, respectively. For thick blood films, at malaria per WBC 100 cells was a highest parasite found (ratio 14.5) following by per WBC 50(13.2), 200(12.9), 300(13.1), 400(12.7), and 500(12.6) cells

Conclusions

The results showed that thin blood films at malaria per RBC 5000 cells was a highest parasite found (ratio 0.78). For thick blood films, at malaria per WBC 100 cells was a highest parasite found (ratio 14.5). This is the first report about assessment of parasite density in thick and thin blood films.

ESP16-0168
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

INCIDENCE OF G6PD DEFICIENCY IN PATIENTS WITH MALARIA

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Background

Glucose-6-phosphate dehydrogenase (G-6-PD) plays a key role in regeneration of NADPH and maintenance of cellular redox balance. G-6-PD deficiency can lead to acute hemolytic disease, anemia, and various complications which can lead to death. Previous studies showed that number of population with G-6-PD deficiency in Thai-Burma border was 13.7% compared to those of Southeast Asian population in non-endemic area such as 3.9 in Cambodian which indicated that population with G-6-PD deficiency has a protective factor for malaria infection. Previous studies showed that malaria cannot infect defected red blood cells to growth.

Methods

This study aimed to determine the incidence of G-6-PD deficiency in malaria patients at medical laboratory, Phop Phra Hospital, Tak Province during 2013-2015 by Fluorescence Spot Test as a screening test.

Results

The results showed 272 patients were infected with malaria. Among these patients, eighteen patients were G-6-PD deficiency (6.6%). This study indicated that population lived in malaria endemic area may develop G-6-PD deficiency which is a protective factor for malaria infection. In addition, data of this study will lead the physician to avoid treatment patients with malaria and G-6-PD deficiency by primaquine, a drug causing hemolysis, which resulting in efficiently treatment of patients with malaria.

Conclusions

This study showed the high prevalence of G6PD deficiency which is health awareness from potential hemolytic reactions due to treatment of malaria by Primaquine. This findings will help to recognize and diagnose malaria related G6PD deficiency as well as identify risk/protective factor and awareness of treatment in endemic area of malaria in Thailand.

ESP16-0081
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

COMPARISON OF HEMOGLOBIN LEVEL BETWEEN MONOINFECTION VERSUS MIXED INFECTION OF SOIL TRANSMITTED HELMINTHS IN SCHOOL AGE CHILDREN

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Background

Soil transmitted helminths infection (STH) is one of major health problem in Indonesia. More than 50% of school age children are infected to either ascaris, trichuris, hookworm or mixed infection. This disease can cause anemia which potentially reduces cognitive, retards their growth and prone to other infection.

Methods

A cross sectional study was done in school-age children in North Sumatera, Indonesia. Kato Katz technique was assessed from stool samples to distinguish soil transmitted helminths to either *A.lumbricoides, T.Trichiura* or hookworm. Complete blood count was done to measure morphology profile. Un-paired ttest and Mann Whitney test were carried out to compare the hemoglobin level and other measurement.

Results

Among 142 children screened, 92 (64.7%) was infected with STH (49 mono infection, 43 mixed infection). Among mixed infection group, 38 children were infected with *A.lumbricoides* + *T. Trichuria* and 3 children were infected with *A.lumbricoides* + *T. Trichuria* + hookworm. Ten children refused their blood to be taken for analysis, with 41 included in each group. Hemoglobin level in mono infection was 13.28gr/dL compared to 12.21gr/dL in mixed infection, p=<0.001. Mean corpuscular volume (MCV) and Mean corpuscular hemoglobin concentration (MCHC) was significantly lower in mixed infection, p=0.03, p=0.02, respectively. Anemia was found in 7 children from mixed infection group compared to none from mono infection group, p=0.012. Microcytic and hypochromic red blood cells were seen from peripheral blood of anemia patients.

Conclusions

Hemoglobin level in children with mixed infection of soil transmitted helminths was lower compared to mono infection. Complete blood count and red blood cells result were consistent with form of iron deficiency anemia.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0512
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

ARE THERE ANY DIFFERENCES BETWEEN INTERNATIONAL ADOPTEES FROM ETHIOPIA VS VIETNAM/INDIA?

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Title of Case(s)

Are there any differences between international adoptees from Ethiopia vs Vietnam/India?

Background

In 2014, 824 children from abroad were adopted by Spanish families. From Asia around 428, with an increasing trend of children from Vietnam/India. From Africa around 92, being mostly Ethiopians.

Methods:
Descriptive retrospective study comparing characteristics at arrival of children from Ethiopia vs India/Vietnam in a Spanish Reference Unit of Tropical Diseases and International Adoption.

Case Presentation Summary

Results:
We analyzed 56 children: 26 Ethiopia, 30 India/Vietnam. Epidemiological, clinical and Tropical-Infectious results are described in table. The three positive serology-tests for HBV were diagnosed two of chronic and one of resolved.

	India-Vietnam N:30	Ethiopia N:26	p
Age: median	35.5months	17months	0.02
Sex: M/F	10/20	19/8	
Previous diagnosis Most prevalent	16 Anemia	13 Diarrhea	

Serology-tests home-country (HIV, HCV, Syphilis, HBV) Positive	19 3(HBV)	24 0	
BCG-scar	20	19	
Tuberculin-skin-test >10mm Positive IGRA-test Considered/treated as latent tuberculosis	3 0 1 (>15mm)	4 2 2	
Nutritional-parameters: Weight <2SD Height <2SD HC <2SD	 7 11 8	 8 10 3	
Symptoms at arrival	27 Respiratory(12/27)	21 Digestive(17/21)	
Blood-tests: Haemoglobin mg/dl: mean±SD Eosinophils >500	 12,35±0,2018 5	 11,70±0,2174 2	 0.036
Serology-tests parasites: *Strongiloides Stercoralis* *Schistosoma* *Toxocara canis*	 2/24 2/23 1/24	 1/19 1/18 1/18	
Stool-testing parasites: Multi-infestation *Entamoeba coli/dispar* *Endolimax nana* *Blastocistis* *Giardia liamblia*	5/30 5/5 3 5 2 2	16/26 5/16 0 2 1 16	

Hymenolepis nana	2	2	

Learning Points/Discussion

Conclusions:

Ethiopian children are younger and mostly boys. Both populations presented similar growth delays. Infectious issues were found in most, especially parasite infections. More children with parasites were identified among Ethiopians, with a strikingly high prevalence of *Giardia lamblia.* Multi-infestation was more prevalent in Asians.

Beyond these differences regarding country of origin, high prevalence of findings among international adoptees is reflected. Thorough nutritional and infectious-tropical checkup at arrival is necessary.

ESP16-0220
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

THE PATHOLOGY OF PLATELET COUNT IN MALARIA- BASIS FOR POLICY ON PLATELET TRANSFUSION

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Background

Background

Malaria is endemic in Mangalore and is showing an increasing trend. Among 475 patients confirmed with malaria in past two years, 20 were children age ranging from 3 months to 15 years (Male: 15 Female 5). Malaria affects all blood components and thrombocytopenia is a frequent complication. The objective was to analyse incidence of thrombocytopenia in children with malaria and to review pathogenesis

Methods

Methods:

Records of all patients treated for malaria (*P.vivax /P.Falciparum* or both) were reviewed. The diagnosis was confirmed by Quantitative buffycoat and peripheral smear. Haematological profile (Haemoglobin, Total WBC count, Platelet count) was retrieved. Severity of thrombocytopenia was graded based on platelet count (mild- 1,40,000- 90,000 cells/µl moderate- 90,000 to 50,000 cells/µl and severe <50,000 cells/µl). Data was analysed using chi square test.

Results

Results:

11 children had *P.vivax*, 3 had *P. Falciparum* and 6 had both. Thrombocytopenia was observed in 15 children (75%) (Mild-4, moderate-6, severe-5). (Chi square-0.06) There was no significant difference in severity between species or when both are present. All patients were treated with first line antimalarial drugs. Children with severe thrombocytopenia were closely monitored and no transfusion was given. The platelet count reverted back to normal after transient period of 2 to 3days. There was no death reported in children.

Conclusions

Conclusions

In view of inherent biological characteristics, *P.vivax* is more difficult to eradicate than *P.Falciparum.* Thrombocytopenia in *P.vivax* is known and incidence in India ranges from 43% to 80%. Immune mediated lysis and sequestration in spleen, oxidative stress damage have been reported as mechanisms. As megakaryocytes are normal and evidence of decreased thrombopoiesis is lacking, thrombocytopenia may be transient. Hence wait and watch policy is required regarding platelet transfusions especially in children.

ESP16-0856
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

INTERNATIONAL PRE-ADOPTION ASSESSMENT: COMMON DISEASES IN ADOPTED CHILDREN AND RELIABILITY OF MEDICAL REPORTS

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Background

Spain is a leading country in International adoption. During the pre-adoption visits we provide parents with information about child´s health and travel advise. The aim of this study is to describe common pathologies in a cohort of internationally adopted children, and to address the reliability of the pre-adoption reports.

Methods

Pre-adoption reports from a Reference Unit for Tropical Diseases January 2012 to June 2014 were reviewed. Data collected included: affiliation, medical background, diagnoses and immunizations. Final adoption was confirmed by telephone.

Results

A total of 263 pre-adoption visits were evaluated, 53% corresponding to girls, aged 2 months to 18 years, coming from: 61% Eastern Europe, 25% Asia, 11% Africa, 3% Latin America. According to 186 available medical reports, 97 (52%) children presented neurological disorders, 30 (16%) malformations, 14 (7.5%) malnutrition, 3 HCV, 3 HBV; 3 tuberculosis, 5 latent tuberculosis, 4 congenital syphilis and 2 HIV.

The adoption was already effective in 118 children, 43 processes were ongoing. In 10 cases the child was not accepted, and in 27 the adoption process was interrupted because of other reasons. 65 children were evaluated after adoption; in 47 cases reports were fully reliable, but 18 resulted inaccurate. Fourteen children showed no pathology at all, despite having different diagnoses in their medical reports, and 4 children presented with diseases previously not diagnosed.

Conclusions

Most international adopted children arriving to Spain come from Eastern Europe and Asia, and medical conditions are common. Pre-adoption reports are generally reliable, and after 70% of pre-adoption visits, the family continues with the adoption process. Pre-adoption advice is recommended in order to ensure that families are aware of the child's health and understand the special needs they are facing, if any.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1051
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

IMPACT OF A PUTSCH ON A MOTHER&CHILD HEALTH CARE CLINIC IN WESTERN AFRICA …. BEHIND THE HEADLINES

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Background

Since 2002 the University Hospital of Brescia, has an ongoing collaboration with the Mother&Child department of the Hospital of the Camillian Fathers in Ouagadougou (HOSCO).

The hospital assists >3800 birth/year and has one of the largest neonatal units with 50 cots. Besides general pediatrics, there is also a large malnutrition-DayHospital and an HIV-service with over 150 children on HAART.

Methods

On September 17th 2015 the country was hit by a coup from the guard regiment of the former president against the transitional government. Trade unions immediately proclaimed an unlimited strike, furthermore, the military enforced a 24/24 curfew.

Most hospitals closed, but the HOSCO stayed open and had to face a significant increase in patients.

Results

During the period from Sept 17-28, 888 women were seen (eight-fold increase). 318 normal births and 107 C-sections were performed (>10 x increase). 41 neonates were hospitalized plus 33 mostly from home deliveries.

From the 72 HIV+ children scheduled for follow-up and pharmacy refill, only 49 were able to come before running out of stock while 23 had an interruption of therapy, which may cause them resistance problems in near future.

Conclusions

All this was made possible as most of the personnel did come to work and stayed there even longer than their shifts. In order to assure safe travel they often were accompanied by ambulances. In addition many Camillian Sisters and Fathers, also those usually not involved with the Hospital, joined forces and some paediatricians even decided to live in the Hospital for the whole period to assure assistance to those in need.

Now, more than 3 months after the putsch, further fall-out becomes evident, as the national ART-distributor is running out of paediatric ARVs and PCR-reagents.

ESP16-0274
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

DISCORDANCES BETWEEN SEROLOGY AND CULTURE FOR STRONGYLOIDES STERCORALIS IN AN ETHIOPIAN ADOPTED CHILD WITH MULTIPLE PARASITIC INFECTIONS

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Title of Case(s)

Discordances between serology and culture for *Strongyloides stercoralis* in an Ethiopian adopted child with multiple parasitic infections

Background

Infectious diseases screening of international adoptees is complex because of the concurrence of different pathogens at same time. We describe an international adopted child born at Ethiopia infected by four different pathogens, two of them *Strongyloides stercoralis* and *Entamoeba histolytica* with a capacity to develop severe clinical complications if not detected promptly with appropriate diagnosis tests.

Case Presentation Summary

A 21-month-old Ethiopian adopted infant was visited at our unit for an initial health screening. Weight (12.4 kg) and height (84 cm) were on p50 according to WHO paediatric growth charts. Skin lesions due to *Molluscum contagiosum*, burns, and scabies were observed. Anaemia, no eosinophilia (472 cells/mm3), and low ferritin level were determined. Serologies for HIV and viral hepatitis were negative. Blood test for malaria and TST for tuberculosis were negative. Parasitological stool exams showed *Hymenolepis nana*, *Trichuris trichiura*, and *Entamoeba* spp. cysts. A feces charcoal culture for *Strongyloides stercoralis* found rhabditiform larvaes. However, serology for *S. stercoralis* was negative. Ivermectin was given with very good response. Stool antigen for *Entamoeba histolytica* was positive and treatment with

metronidazole and paromomycin was given to the child.

Learning Points/Discussion

Eosinophilia determines collection of serial stool samples to rule out intestinal parasitic infection including *S. stercoralis*. However, in our case eosinophilia was absent. Therefore, *S. stercoralis* would not have been detected if we had followed the protocol. Also, discordances between direct and indirect diagnostic methods are not unusual as showed in this case. Different sequencing tests and insistence of the clinician to find out these pathogens was determinant to cure this child preventing potential severe clinical forms in case of immunosuppression.

ESP16-0070
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

TREATMENT OF PEDIATRIC CHAGAS DISEASE - THE AGE-APPROPRIATE 30 MG NIFURTIMOX (NFX) TABLET IS BIOEQUIVALENT TO THE ESTABLISHED 120 MG FORMULATION

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Background

Dosing of NFX in pediatric patients is based on body weight scaling (8 to 30 mg/kg) . In absence of an age-appropriate oral formulation a 120 mg tablet intended for adults is currently used to treat children. This renders dosing - especially in small children - difficult because it requires error-prone measures like tablet breaking. Therefore, an age appropriate pediatric formulation would improve controlling Chagas. We developed a new 30 mg tablet suitable tor children which can also be administered as aqueous slurry .

Methods

We report the results of a single center, randomized, cross over, single dose group comparison study in adult Chagas patients investigating the pharmacokinetics of the 30 mg tablet administered as intact tablet and as aqueous slurry compared to the approved 120 mg tablet. Adult male and female patients diagnosed with chronic Chagas' disease aged 18-45 years were enrolled to receive the following treatments under fed conditions:
Group 1 (n=12) got 4x30mg administered as intact tablet or as a slurry
Group 2 (n=24) received 4 30 mg tablets and one 120 mg tablet.
Non-compartmental pharmacokinetics, safety and tolerability were assessed.

Results

Bioequivalence of the pediatric 30 mg tablet to the 120 mg dose strength was shown with a mean ratio [90%CI] of 104.73% [99.09-110.68%] for AUC and 101.67% [89.41-115.60%] for Cmax. No obvious differences in PK were observed for the slurry application of the dose. Treatments were well tolerated.

Conclusions

In conclusion, bioequivalence of the 30 mg tablet to the established 120 mg dose strength was shown. Therefore, the novel, age-appropriate formulation can be considered suitable for pediatric dosing. Moreover, NFX can be administered as aqueous slurry preapared from the tablets, an important prerequisite for its suitibility to treat small children.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0983
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

HOW OUTCOMES MIGHT BE IMPROVED IN AN OUTBREAK OF TYPHOID FEVER (UGANDA 2015)

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Background

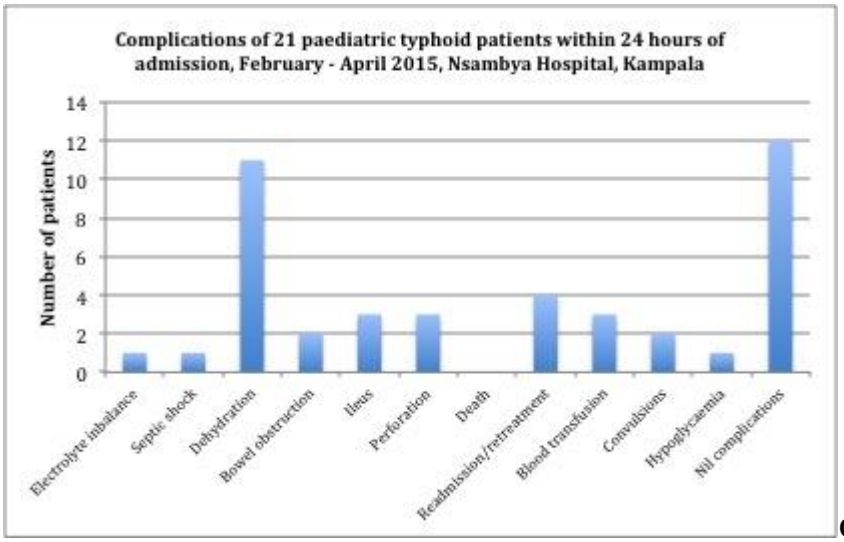
Typhoid fever, caused by the salmonella enterica serovar typhi is a global health problem. There are a reported 21 million cases and 200,000 deaths worldwide, with less reported paediatric statistics and complications. In February 2015, Ministry of Health in Uganda confirmed an outbreak, which affected up to 14,000 people by May, secondary to contaminated water source. We surveyed paediatric cases that were admitted and cared for in a hospital in Kampala during this period to report on the complications seen.

Methods

A survey was conducted over 2 weeks in Nsambya Hospital, a charging non-profit hospital in a Kampala suburb, with 5000 paediatric admissions annually. The author audited clinical notes retrospectively based on the ward admissions book of patients diagnosed with typhoid fever (with clinical and serological evidence) from February to April 2015. Exclusions were for missing notes only.

Results

There were 28 admissions, with notes available for 21 patients. All were malaria RDT negative at admission. The median age was 1 year 4 months (IQR 9 months: 4.5 years). The duration of illness prior to admission ranged 1- 30 days, mean 8.6 days. 81.0% patients had treatment from a health clinic prior to hospital attendance, with 42.9% receiving antimalarials , 38.1% receiving antibiotics. 85.7% patients were positive for salmonella typhi IgM, 61.9% positive for IgG. Blood cultures were taken in 9 cases (42.9%), 1 grew salmonella typhi. 42.9% demonstrated the following complications within 24 hours of admission.



Conclusions

There was a high rate of complications secondary to typhoid. The majority of patients had delayed presentation to hospital following treatment at private clinics. We suggest that better early differentiation from other febrile pathologies, particularly malaria, will help with this.

ESP16-0525
10. TROPICAL DISEASES, TRAVEL MEDICINE AND PARASITIC INFECTIONS

TOXOCARIASIS AS A CAUSE OF EOSINOPHILIA: EXPERIENCE IN A PEDIATRIC TROPICAL REFERENCE UNIT

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Title of Case(s)

TOXOCARIASIS AS A CAUSE OF EOSINOPHILIA: EXPERIENCE IN A PEDIATRIC TROPICAL REFERENCE UNIT

Background

Toxocariasis is a worldwide zoonosis, prevalent in areas with poor hygienic conditions. Although usually asymptomatic in children, it may progress to severe liver, systemic and eye disease. We describe the epidemiology, clinical syndrome, diagnosis and treatment of a series of pediatric patients.

Methods:

Children under 16 years diagnosed with Toxocariasis between 2009-2015 in a Pediatric Tropical Reference Unit were included in the study.

Case Presentation Summary

Results:

A total of 36 children, with a median age 107 months [IQR 9-240], 20 (55%) women, were included. Thirty-four were born outside Spain (32% Asia, 29% Africa, 25% Latin America, 9% Eastern Europe). At diagnosis,16/36 were asymptomatic: 12/36 refered gastrointestinal symptoms, 7/36 skin disorders and 1 respiratory syndrome. Seventy percent (24/36) showed eosinophilia, 14/24 moderate (median:1184 eosinophils/mm3 [IQR 4950-535]. All patients showed a positive EIA serology. There were 17 coinfections with other parasites (7 *Giardia lamblia*, 3 *Strongyloides stercoralis*, 3 *Schistosoma* and 4 multiple parasitosis); one latent tuberculosis;. 1 Trichophitum violaceum mycosis and 1 vertical *HIV* infection. All of them received Albendazole, requiring 14/36 (39%) more than one cycle (4 children 3 cycles and 10 cases 2 cycles). All of them normalized eosinophil count. Evolution was uncomplicated for all.**Learning Points/Discussion**

Conclusion:

Toxocariasis must be included in the differential diagnosis of eosinophilia, due to its potential severity. Diagnosis is based on suspicion and confirmed by serology, as patients are often asymptomatic or have few symptoms.
Only 70% of cases presented with eosinophilia, and thus we recommend to include serology in the screening of immigrant /internationally adopted children.
Albendazole remains the treatment of choice, often requiring 2 or more cycles, in our experience with favourable course.

ESP16-0804
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

THE RATE OF CATHETER-ASSOCIATED BLOODSTREAM INFECTIONS IN PEDIATRIC INTENSIVE CARE UNIT: ONE YEAR EXPERIENCE

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Background

Intravascular catheters are used in intensive care units as well as the services with increased frequency in the management of children. The aim of this study is to evaluate the infections associated with intravascular catheterization.

Methods

Between the years 2014-2015 Augusts, in Medical Faculty of Cerrahpasa, University of Istanbul, Pediatric Intensive Care Unit (PICU), 105 patients and placed 171 intravascular catheters analyzed retrospectively by the patients' medical records.

Results

During the study period, 13 patient had catheter-associated bloodstream infections (CABSI), 6 of them had sepsis, 4 of them had local infection and 3 of them had colonisation. The CABSI rate was 1.88 infections per 1000 central venous catheter (CVC) days. Two deaths following CABSIs were observed. Carbapenem resistant *Klebsiella Pneumoniae* and *Enterobacter Cloacae* were isolated in their cultures. As catheter type, size and location had no risk for catheter related infections. Increased time length for the usage of catheters showed a significant increase in infection incidence. The presence of infection during administration did not show a significant increase in CABSI. The incidence of infection was lower for patients in PICU.

Conclusions

The rate of CABSI was low for our patients. We suggest that, the insertion and care of catheters by skilled persons reduce the complication rates**.**

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0457
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS IN PEDIATRIC INTENSIVE CARE UNITS. OUTCOMES OF THE VINCAT SURVEILLANCE PROGRAM IN CATALONIA-SPAIN, 2012-2014

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Background

Since 2012, medical-surgical pediatric intensive care units have been included in the epidemiological surveillance program of nosocomial infections of Catalonia (VINCAT) to monitor central line-associated bloodstream infections (CLABSI) with a standardized and unified methodology.

Methods

A prospective yearly monitoring was carried out by experienced and trained personnel of participant units. The follow-up included daily assessment of admissions and central line utilization, as well as individual data of patient who developed CLABSI. This information was centralized trough a on-line specific program. The definitions for central line utilization and CLABSI used in this program were similar to the ones used by the National Healthcare Safety Network of USA (NHSN). CLABSI rate and central line utilization ratio were calculated globally and stratified by unit complexity.

Results

The program has been implemented in 6 of the 7 pediatric intensive care units of Catalonia. The incidence rate (CLABSI/patient-days with central line x 1000) was 3.2‰ in 2012 and decreased significantly the next two years (2.8‰ in 2013; 2.9‰ in 2014). The central line utilization ratio remained stable (0.61 global). The incidence rate was higher in the more complex units (2.95‰ vs 1.37‰) accordingly with a higher central line utilization rate (0.67 vs 0.45). The stronger decrease occurred in less complex units, from 5.48‰ in 2012 to 0.18‰ in 2014. Isolated microorganisms were mainly gram-negative bacilli (35.82%), coagulase negative staphylococcus (29.85%) and candida spp. (19.4%).

Conclusions

The incidence rates in the last two years were in the range of international standards (percentile 75 NHSN). The main impact of the program in reducing infection rates was observed in less complex units. A significant increase in the proportion of CLABSI caused by gram-negative bacilli was observed in the last year.

ESP16-0803
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS IN NEONATAL INTENSIVE CARE UNITS. OUTCOMES OF THE VINCAT SURVEILLANCE PROGRAM IN CATALONIA-SPAIN, 2012-2014

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Background

Since 2012, neonatal intensive care units have been included in the epidemiological surveillance program of nosocomial infections of Catalonia (VINCAT) to monitor central line-associated bloodstream infections (CLABSI) with a standardized methodology.

Methods

A prospective continuous monitoring was carried out by experienced and trained personnel of each participant unit. The follow-up included daily assessment of admissions and central line utilization, as well as individual data of patient who developed CLABSI. This information was centralized trough an on-line specific program. The definitions for central line utilization and CLABSI used in this program were similar to those used by the National Healthcare Safety Network of USA (NHSN) but include some differences regarding skin contaminating microorganisms. CLABSI rate and utilization ratio were calculated globally and stratified according to unit complexity and birth weight category.

Results

The program has been implemented in 14 neonatal intensive care units, but only data of 12 units that met quality control were included. On 2014, the incidence rate (CLABSI/patient-days with central line x 1000) was 4.55‰, with a central line utilization ratio of 0.39. We observed a

significant decrease in the incidence rate for the second consecutive year (4.91‰ in 2013; 6.51‰ in 2012), while the overall utilization rate remained stable. The stronger decrease occurred in infants less than 1000 gr. at birth weight (9.73‰ in 2012; 6.94‰ in 2013; 5.91‰ in 2014). The most frequently isolated microorganisms were coagulase negative staphylococcus (47.4%).

Conclusions

Despite the observed decline in the incidence of CLABSI rates, additional strategies are needed to improve the program results. Infection rates differ significantly between unit complexity and birth weight categories. The stronger impact of the program in reducing infection rates was observed in the more at risk category.

ESP16-0242
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

A POINT PREVALENCE STUDY OF ANTIMICROBIAL PROPHYLAXIS IN SURGICAL PROCEDURES IN THE PEDIATRICS SETTING

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Background

KK Women's and Children's Hospital has no published data on adherence rates to the surgical antimicrobial prophylaxis pediatric guidelines and the impact on the incidence of surgical site infections (SSIs). This study aimed to evaluate adherence and association between timing of administration of the prophylactic antimicrobial and the incidence of SSI, 30-day SSI related readmission and 30-day SSI related mortality. The total duration of prophylactic antimicrobial was also evaluated.

Methods

Point prevalence study of prophylactic antimicrobial use in 158 patients who undergone pediatric surgical procedures. Patient and surgery data were collected in a 3-month period with recording of the incidence of SSIs conducted 30-days post-discharge. Chi square test was used to evaluate the relationship between the timing of the first dose and selected patient or surgery characteristics. Logistic regression was used to evaluate the association between timing of the first dose and total duration of therapy with the incidence of SSIs.

Results

Data was analyzed based on the appropriateness of the timing of the first dose. Compliance to the guidelines for the studied parameters was low; 81.5% of antibiotic entries had an inappropriate timing of administration; 13.9% and 5.0% of the antibiotic entries was a single prophylactic dose in the appropriate and inappropriate timing arms respectively. Following logistic regression analysis, association between timing of the first dose and total duration of therapy with the incidence of SSIs were not statistically significant [$P<0.05$].

Conclusions

This study showed a lack of compliance to the guidelines for the timing of administration and duration prophylactic antibiotics. Further assessment must be made to evaluate the extent of non-compliance for other components of the guideline. Interventions may be required to correct noncompliance for the improvement of antimicrobial use.

ESP16-0392
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

LONGER DURATION OF URINARY CATHETERIZATION INCREASES CATHETER-ASSOCIATED URINARY TRACT INFECTION IN PEDIATRIC INTENSIVE CARE UNIT

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Background

Catheter-associated urinary tract infections (CAUTI) are common, accounting for 30% of healthcare-associated infections. To date, few studies have addressed the issue of pediatric CAUTI. The aim of our study was to assess the risk of CAUTI in relation to the duration of catheterization.

Methods

Children with an urethral catheter seen in the pediatric intensive care unit between April 2012 and June 2015 at Tokyo Metropolitan Children's Medical Center in Japan were included. CAUTI was identified either using the diagnostic criteria of the CDC or through agreement of the clinical diagnoses of the infection control team and primary physicians. CAUTI cases were reviewed for patient data and isolated organisms. Duration of catheterization and the CAUTI incidence rate were analyzed.

Results

Among 1,894 catheterizations, 48 CAUTI cases were identified. The overall incidence was 4.87 / 1,000 catheter-days. Among the CAUTI cases, 24 were boys. The median age was 13 months (IQR 7-37 months) and the median duration of catheterization was 8 days (IQR 5.5-13.5 days). The isolated bacteria were *Escherichia coli* (35%), *Enterococcus faecalis* (16%), and *Pseudomonas aeruginosa* (13%). Two species were isolated in each of nineteen cases (40%). The incidence of CAUTI at <7 days and ≧7 days was 3.59 / 1,000 catheter-days and 6.06 / 1,000 catheter-days, respectively ($p<0.001$). Each extra day of catheterization increased the risk of CAUTI (odds ratio 1.09, 95%CI 1.06-1.12).

Conclusions

Longer duration of catheterization increased the risk of CAUTI. Prompt removal of the catheter is therefore crucial in pediatric patients.

ESP16-0537
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

COULD LONG-TERM AZITHROMYCIN REDUCE PSEUDOMONAS AERUGINOSA VENTILATOR ASSOCIATED TRACHEOBRONCHITIS AND PNEUMONIA IN PATIENTS WITH TRACHEOSTOMY AND MECHANICAL VENTILATION?

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Background

Among long-term tracheostomized patients using mechanical ventilation, ventilator-associated tracheobronchitis (VAT) and pneumonia (VAP) are frequent complications, even in “Hospital at Home” program patients. These patients are at high risk for exacerbations and hospitalizations. Macrolide treatment has shown to reduce exacerbations in moderate-to-severe chronic obstructive pulmonary disease in adults, asthma and cystic fibrosis. The aim of this preliminary study is to evaluate the safety and efficacy of long-term azithromycin use in pediatric outpatients with tracheostomy and mechanical ventilation with high *Pseudomonas aeruginosa* VAT and VAP incidence density rates.

Methods

Patients were recruited between January 2015-January 2016 at Children with complex chronic disease unit in Hospital La Paz (Madrid, Spain). We evaluate safety and efficacy of azithromycin 10 mg/kg/day, three day-a-week for 6 months (AZI) in patients with high *Pseudomonas aeruginosa* VAT and VAP incidence density rates defined by American Thoracic Society and Infectious Diseases Society of America criteria. The primary outcome in this preliminary study was the reduction in the number of exacerbations and hospitalizations. No different tracheostomy care measures were conducted in these patients during the study period.

Results

Three long-term tracheostomized patients using mechanical ventilation were included. All of them had frequent *Pseudomonas aeruginosa* VAT and VAP with high incidence density (16.4/8.2/20; N/1000 ventilation-days) requiring emergency attention and/or hospitalization. After azithromycin 10 mg/kg/day, three day-a-week was started, incidence density descend to 0/3/0, after 5-11-3 months follow up. No side effects were documented.

Conclusions

Long-term azithromycin treatment seems to be safe and effective in our preliminary study to reduce *Pseudomonas aeruginosa* VAT and VAP in pediatric patients with tracheostomy, reducing infection exacerbations and hospitalizations.

ESP16-1052
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

RECURRENT INTRAVENTRICULAR CATHETER INFECTION IN PEDIATRICS: CASE REPORT

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Title of Case(s)

RECURRENT INTRAVENTRICULAR CATHETER INFECTION IN PEDIATRICS: CASE REPORT

Background

Health care−associated infections in pediatrics are a major clinical problem resulting in increased morbidity and mortality. Bacterial infections of intraventricular catheters are often difficult to treat with antimicrobial therapy alone, even if appropriate targeted intravenous antimicrobial treatment is prescribed. Often, recurrence may occur even if proper management is performed.

We describe the case of a girl with recurrent infection of the intraventricular catheter.

Case Presentation Summary

A 4 years 10 months old girl with a progressive neurodegenerative lysosomal storage diseases is followed by our institution for an experimental study, consisting of intraventricular recombinant enzyme replacement therapy every two weeks. After 1 year of uncomplicated procedures, her routine CSF sample showed a bacterial infection by Propionibacterium acnes, which was first treated with intravenous targeted antimicrobial therapy. Given the failure of conservative treatment, on Day 7 catheter substitution was performed, jointly with intramuscular targeted antimicrobial therapy; microbiological and clinical recovery rapidly occurred. After 6 months, a new episode of intraventricular bacterial infection occurred; a Propionibacterium acnes with different antimicrobial sensitivities was isolated. An immediate catheter replacement was performed, leading to immediate microbiological and clinical recovery.

Learning Points/Discussion

Infections of intraventricular catheters are often difficult to treat with antimicrobial therapy alone; few studies on intraventricular drug dosing in pediatrics are to date available. In our experience, removal of infected catheter is the most efficient measure in intraventricular catheter infections. However, further studies on pharmacokinetics of intraventricular antimicrobial drugs are needed in order to avoid invasive procedures such as device replacement.

ESP16-0118
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

NOSOCOMIAL INFECTIONS IN THE PAEDIATRIC INTENSIVE CARE UNIT AND MORTALITY: THREE YEARS EXPERIENCE

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Background and Objective

The aim of this study was to evaluate the rates of health care associated infections (HCAI) in paediatric intensive care units (PICU) and HCAI-related mortality.

Methods

HCAI surveillance results between 2012 and 2014 were evaluated in 3-month periods based on the CDC 2008 criteria.

Learning Points Discussion

A total of 1378 patients were hospitalised in the PICU over the period of three years, and HCAI developed in 7% of these patients (100/1387). In 100 patient with HCAI, totally 139 HCAI attacks developed (average 1.39 attacks per patient), 25% of patients had >2 attacks. It was found that HCAI rate was 10% (139/1387) and HCAI incidence density 11,27/1000 patient/hospital day.

Throughout the study, it was found that hospital bed occupancy rate was 95%-113%, patient to nurse ratio 3.37-4.14, rate of ventilator use 0.24-0.57, rate of central catheter use 0.09-0.36, rate of urinary catheter use 0.13-0.39. As far as the evaluation was concerned, the rates of healthcare workers complying with hand hygiene varied between 45% and 57%.

It was estimated that total crude in PICU mortality was 11.1%, crude mortality in patients with HCAI 47%, without HCAI 8.31% ($p<0.001$), and HCAI-attributed excess crude mortality 38.7%. There was statistically significant relationship between HCRI rate and total patient mortality rate ($r=0.54$; $p=0.032$). Statistically significant relationship was also found between mortality rate in patients with HCAI ($r=0.66$,$p=0.006$), HCAI-attributed crude net mortality ($r=0.62$, $p=0.10$) and Patient/Nurse ratio.

It was found that PICU HCAI rates in our study were higher than those in the developed countries and lower than those in the developing countries.

ESP16-0333
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

WHERE SHOULD INTRAVASCUALR CATHETERS BE PLACED IN PEDIATRIC PATIENTS IN INTENSIVE CARE?

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Background

Little is known about ideal sites for catheter placement in children. We aimed to assess the relationship between the insertion site and risk of catheter-related blood stream infection (CRBSI) in pediatric intensive care unit (PICU).

Methods

Patients with intravascular catheters seen in the PICU between April 2014 and March 2015 at Tokyo Metropolitan Children's Medical Center were included. Medical records were reviewed for patient characteristics, types and sites of intravascular devices, and duration of placement. CRBSI incidence in relation to insertion site was examined.

Results

415 patients were included. The median age was 1.5 years (IQR 5 months-6.5 years) and 42% were males. The median length of PICU stay was 6 days (IQR 3-10 days). The total number of intravascular catheters was 1,038. The sites of 343 central venous catheters (CVCs) were the jugular vein (50%), the subclavian vein (8%), the femoral vein (35%), and unknown (7%). The sites for 203 peripherally inserted central catheters (PICCs) were the upper extremities (72%), the lower extremities (21%), and unknown (7%). The sites for 512 arterial catheters (ACs) were the upper extremities (72%), the lower extremities (25%), and unknown (5%). The median duration of placement of CVCs, PICCs, and ACs was 5 (IQR: 3-7 days), 6 (IQR: 4-12 days), and 4 days (IQR: 3-8 days), respectively. CRBSI incidence was 1.07 per 1000 catheter-days. Patients with CRBSI experienced longer PICU stay (p=0.001) and higher mortality (p=0.014). CRBSI risk was higher when the lower extremities were used as the site of insertion for any intravascular device (p=0.024).

Conclusions

CRBSI incidence correlated with longer hospitalization and higher mortality. Using the lower extremities as the insertion site for intravascular devices also increased the risk of CRBSI among children.

ESP16-0291
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

REGISTERED NURSES' KNOWLEDGE, ATTITUDES AND PRACTICES REGARDING THE SPREAD OF NOSOCOMIAL INFECTIONS

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Background

Nosocomial infections (NIs) are infections that develop in patients receiving medical care in a hospital or other healthcare facilities. Episodes of NIs are recognized in hospitalized patients world-wide. They are caused by pathogens such as bacteria, viruses and parasites present in the air, surfaces or equipment often transmitted by indirect and direct contact. The burdens of NIs include prolonged duration of hospitalization for patients resulting in increased costs of healthcare and deaths. Implementation of safe patient care activities is the role of healthcare workers such as physicians and nurses. It has been documented in the literature that at the time of their graduation from their professional education, healthcare professionals have sufficient knowledge to practice patient safety and infection control guidelines. However, the evidence suggests otherwise since healthcare workers including nurses are implicated in the transmission of nosocomial infections. With nurses having the most contacts with patients; understanding of their knowledge, attitudes and practice patterns with regard to the spread of NIs may provide one approach by which this health care issue would be addressed.

Methods

This exploratory, cross-sectional and descriptive study was conducted using on-line survey responses from 352 registered nurses. Data was analyzed with descriptive and inferential non-parametric statistics.

Results

The participants demonstrated high levels of knowledge regarding the spread of nosocomial infections, adherence to recommended guidelines of infection control practices, and positive attitudes. The results of correlation analysis indicated a significant positive correlation between organizational support and respondent's knowledge and weak but significant positive correlations between organizational support and respondents' attitudes and practices.

Conclusions

Findings in this study suggest that nursing education, concerted efforts of infection control and organizational support play pivotal roles toward reducing the spread of NIs.

ESP16-0667
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

ACUTE APPENDICITIS IN HOSPITALIZED CHILDREN AND ADOLESCENCT : REGRESSION ANALYSIS OF FACTORS ASSOCIATED WITH PERFORATION OUTCOME

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Background

Acute appendicitis is one of the most common causes of acute abdomen in children. Late surgical intervention is often associated with increased perforation and fatal outcome. Apply multivariate regression analysis to determine the significance of clinical variables for perforation outcome.

Methods

Retrospective formal systemic review of 552 cases under 18 years of age were analyzed between January 2011 through December 2014. The diagnostic study used ultrasound to determine if certain sonographic features correlated with appendiceal pathological findings. The cut-off diameters of appendicitis was more than 6 mm.

Results

The total number of non-perforated appendicitis were 430 (77.8%) and perforated appendicitis were 122 (22.1%) during 4 years. The confirmed appendicitis males were 330 (59.8%) and females were 222 (40.2%). Among the perforated cases, the males were 68 (55.7%) and the females were 54 (44.3%). The perforation rate of preschool age (3-6 year) was 28/54 (51.9%), elementary school age (7-12 year) was 56/241 (23.2%), middle school age (13-15 year) was 24/129 (18.6%) and high school age (16-18 year) was 14/128 (10.9%). Clinically vomiting and diarrhea symptoms were more severe in perforated appendicitis ($p<0.001$) and laboratory inflammation index (WBC and CRP) were more increased in perforated appendicitis ($p<0.001$). The most common microorganisms were *Escherichia coli* (50%) and the next were *Pseudomonas aeruginosa, Streptococcus viridians, Proteus penneri, Enterococcus avium, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus hominis*.

Conclusions

The overall perforation outcome of childhood and adolescence was 22.1 %. The perforation portion of acute appendicitis under 8 years was 86.1% among the peritonitis. The sex ratio was more predominant in males (59.8%). The most common microorganism was *E.coli* (50%). No mortality was recorded from the disease.

ESP16-0234
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

PREDICTORS OF MORTALITY IN STAPHYLOCOCCUS AUREUS BLOOD STREAM INFECTION IN LEVEL III NEONATAL INTENSIVE CARE UNIT NEW DELHI

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Background

Staphylococcus aureus (*SA*) Blood Stream Infection (BSI) is a frequent health care associated infection in newborns resulting in increased mortality, morbidity and length of hospital stay. Resistance to methicillin is reported in 8%-28% of cases. Reported mortality from all cause sepsis is 18%-24% and from *SA* sepsis is 9%-12% However none of the study has evaluated the predictors of mortality in these babies.
Objective: was to identify predictors of mortality in babies with *SA* Blood Stream Infection

Methods

It was a Retrospective Cohort Study between January 2013 and December 2014 in a NICU in New Delhi. Study population included babies who grew *SA* on blood culture. Data on patient demographics, underlying diseases, medications, central catheters, nutrition, ventilator use etc. was retrieved. Risk factors were evaluated from the time of admission until the onset of BSI and then till discharge or death.Data analysis was performed using SPSS Version 20.0. Risk factors were evaluated using Univariate and Multivariate Logistic Regression Analysis. P values <.05 were taken as significant. Adjusted Odds Ratios (aO.R.) and 95% Confidence Intervals (C.I.) were calculated for significant variables

Results

Thirty one out of total of 4038 admitted newborns developed *SA* BSI, 22 of which were by *MRSA* and 9 *MSSA* (Incidence 77 and 54 per 10000 respectively). Eleven out of 22 babies with *MRSA* and 3 out of 9 babies with *MSSA* died (p 0.4). Male gender, birth weight, asphyxia, ventilation duration, surfactant and steroids use did not significantly influence mortality. Factors associated with significantly high mortality were prematurity, ventilation, vasopressor,

TPN and prolonged duration of stay

Table 1. Univariate analysis

Variable	Survived (n=17)	Died (n=14)	O.R	Confidence interval		P Value
Male Sex	12	7	0.42	0.09	1.83	0.25
Gestation (weeks) Mean (SD)	34.88 (4.05)	30.79 (4.73)	0.81	0.68	.97	0.02
Birth Weight (grams) Mean (SD)	1779 (703)	1436(906)	0.99	0.99	1.00	0.24
Duration of stay (Days) Mean (SD)	24.8 (14.9)	40.9 (21.4)	1.05	1.00	1.10	0.03
Ventilation	12	2	45.00	5.50	368.15	0.00
Duration of ventilation(Days) Mean (SD)	3.5 (2.1)	9.75 (9.8)	1.26	0.71	2.24	0.42
Vasopressors	4	11	11.92	2.18	65.15	0.01
APGAR <7 at 1 Min	3	6	3.50	0.68	17.96	0.13
Surfactant	4	7	3.25	0.70	15.07	0.13
Steroids	4	6	2.43	0.52	11.39	0.26
TPN	3	9	8.40	1.60	44.10	0.01
MRSA	11	11	2.00	0.39	10.09	0.40

Table 2. Multivariate Logistic Regression Analysis

Factors	Odds ratio	Confidence Interval		P Value
Ventilation	47.77	4.40	518.233	0.001

Multivariate regression analysis revealed that ventilation was an independent risk factor for mortality

Conclusions

Ventilation is an important independent contributor to mortality in *SA* BSI. In newborns mortality associated with *MRSA* and *MSSA* is comparable

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0167
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

EPIDEMIOLOGY AND CLINICAL FEATURES OF HOSPITAL-ASSOCIATED VIRAL INFECTIONS IN PEDIATRIC PATIENTS IN A TERTIARY CENTER IN THAILAND

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Background

Background: Hospital-associated viral infections (vHAI) in pediatric patients have been less aware of in developing countries. We evaluate incidence and trend of vHAI over the 5 year-period in a tertiary care center in Thailand.

Methods

Methods: This retrospective study was conducted at Siriraj hospital, a 350 pediatric bed-tertiary care center in Bangkok, from 2009 to 2013. The episodes of vHAI collected in routine surveillance were analyzed. The vHAI was defined as the new onset of the identifiable viral infections occurred after hospitalization for at least 48 hours and longer than the incubation period for the specific viruses. Medical records were reviewed for clinical features and outcomes.

Results

Results: There were 264 vHAI found and were classified in the two diagnosis groups, gastroenteritis (GE) and respiratory tract infection (RTI), with the incidence of 0.69/1,000 patient-days for GE, and 0.79/1,000 patient-days for RTI, respectively. The most common organism of RTI was RSV (46%) and all of GE was caused by rotavirus. One third of hospital acquired pneumonia were caused by respiratory viruses. More than 90% of the patients were younger than 5 years. 58% of patients with GE and 98% of those with RTI had underlying conditions. The median onset of vHAI was 12 days after hospitalization. 16% of rotavirus GE had respiratory symptom and 23% of RTI had gastrointestinal symptoms. 67% of RTI episodes involved lower respiratory tract. Antibiotics were prescribed in 61% of all vHAI and oseltamivir was prescribed in 33% of all RTI. Two (1.4%) patients with RTI died from RSV pneumonia.

Conclusions

Conclusion: Rotavirus and RSV were the most common viruses causing vHAI. Infection control strategies should concern vHAI more especially among children with underlying conditions.

ESP16-0218
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

FACTORS INFLUENCING THE CLINICAL OUTCOME IN CHILDREN IN INTENSIVE CARE UNITS IN A TERTIARY CARE HOSPITAL IN INDIA

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Background

Background and Objective: 8 children (7 males: 1 female, 3 months to 5 years) among 514 inpatients children (1.7%) and 38 neonates (3.2%) (23 males: 15 females) among 1157 neonates required ICU care. A 5 year old child with post HSV encephalitis required readmission due to seizure as complication. Hence the objective was to analyse factors influencing outcome in children admitted for infections in intensive care units (ICU)

Methods

Methods: The study was done as part of infection control surveillance program in ICU (January 1-November 30) All children who were admitted to ICU for infections were included. The type of infection, appropriate therapy, co-morbid conditions and duration of hospital stay were correlated with clinical outcome.

Results

Average length of hospital stay - 7 days (2 days to 23 days). Children were treated with antibiotics as per antibiotic policy. Anaemia and increased neutrophil count were common features. The outcome included 7 discharges and one death.

All babies with symptoms of sepsis were treated with cefiximine (Taxim). (37 discharges and one death). 36 babies had late onset ranging from 3 to 22 days. 3 cases of klebsiella prompted infection control team to investigate for source.

Coagulase negative Staphylococcus, staphylococcus aureus, Klebsiella, mycobacterium tuberculosis and candida were reported.

Conclusions

Conclusions: Host defenses to microbial invasion include antigen-independent immunity and specific or adaptive immunity. As newborns have a naïve adaptive immune system, early antibiotic therapy on presumptive diagnosis of sepsis has facilitated good outcome. The duration of hospital stay did not influence clinical outcome (r-0.1) but indirectly influenced hospital economics.

The authors acknowledge support of infection control team.

ESP16-0855
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

ASSESSING ADHERENCE TO THE WORLD HEALTH ORGANIZATION HAND HYGIENE TECHNIQUE RECOMMENDATIONS AMONG HEALTHCARE WORKERS OF A NEONATAL INTENSIVE CARE UNIT

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Background

Hand hygiene is a cornerstone for preventing healthcare-associated infections. Training sessions are performed regularly in our centre to improve compliance with the World Health Organization (WHO) recommendations. These are the results of a study performed to measure the adherence to proper hand hygiene technique during the training sessions for the healthcare workers (HCW) in the neonatal intensive care unit (NICU).

Methods

The WHO recommends an 8 step technique for ABHR: 1. Application of the product; 2. Rubbing palms 3. Palm over dorsum; 4. Palm to palm (fingers interlaced); 5. Back of fingers; 6. Thumbs; 7. Fingertips, and 8. Drying.
In 2015 four alcohol-based hand rub (ABHR) training sessions were conducted in the NICU. During these sessions, the attending HCW where observed while performing ABHR, and the number of steps from 2 to 7 performed by each HCW was counted.

Results

There were 118 observations, with some HCW observed more than once. 61 observations corresponded to nurses, 36 to physicians, 16 to auxiliary nurses and 5 to other HCW. The age of the participants ranged from 20 to 62 years.
Two of the 6 steps were performed in 10 observations (8,47%); 3 steps in 22 (18,64%); 4 steps in 32 (27,12%); 5 steps in 38 (32,20%), and the complete 6 steps were observed in 16 occasions (13,56).

Conclusions

Most healthcare workers do not complete the sequence for ABHR recommended by the WHO.

ESP16-0325
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

CATHETER-RELATED BLOOSTREAM INFECTION DUE TO MULTIDRUG RESISTANT ELIZABETHKINGIA MENINGOSEPTICA

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Title of Case(s)

CATHETER-RELATED BLOOSTREAM INFECTION DUE TO* MULTIDRUG RESISTANT *ELIZABETHKINGIA MENINGOSEPTICA

Background

Elizabethkingia meningoseptica is gram negative bacillus, it has been reported as cause of nosocomial bacteremia, meningitis, pneumonia, sepsis especially in premature neonates, immune deficient patients and those had prolonged hospitalization or prolonged use of antimicrobial agents. Here we present a case with catheter related bloodstream infection due to *Elizabethkingia meningoseptica* and we aim to discuss unique antibacterial susceptibility pattern of *Elizabethkingia meningoseptica* and outcome of infection.

Case Presentation Summary

A 7-month old girl with factor-VII deficiency and hydrocephalus was consulted for evaluation of fever. She was lethargic and febrile without other abnormal physical finding, had subclavian and Port catheters. She had been hospitalized for last 2 months in neurosurgery clinic, and had prolonged antimicrobial usage. Laboratory investigation showed elevated acute phase reactant, later *Elizabethkingea meningoseptica* was grew in blood cultures taken from subclavian catheter and peripheral vein. Blood culture could not taken from port catheter. Subclavian catheter was removed, ciprofloxacin was initiated according to antibiotic susceptibility results. But for clinical improvement was not observed, she was still sick-appeared, lethargic and subfebril, at the third day of this treatment even if *Elizabethkingea meningoseptica* is gram negative bacillus, we added vancomycin and rifampicine to treatment. At the second day of combination treatment she appear very well, her fever subside. Control blood culture taken at the beginning of combination treatment remained sterile, treatment was completed to 14 days.

Learning Points/Discussion

Prompt treatment of infections caused by *Elizabethkingia meningoseptica* is seriously effect prognosis and clinical outcome. Awareness of inconsistency between *Elizabethkingia meningoseptica's* susceptibility test and clinical response, and knowledge of its sensitivity to some antibacterials that are actually effective against gram positive bacteria is very important for applying appropriate treatment.

ESP16-0481
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

SURGICAL SITE INFECTION DUE TO COLISTIN RESISTANT KLEBSIELLA PNEUMONIAE IN A CHILD

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Title of Case(s)

SURGICAL SITE INFECTION DUE TO COLISTIN RESISTANT *KLEBSIELLA PNEUMONIAE* IN A CHILD

Background

Health care associated infections such as surgical site infections, especially caused by multi-drug resistant (MDR) gram negative microorganisms are increasingly detected. Herein we report a case of surgical site infection due tocolistin resistant *Klebsiellapneumoniae*.

Case Presentation Summary

A ten-year-old boy who underwent right transhumeral amputation following a car crash had been hospitalized in the pediatric intensive care unit for multiple cranial bone fracture. On the sixth day of admission, he had fever and purulent discharge from transhumeral amputation site. His drainage culture yielded*Klebsiellapneumoniae* susceptible to only tigecycline and amikacin by E-test. Minimal inhibitory concentration for colistin and tigecycline were6 mcg/ml (resistant) and 0.75 mcg/ml (sensitive) respectively, by E-test.Tigecycline and amikacin were started and continued for 14 days. The patient's clinical condition and purulent discharge from surgical site recovered.

Learning Points/Discussion

Health care associated infections, especially due to MDR gram negative microorganisms are in increasing clinical challenge because of limited options of antimicrobial treatment. With the increase in multi-drug resistance of gram negative microorganisms, appropriate treatment for infections caused by these bacteria has become more difficult. Tigecycline may be an alternative drug in MDR gram negative bacteria infections in children.

ESP16-0347
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

VENTILATOR-ASSOCIATED PNEUMONIA IN A TERTIARY CARE CHILDREN'S UNIVERSITY HOSPITAL: A PROSPECTIVE STUDY

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Background

Ventilator-associated pneumonia (VAP) is a common healthcare-associated infections in childhood. The 2014 report of the European Centre for Disease Prevention and Control estimated for VAP a mean device-adjusted rate of 10.1/1000 and 6.6/1000 ventilation-days in European and Italian patients, respectively. Despite the international data available in selected groups of patients, there is a lack of large and good quality studies. The present survey is a prospective cohort-study monitoring for 6 months the occurrence of VAP in an Italian tertiary care children's hospital.

Methods

The study involved all children admitted to Meyer Children's University Hospital, Florence, Italy who were mechanically ventilated between the 15th of October 2014 and the 14th of April 2015. VAP was defined according to the Center for Disease Control and Prevention criteria. VAP incidence rate with 95% confidence intervals (95%CI) was calculated and stratified for the study variables. For each factor the relative risk and 95%CI were evaluated. Statistical analysis was performed using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL), $p<0.05$ was considered statistically significant.

Results

One hundred and forty-seven mechanically ventilated children with a median age of 5 months were included in the study, resulting in overall 1627 ventilation-days. The incidence of VAP in our study was 8.6/1000 ventilation-days (95%CI: 4.90-14.09). VAP rate was statistically significant higher in patients admitted to intensive care unit ($p=0.031$) and in children with nasotracheal intubation ($p=0.014$).

Conclusions

VAP incidence in our study was consistent with national and European data. Monitoring healthcare associated infections is the best way to assess the risk factors for infection globally and specifically for each institution. Moreover, it helps in planning preventive interventions to reduce patient's morbidity and mortality, save costs and control resistant-microorganisms spread.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0647
11. HEALTHCARE-ASSOCIATED AND SURGICAL INFECTIONS

CARBAPENEM-RESISTANT KLEBSIELLA PNEUMONIAE URINARY TRACT INFECTIONS IN INFANTS WITH A HISTORY OF HOSPITALISATION IN A NEONATAL INTENSIVE CARE UNIT

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Title of Case(s)

CARBAPENEM-RESISTANT KLEBSIELLA PNEUMONIAE URINARY TRACT INFECTIONS IN INFANTS WITH A HISTORY OF HOSPITALISATION IN A NEONATAL INTENSIVE CARE UNIT

Background

Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) has become a major cause of nosocomial infections worldwide but CRKP urinary tract infection (UTI) in healthy individuals is rare.Here we report a series of infants presented with UTI caused by CRKP and discuss their aetiology.

Case Presentation Summary

Between April 2009 and March 2011, a CRKP outbreak emerged in the Neonatal ICU of our Hospital that involved 15 neonates hospitalized for a median of 37 days (range 20-275). The neonates developed a clinical CRKP infection after a median of 8 days (range 4-115) from admission. CRKP was isolated from 17 positive cultures; blood (10/17), CSF (2/17) or urine (5/17). Among the 5 neonates that developed CRKP UTI, only one had an underlying urological abnormality.

Starting from October 2009 through July 2012, 9 infants, all males, were admitted in the Department of Paediatrics with urinary tract infection caused by CRKP. The median age at presentation was 3.9 months (range 1-19.3 months). History revealed that they had all been hospitalized in the NICU during the long-lasting CRKP outbreak for a median of 17 (range 1-275) days but no CRKP UTI infections were documented during their stay in NICU. They presented with CRKP UTI 15 to 567 (median 42.5) days after NICU discharge. Only two children had urological abnormalities. The antibiotic susceptibility patterns of all isolates from NICU and paediatric ward were identical.

Learning Points/Discussion

These cases illustrate that hospital–acquired asymptomatic carriage of CRKP may well provoke community–onset multidrug resistant UTIs in healthy children months later and stresses the value of detailed history and source investigation in patients with unusual pathogens.

ESP16-0123
12. ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

SCRUB TYPHUS PRESENTING AS SEVERE LEFT VENTRICULAR DYSFUNCTION IN AN ADOLESCENT CHILD

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Title of Case(s)

SCRUB TYPHUS PRESENTING AS SEVERE LEFT VENTRICULAR DYSFUNCTION IN AN ADOLESCENT CHILD

Background

Scrub typhus is a rickettsial disease endemic in Northern parts of India.This case report highlights the presemptive early institution of oral/IV Doxycycline antibiotic in a sick child like ours of Tropical Fever with multiorgan failure.In our patient also doxycycline was started empirically till reports of scrub serology came positive,Child was dicharged after 14 days of hospital stay in a stable condition.

Case Presentation Summary

A 13 year old male child came to our emergency department with complaints of fever,vomiting for 5 days and yellowish discoloration of eyes,pain abdomen for 2 days prior.On examination child was responsive only to painful stimulus.Child had a pulse rate of 56 beats/minute,respiratory rate of 36/minute,B.P. of 88/60 mmHg,Temperature of 38 degree Celsius.Peripheral pulses were feeble with well palpable central pulses,Capillary refill time of 4 seconds.EKG done showed a prolonged QTc interval of 0.8 seconds.On auscultation heart sounds were muffled with bilateral basal crepitations.Laboratory investigations revealed a low platelet(54000/dl) and low hemoglobin(8.8gm/dl) levels.Creatinine kinase MB fraction levels were increased.Skiagram chest showed cardiomegaly.Echocardiography revealed an ejection fraction of 20% with hypokinetic left ventricle.As there was a travel history to an area endemic for scrub typhus,child was evaluated for the same.Scrub typhus serology was positive and child was started on oral doxycycline,slowly child started improving ,his ejection fraction improved and was discharged on day 14th of hospital stay in a stable condition.

Learning Points/Discussion

Doxycyline should be started early as a management strategy in sick children with Tropical Fever .Clinicians should be aware of this serious cardiac manifestation of scrub typhus, especially in patients living in or returning from areas endemic for scrub typhus.

ESP16-0312
12. ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

HEPATOSPLENIC CAT SCRATCH DISEASE IN CHILDREN: REPORT OF 11 CASES AND REVIEW OF THE LITERATURE.

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Title of Case(s)

Hepatosplenic cat scratch disease in children: report of 11 cases and review of the literature.

Background

Cat scratch disease is the most frequent presentation of *Bartonella henselae* infection. This disease is transmitted by cat scratches or bites. The typical form is a large and rough lymphadenopathy, with no general signs. In a few cases, the symptoms are aspecific and various, which makes the diagnosis difficult.

Case Presentation Summary

We reviewed 11 cases of hepatosplenic cat-scratch disease at our tertiary level Children's Hospital (Toulouse, France). One transplant patient received immunosuppressive therapy. The mean age was equal to 13 years (range 2 to 15 years). The chief complaint was fever. The duration of symptoms before diagnosis was 3 to 100 days (mean, 24 days). Nine patients had lymphadenitis and four had needle aspiration. Abdominal pain was present in 7 patients (64%). Seven children were treated with intravenous antibiotics, eight of them received macrolide therapy. Only four patients received rifampicin in combination. Once efficient therapy was initiated alone or in combination, improvement was noted within 1 to 30 days (mean, 8 days).

Learning Points/Discussion

Macrolide as Azithromycin should be considered in the initial antimicrobial treatment of hepatosplenic cat-scratch disease.

ESP16-0397
12. ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

CLINICAL CHARACTERISTICS OF DENGUE SHOCK SYNDROME CHILDREN WITH RECURRENT SHOCK IN SURABAYA

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Background

The most common danger in dengue virus infection is shock. Some patients will also suffered from recurrent shock.

To objective of this study was to describe clinical characteristics of children who had dengue shock syndrome (DSS) with recurrent shock

Methods

This cross sectional study was conducted in children hospitalized with dengue hemorrhagic fever (DHF) grade III and IV in Dr. Soetomo Hospital Surabaya from Januari 2013 until December 2014. Data were collected from medical record. We used the criteria from WHO-SEARO 2011 Guideline.

Results

One hundred and two children with DSS were included, mostly with DHF III (93.1%). Female outnumbered male (3:2) and the median age was 7 years (range 1-16). Twenty six children (25%) got recurrent shock. Among those group, all children had the history of fever previously, 50% had headache, and 70% reported abdominal pain. Most children with recurrent shock (88.5%) showed good nutritional status. One patient had the first episode of shock on the end of second day of illness, three others on the third day, and the rest on the fourth day and after. Fourteen children showed bleeding history, mostly as petechiae on the skin. Only half of the patients showed positive Rumpel Leede (RL) test on admission. The lowest thrombocyte level was 4000 /cmm. The highest hematocrite level was 56%. Eighty five percents children had hematocrite level above 40% since the first day of hospitalization.

Conclusions

Most DSS patients had DHF III. Recurrent shock only happened in one forth of those children. Many had pain in many parts of the body but less than half showed bleeding manifestations. The first episode of shock could happened as early as second day of illness. Many patients had high hematocrite level.

ESP16-0156
12. ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

CUTANEOUS LEISHMANIASIS IN NONENDEMIC AREA OF TURKEY

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Background

Leishmaniasis is a worldwide infectious disease caused by a protozoan parasite of the *Leishmania* genus. Leishmaniasis is endemic in southeastern Turkey and the neighboring Middle Eastern countries. Cutaneous leishmaniasis (CL) is the most common type in Turkey.

Methods

Samples were stained with Giemsa and also incubated to Novy-Nicolle-McNeal media.

Results

A total of 16 CL patients [11 (69%) boys and five (31%) girls] were admitted to a tertiary care hospital in Ankara between January 2014 and December 2015. The mean age was 74.3±32.3 months. Of these patients, two (12.5%) were Turkish citizens, 14 (87.5%) were Syrian citizens. The duration of symptoms before presentation was 10.5±15 (median 5.5 months) months. Single lesions were the most commonly seen in seven (43%) patients, whereas double and multiple lesions were observed in six (37%) and in one (6%), respectively. The face and neck was commonly involved site (87.5%). Skin smears for parasitologic examination were performed in all of the patients, and these were positive in nine (56%) patients. *Leishmania* spp. culture was positive in one patient whose smear examination revealed no amastigotes. Two patients (%12.5) with limb lesions were treated by intralesional meglumine antimoniate (Glucantime®) twice weekly for three weeks. One patient who had pulmonary stenosis treated with liposomal amphotericin B (AmbiSome ®) as an initial therapy because of the presence of cardiovascular risk. Thirteen patients were treated with intramuscular Glucantime® for two weeks. Intravenous AmbiSome ® was commenced to two of these patients who were unresponsive to systemic Glucantime®.

Conclusions

In conclusion, especially in patients with painless cutaneous lesion(s) who came from endemic areas like Syrian or who had history of travel to endemic areas, CL should be kept in mind in nonendemic areas also.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0686
12. ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

TICK-BORNE ENCEPHALITIS IN CHILDREN AND ADOLESCENTS IN THE WEST BOHEMIAN REGION (CZECH REPUBLIC) BETWEEN 1960 AND 2015

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Background

West Bohemian Region (currently Pilsen and Karlovy Vary Regions) is a high tick-borne encephalitis (TBE) endemic region in the Czech Republic.

Methods

We analysed all reported epidemiological and clinical data about TBE among children and adolescents in the period 1960-2015, retrospectivelly.

Results

Over the years the risk of transmission in particular areas of the region has changed. The current (year 2015) highest reported incidence rate is in the Pilsen-North District (9.2 per 100,000 inhabitants p.a.). Between 1960 and 2015, 482 cases of TBE in children and teenagers were confirmed by laboratory testing in Pilsen and Karlovy Vary Regions, i.e. 3.7per 100,000 inhabitants p.a. The highest incidence rate for both male and female sexes (6.5 and 4.3 respectively) concerns the same age group 15-19 years. Of all the reported cases, one case was fatal (a 15-year-old boy, 0.2%). One of the sick reported TBE vaccination. Tick bite was reported from 283 patients (58.7%). In 7.6% of cases, patient's history showed data on the consumption of non-pasteurized milk or non-pasteurized diary products. As a result of the gradual infection season prolongation, the transmission can currently occur anytime between March and November. The preschool category (under 5 years of age) reported the highest incidence in June and September, while schoolchildren fall predominantly in the standard summer holiday months of July and August. During the monitored period there was no altitude shift of infection transmission occurring in the higher altitudes. Based on officially available data, 37.6% of the Pilsen Region´s young population has been vaccinated, so far.

Conclusions

Risk behavior - the consumption of non-pasteurized milk together with low vaccination coverage may hardly influence the unfavorable tick-borne encephalitis epidemiological situation.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0644
12. ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

INGUINAL MASS IN AN ADOLESCENT GIRL. WHAT IS THE ETIOLOGY?

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Title of Case(s)

Inguinal mass in an adolescent girl. What is the etiology?

Background

Inguinal lymphadenopathies during adolescence are usually due to neoplastic disorders or infectious diseases (originated by streptococcus, cytomegalovirus, Epstein-Barr, toxoplasma, HIV and mycobacterium). But other possible etiologies should be considered.

Case Presentation Summary

We report an 11-years-old girl with history of a painful inguinal mass with progressive growth without inflammatory signs or fever. As a result of lack of improvement with oral flucloxacillin, she became hospitalized to do endovenous antibiotherapy (flucloxacillin plus clindamycin) and for further investigation. Laboratory tests revealed acute-phase reactants lightly elevated without leucocytosis (WBC 8700; c-reactive protein 7,2 mg/L; sedimentation rate 45 mm/h) and ultrasound exam showed “inguinal mass (3cm x 2cm) with a liquefied area associated with inflammation of subcutaneous tissue, compatible with an adenophlegmon”. Infection causes, such as, streptococcus, cytomegalovirus, Epstein-Barr virus, toxoplasma and mycobacterium tuberculosis, have been excluded and microbiological analysis of surgery resection was negative. Besides negative history of animal contact, bartonella serology was positive and the patient was treated with azytromycin. After a more detailed anamnesis it was possible to identify the contact with a friend’s cat, which was also treated.

Learning Points/Discussion

Cat-Scratch Disease (CSD) is a relatively common zoonosis, whose incidence in Portugal is probably underestimated. It is mainly characterized by self-limiting lymphadenopathy in the draining site of a cat scratch or bite. CSD should always be considered when there is no adenitis improvement with antibiotherapy correctly instituted, even if there is no epidemiologic context.

ESP16-0628
12. ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

SPLENIC BARTONELLOSIS - RARE CAUSE OF FEVER OF UNKNOWN ORIGIN
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Title of Case(s)

SPLENIC BARTONELLOSIS - RARE CAUSE OF FEVER OF UNKNOWN ORIGIN

Background

Fever of unknown origin is a diagnostic challenge in daily practice. Although most underlying causes are common, when atypical manifestations are present and the investigation doesn't lead to an obvious diagnosis, infrequent causes should be considered.

Case Presentation Summary

Previously healthy 14 year-old boy presented with 4-week history of fever, weight loss of five kilos and night sweats. His immunization program was updated. He lived in a rural region, didn't consume unpasteurized dairy and had no recent travels. Physical examination revealed cervical and inguinal lymphadenopathy (1,2 cm) with no inflammatory signs, abdominal pain, left shoulder discomfort and upper left abdominal tenderness at palpation.
Bloodwork showed haemoglobin 12,6 g/dL, 7,9x10^9/L leucocytes, 6,8% monocytes, 101 mm/h sedimentation rate and reactive C protein 139,2 mg/L, with no other abnormal results. Cervical echography ultrasound revealed accessory spinal and jugulocarotid lymphdenopathy with insuspect morphologic appearance and number, and no signs of absceded collections. At both abdominal ultrasound and CT scan, there was mild spleen enlargement with multiple hypoecogenic and hypodense infracentimetric lesions all over the splenic parenchyma, resembling micro-abscesses, Among other etiologic investigation, serologic testing was positive for *Bartonella henselae*. A 6-week treatment with rifampicin and ciprofloxacin resolved the fever and splenic nodules. Further enquiry revealed contact with an infected cat.

Learning Points/Discussion

Splenic bartonellosis is an atypical, rare presentation of the cat-scratch disease (5-14%) and poses itself as an important cause of prolonged fever in children. Rare clinical forms as splenic bartonellosis may have a prolonged course and need antibiotic treatment. However, the prognosis of these frequently undersuspected presentations is typically good, so as the prognosis of common cat-scratch disease.

ESP16-0084
12. ZOONOSES, VECTOR-BORNE AND EMERGING INFECTIONS

GENETIC DIVERSITY OF ORIENTIA TSUTSUGAMUSHI IN PAEDIATRIC PATIENTS OF SCRUB TYPHUS FROM NORTH INDIA

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Background

Scrub typhus, caused by the intracellular bacterium *Orientia tsutsugamushi*, is a zoonotic disease transmitted by the bite of the trombiculid mite. As there is great variation in antigenicity of *O. tsutsugamushi*, it is important to know the prevailing antigenic types for the success of diagnostic immunoassays and prospective vaccine candidates. Therefore, the current study was planned to identify the genotypes of *O. tsutsugamushi* circulating in Indian children suffering from scrub typhus in North India.

Methods

Whole blood was collected from children with suspected scrub typhus over a period of six months. The PCR products of a nested PCR targeting the 56kDa gene were sequenced and aligned using the ClustalX 2.1. A phylogenetic tree was constructed using our sequences and those obtained from the GenBank database by NJ algorithm using MEGA6 software. The evolutionary distances were computed using the Maximum Composite Likelihood method.

Results

Out of a total of 78 patients, 30, 17, 13, 11, 3, and 1 each were from Haryana, Himachal Pradesh, Punjab, Chandigarh, Uttar Pradesh, Uttarakhand and Nepal. Out of 30 positive PCR, sequencing of 26 isolates revealed that 62% of strains (n=16) clustered with Boryong B119, Boryong IIOC1223 and Boryong IIOC1221 which were 50%, 25% and 12.5% of Haryana, HP and Punjab respectively had 98%–100% sequence similarity with the Boryong strains. In remaining 23% (n=6) clustered with TH2033 strains, which is Karp-like prototypes. The Gilliam, Kawasaki, TH2191 and cloneT1125175 were also present.

Conclusions

O. tsutsugamushi strains circulating in Indian children share great similarity with Boryong strains and is widespread over a large area of north India. Boryong strains should be included in diagnostic assays as well as vaccines for scrub typhus for the Indian population.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0669
13. EPIDEMIOLOGY AND PUBLIC HEALTH

ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF DIARRHOEAIC BACTERIAL PATHOGENS FROM PAEDIATRIC PATIENTS IN LAGOS, NIGERIA

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Background

Acute diarrhoea associated with bacterial enteropathogens is an important cause of morbidity and mortality in infants and young children in most developing countries..The major challenge usually faced has to do with the increasing numbers of probable causative agents. The study was investigated to determine the prevailing bacterial enteropathogens and the patterns of antimicrobial susceptibility exhibited.

Methods

A total of 160 faecal samples were collected from infants and children presenting with symptoms of diarrhoea in three referral public health care centres in Lagos State. Stools samples were processed by standard bacteriological methods, the isolates were identified by standard procedures and were further subjected to antimicrobial susceptibility testing using standard methods.

Results

A total of 102 of the 160 faecal samples evaluated were positive for bacterial growth given a prevalence of 63.8%. The isolates were, made up of seven (7) bacteria genera. Co-existence of two or more bacterial enteropathogens were identified. *Enterobacter* spp. (47.1%) was found to be the predominant enteropathogen identified, followed by *Escherichia coli* (20%), *Klebsiella* spp. (11.4%), *Acinetobacter* spp. (8.6%), *Citrobacter* spp. (5.7%), *Salmonella* spp. (4.3%) and *Alcaligenes faecalis* (2.9%). The highest risk of diarrhoea was observed in age group 3 - 5 years. Antimicrobial susceptibility testing revealed that over 90% of the isolates susceptible to gentamicin, pefloxacin, augmentin, while over 60% of the isolates were susceptibility to co-trimoxazole.

Conclusions

This study revealed wide range of enteropathogens associated with childhood diarrhoea with *Enterobacter* species being the most prevalent organism. Gentamicin, perfloxacin and augmentin still proved effective against enteropathogens-associated childhood- diarrhoea. A need to adopt strategies of looking beyond routine identification of convectional diarrhoeaic agents for effective public health management of childhood diarrhoea is advocated

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0418
13. EPIDEMIOLOGY AND PUBLIC HEALTH

IMMUNIZATION AGAINST MENINGOCOCCAL B DISEASE IN CHILDREN AGED ≤14 YEARS. VALENCIAN REGION (SPAIN). YEAR 2015.

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Background

The meningococcal B vaccine is free of charge for risk groups established by the Heatlh Authority of the Valencian region (Comunidad Valenciana-CV) since 2014. The acquisition of the vaccine in chemists for general population is available since October 2015. The aim of the study was to evaluate meningococcal B immunizations in children aged ≤14 years registered in the Vaccination Information System (SIV) of CV in 2015.

Methods

Descriptive analysis of meningoccocal B immunizations registered in SIV by sex, age, risk group and dose.

Results

1,244 doses in children aged ≤14 were registered in SIV (53% of the global doses in all ages). 50.9% in males. The 30.1% were aged 0-11 months; 41.9% 1-4 years; 18.57% 5-9 years; 9.3% 10-14 years. 88.2% were first doses and 11.2% second ones. 82.56% were No-risk children, 6.43% had asplenia or splenic dysfunction.; 6.35% were meningococcal B contacts; 2.73% were deficient in properdina or terminal complement and 1.9% had a previous meningitis by serotype B.

Conclusions

Most of vaccinated children were aged less than 5 years. Only 18% of free of charge vaccinated children had some risk factor associated. Most children were healthy and had only one administered dose due to shortages of vaccines in chemist.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0454
13. EPIDEMIOLOGY AND PUBLIC HEALTH

SYSTEMATIC VACCINATION VERSUS INDIVIDUALIZED CALENDAR AGAINST PNEUMOCOCCUS IN THE VALENCIAN REGION, 2015

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Background

In 2015, the tridecavalent pneumococcal conjugate vaccine (PCV13) was included in the children vaccination program in the Valencian Region (Comunidad Valenciana – CV) Spain. Previously, the personal decision of parents vaccinating their children by private funding already generated nearly 70% overall coverage. Despite of the official recommended schedule (2 +1), some pediatricians still advise the standard 3 + 1 schedule to all children considering it necessary to achieve herd immunity.

The objectives are to determine the vaccination coverage and employed schedules of PCV13 in children born between the 1st of January 2015 and the 30th of September 2015 and to analyze the additional cost of the unnecessary third dose for parents and the public health system.

Methods

A descriptive cross-sectional study based on information from immunization and population records was done. Socio demographic variables, age, number of administrated doses, batch number and belonging or not to a risk group were analized.

Results

The average first dose vaccination coverage was 93.6%, it was 88.5% for the second and 20.4% for the third dose. Of the children receiving a third dose, 92.6% did not belong to any risk group, supposing a cost of 158,176.48 and 43,304.80 euro for parents and the public health system respectively.

Conclusions

Since the inclusion of PCV13 in the children vaccination program, high vaccination coverages have been reached. The indication of a third dose at 6 months should not be advised except for children belonging to risk groups. The added cost for both parents and the public health system are important. For the benefit of the population and vaccination programs, our clinical decisions should be more evidence based.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0914
13. EPIDEMIOLOGY AND PUBLIC HEALTH

PREVALENCE OF HEPATITIS E VIRUS ANTIBODIES in TURKISH CHILDREN THE CHANGE in LAST 15 YEARS

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Background

Infection of hepatitis viruses A, B and E are community health problems in developing countries and most common acute viral hepatitis in children. Hepatitis E virus (HEV) causes epidemics in developing countries. Turkey represents a bridge between HEV endemic and non-endemic areas, and HEV may cause epidemics in Turkey. The epidemiology of HEV infections in children is best defined by measuring humoral antibodies. For this reason the purpose of this study was to detect the change in the prevalence of HEV antibody by systematic reviews in published medical literature between the years of 2000-2015 in Turkey.

Methods

The study was planned and conducted in accordance with the declaration of PRISMA. To find the published series, two national databases (ULAKBIM and TURK MEDLINE) and one international databases (PubMed) were searched. Published manuscripts were evaluated according to the determined criteria for acceptance and rejection. For each study, anti-HEV IgG and anti-HEV IgM antibody rates were collected as a common unit

Results

After screening according to the applied acceptance and rejection criteria, 13 studies published between 2000 and 2015 were included in the study for evaluating HEV antibodies seroprevalance. Anti-HEV IgM 4.15±4.73 and anti-HEV IgG 4.24±4.67 (Mean±SD) between 2000 and 2015. Anti-HEVIgG seroprevalance under the five years 2.56±2.63, five to nine years 2.00±2.47, ten to sixteen years 2.03±2.73, respectively. Detailed HEV antibodies rates, author and publication date were presented in the Table.

Conclusions

In conclusion, we evaluated more than 5000 Turkish children HEV antibody prevalance over the fifteen years period. Frequency of HEV infection varies greatly depending on geographic region, socioeconomic level, age and various risk factors. To take preventive measures to protect themselves from infection with HEV is important to know the prevalence of HEV.

Systematic Review Registration (Please input N/A if not registered)

ESP16-0580
13. EPIDEMIOLOGY AND PUBLIC HEALTH

DIAGNOSIS AND TREATMENT OF CHILDREN WITH ACUTE DIARRHEA IN A TERTIARY CENTER IN TURKEY: MEDICAL COST ANALYSIS

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Background

Well-defined guidelines for diagnosis and treatment of acute diarrhea have been published in the literature, however in many cases these guidelines are not followed, which leads to unnecessary tests and treatments. The cost of these unnecessary tests and treatments constitutes an important percentage of health care expenses. In this study, we analyzed the cost of diagnostic and therapeutic procedures performed for patients with acute diarrhea that were admitted to pediatric emergency department and outpatient clinic at the tertiary center in Turkey.

Methods

A total of 342 patients under the age of 18 that were admitted to the pediatric emergency department and pediatric outpatient clinic, and were diagnosed with acute diarrhea were included to the study. The clinical features, diagnostic and treatment approaches as well as the medical costs of these patients were analyzed.

Results

The mean age of the patients was 58.2+56.4 months. Dehydration was not detected in 95% of patients. The diagnostic tests were performed in 257 patients (75.1%) and the most common test was the stool examination (52.6%). Moreover, the most common treatment was intravenous fluid therapy (14.6%) and 244 (71.3%) patients were discharged with only specific feeding recommendations. The mean total cost was 15.90+9.26 Euros, the mean laboratory test cost was 7.70+6.73 Euros, and the mean cost for treatment provided in the hospital was 1.83+4.30 Euros. Seventy percent of diagnostic testing costs and ninety percent of treatment costs were unnecessary according to the ESPHGAN guideline on diagnosis and treatment of acute diarrhea.

Conclusions

We believe that the health workers, especially pediatricians, can reduce the medical costs pertaining to diagnosis and treatment of acute gastroenteritis by following recommended procedures outlined in the guidelines.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0077
13. EPIDEMIOLOGY AND PUBLIC HEALTH

EVALUATION OF MATERNALLY ACQUIRED MEASLES, MUMPS, RUBELLA AND VARICELLA ANTIBODIES IN THE FIRST 6 MONTHS OF LIFE

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Background

The duration of maternal antibodies may be affected by regional variation therefore seroepidemiological studies from different parts of the world are needed.The main objective of our study was to evaluate the seropositivity of the mothers and their infants against measles, mumps, rubella and varicella in the first 6 months after delivery.

Methods

This prospective, multicenter study was conducted between May 2013 and May 2014 in 2 University hospitals, 1 private hospital located in Istanbul and 1 public hospital located in Ankara, Turkey. The mothers completed a detailed questionnaire. Blood samples were collected by venopuncture from 209 mothers and from all infants(n:209) at 1 month and 6 months of age. The determination of Ig G antibody values against measles, mumps, rubella, varicella were carried out by Enzyme-linked immunosorbent assays. All tests were performed according to the manufacturer's instructions.

Results

The seropositivity of mothers was 95.7% for measles, 92.8% for mumps, 92.8 % for rubella, and 96.7% for varicella. Majority of infants lost maternal antibodies at 6 months of age. Of all 6 month-old infants 25% was seropositive for measles. This figure was 14.6% for mumps, 23.2% for rubella and 17.1% for varicella. The proportion of seropositive infants born to seropositive mothers was higher than those born to seronegative mothers at 1 month of age (p=0.001).

Conclusions

Our study is the first cohort study conducted in Turkey and our results showed that majority of infants at 6 months of age were susceptible for MMRV infection. As the epidemiology of the diseases changes in time, it is important to carry out such studies in each country.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0336
13. EPIDEMIOLOGY AND PUBLIC HEALTH

WHAT CAN THE CURRENT INFLUENZA VACCINATION POLICY FOR CHILDREN IN SWEDEN HOPE TO ACHIEVE BASED ON EPIDEMIOLOGICAL DATA FROM 16 INFLUENZA SEASONS?

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Background

Influenza is a common pathogen in the young pediatric population. Viral strain, herd immunity and climate contribute to varying hospitalization rates from year to year. Monitoring over several seasons is required to characterize patterns of influenza epidemics in children. The current policy is to vaccinate children with known risk factors for severe influenza infection.

Methods

Retrospective study of hospitalized children 0-17 years of age with influenza infections during 16 seasons spanning from December 1997 to May 2013 in the northern Stockholm area. Information about comorbidities, complications and length of stay was collected annually from patients' records with virologically confirmed influenza.

Results

887 cases of confirmed influenza infections were found during the studied period. On average, 51% of the children had complications and 39% of admitted children had comorbidities. Intensive care treatment was required for 19% of children with comorbidities and for 6% of previously healthy children. Six children, three of which previously healthy, died of their influenza infection during the studied period.

Conclusions

Our study highlights the importance of vaccination in known risk-groups to prevent the majority of severe infections. At the same time, by targeting children with risk factors only, the current Swedish vaccination policy fails to prevent the majority of hospitalizations accounted by previously healthy children.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0305
13. EPIDEMIOLOGY AND PUBLIC HEALTH

MOLECULAR ANALYSIS OF ISOLATED ENTEROVIRUSES IN KOREAN CHILDREN

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Background

Enterovirus(EV) infection in children can manifest various diseases from asymptomatic infection to nonspecific febrile illness, hand-foot-mouth disease, and aseptic meningitis. This study was aimed to analyze the serotype, genetic strain and epidemic pattern of EVs during the epidemic season of hand-foot-mouth disease in children.

Methods

We collected the stool samples from the admitted pediatric patients in Inha University Hospital. Serotype identification were performed by semi-nested RT-PCR amplification of the genomic region coding viral structural protein VP1 for identification of EVs. Sequence data for each isolate was formatted and compiled into contiguous segments and phylogenetic trees were constructed by neighbor joining method.

Results

A total of 52 VP1 sequencing of EVs were analysed; coxsackievirus B5 (17, 32.7%), coxsackievirus A16 (11, 22.2%), coxsackievirus A2 (8, 15.4%), enterovirus 71 (6, 11.5%), echovirus 11 (3, 5.8%) and coxsackievirus A14 (2, 3.8%), coxsackievirus A6(1, 1.9%), coxsackievirus A12(1, 1.9%), coxsackievirus B2(1, 1.9%), echovirus 9 (1, 1.9%) and echovirus 25 (1, 1.9%). Coxsackievirus B5 strain 09-5428 and CF199017CSF_FRA_11 were the most common isolates (58.8%), followed by 17Y (23.5%), 13107-4/Kanagawa/JPN/2013 (11.8%) and CB5/Okinawa/13/2012 (5.9%). Coxsackieviruses A16 isolate 12MC7_2012.02_XH was predominant strain in coxsackievirys A16 serotype (72.7%). Human enterovirus 71 isolate H11-24-KOR and isolate H11-40-KOR accounted for the majority of EV71 serotype (66.6%). Phylogenetic relationship tree revealed 4 distinct clusters.

Conclusions

Though diverse EV serotypes circulated among children, this study shows the molecular similarity within the genetic clusters. Our data will provide the scientific evidence for prevention and management of EV infection.

Acknowledgement: This research was supported by national enterovirus surveillance system (4800-4850-300) of the Korea Centers for Disease Control and Prevention

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0455
13. EPIDEMIOLOGY AND PUBLIC HEALTH

DECLINE OF VACCINATION COVERAGE AGAINST MEASLES IN COHORTS BORN 2011-2013 IN SLOVAKIA: A REASON FOR CONCERN?

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Background

In Slovakia vaccination against measles was introduced in 1969. At present, we use trivalent vaccine (measles, mumps and rubella), first dose is recommended for children aged 15–18 months (MCV1) and the second one for 10 years old (MCV2). Our objectives include analysis of measles vaccination coverage in cohorts of Slovak children aged 24-months (MCV1) and 10 years (MCV2) at national and regional levels.

Methods

Retrospective review of vaccination coverage of measles reported from 2000 to 2015. Cohort studies evaluating measles vaccination coverage in 24-months-old children born between 1998 and 2013 (MCV1) and 10-years-old children by age-group from 1987 to 2003 (MCV2) were conducted. The epidemiological data were obtained from the Epidemiological Information System of the Slovak Republic. Data on vaccination coverage were obtained from the annual administrative monitoring in Slovakia.

Results

In Slovakia, no endemic measles cases were reported during 2000-2015. Since 1999, measles has been eliminated, only imported cases were reported in our country. The vaccination coverage remained at the highest levels (98.0-99.9%) during the whole studied period. The reported annual vaccination coverage ranged from 93.9% to 99.9% at national level and from 90.1% to 99.9% at regional levels in the controlled cohorts. In the last children cohorts (born in 2011, 2012, 2013) vaccination coverage decreased from 93.9% to 96.8%.

Conclusions

Timing and timeliness of measles vaccination influenced effective population vaccination coverage and herd immunity. Increasing of anti-vaccination activities and risk populations (Romany population and migrants) are the main risk factors affecting the vaccination coverage.

Our analysis showed the positive impact of vaccination against measles on the epidemiological situation in Slovakia. This work was supported by the Slovak Research and Development Agency under Contract No. APVV-0096-12 (EPIBIOMAT).

ESP16-0311
13. EPIDEMIOLOGY AND PUBLIC HEALTH

PATTERN OF BETA-LACTANS ANTIMICROBIALS' CONSUMPTION IN PEDIATRIC HOSPITAL SECTOR

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Background

Objective: to scrutinize the proportions of beta-lactam antimicrobials classes consumption in the pediatric wards of an Infectious Diseases clinic

Methods

Reference population was represented by all the patients (0-14 years old) admitted to the pediatric wards of our 500 beds hospital in the first semester 2015. Antibiotic consumption was expressed as number of DDDs per 100 bed days and data were allocated to the Anatomic Therapeutic Chemical Classification (ATC) subgroups. The proportions of consumption of beta-lactam penicillins (ATC group 101C) and other beta-lactam antimicrobials (ATC subgroup J01D) in our study (ROU) were compared with the proportions of consumption of the similar ATC subgroups reported at European Union (EU) level in 2011

Results

In our study consumption of J01C antimicrobials was with 18.6 % lower than in UE ($p< 0.05$) while consumption of J01D antimicrobials was with 19.3 % higher than in UE ($p< 0.05$) (See Table nr. 1)

Table 1 – Proportions (%) of consumption (DDD/bed days) of antimicrobial by selected classes in the study population and European Union (*) respectively

ATC 01 Subgroups	ROU	UE	Difference	P value
J01C Beta-lactam penicillins	17.9	36.5	- 18.6	0.004145
J01D Other Beta-lactam antibacterials	42.6	23.3	+ 19.3	0.002633
Other (J01B, J01G, J01R and J01X)	39.5	40.2	- 0.7	1.000000

(*) http://www.ecdc.europa.eu/en/publications/Publications/antimicrobial-consumption-europe-surveillance-2011.pdf

Conclusions

The main signification of the discordant data shown above is that in the study population the use of cephalosporin and carbapeneme surpass the use of penicillins which represents a deviation from published guidelines and medical evidences.

ESP16-0314
13. EPIDEMIOLOGY AND PUBLIC HEALTH

SUSCEPTIBILITY TO ERYTHROMYCIN OF GROUP A BETA – HEMOLYTIC STREPTOCOCCUS ISOLATES FROM PEDIATRIC PATIENTS

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Background

Resistance to Erythromycin is rising making difficult treatment of infections with Group A Beta – Hemolytic *Streptococcus* (GABHS) in patients allergic to beta lactam antimicrobials. ***Aim***: describe prevalence of GABSHS susceptible to Erythromycin and search for risk factors associated with this, in children.

Methods

Susceptibility to antimicrobials of nasopharyngeal GABHS isolates in 2014 in our 500 beds clinic of infectious and tropical diseases was displayed in MS Excel®) table format; along with each isolate was added the date of isolation and age and gender of patient source. A single isolate per patient was included in analysis. Rates and statistical comparing were done with Epi Info 2000 software. CLSI criteria for disk diffusion test and result interpretation was used.

Results

A total of 481 isolates were analyzed; the median age of source patients was 12 years, and the male / female ratio was 0.89.

The prevalence of GABHS susceptible to Erythromycin was 80.9% (CI 95%: 77.0% - 94.2%)

Prevalence of susceptible isolates was similar by gender (girls77.5% vs boys83.5%) ($\chi 2$: 2.8309; df: 2; p: 0.2428), by age group (preschool 80.0% vs school 81.1%) ($\chi 2$: 4.5441; df:2; p1031) and patient type (inpatient: 79.4% vs outpatient: 81.6%) ($\chi 2$: 1.0546; df:2; p: 0.5902) bat was statistical significant higher in cold season (November to February) than in rest of the year (cold season: 88.3% vs warm season 75.8%)($\chi 2$:12.0824; df: 2: p:0.0024).

Conclusions

Clinicians should be averted that in warm season one in five patients may be carrier or infected with a GABHS

ESP16-0210
13. EPIDEMIOLOGY AND PUBLIC HEALTH

BURDEN OF HEPATITIS B SURFACE AND ENVELOPE ANTIGENAEMIA IN ADULTS AND CHILDREN IN A TERTIARY HOSPITAL IN A DISADVANTAGED REGION OF NIGERIA: 2000 -2015

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Background

Hepatitis B infection is endemic in sub-Saharan Africa and Nigeria bears a disproportionately higher burden of this infection. Hepatitis B vaccination, a proven intervention for preventing the morbidity remains low especially in this region of the country. No National guidelines exist for the management of Hepatitis B. This is a survey of test results within the study period.

Methods

Records of Hepatitis B surface and envelope antigen rapid strip assay test results from adults and children in the central medical microbiology unit from 2000-2015 were retrieved and analyzed. Each test strip incorporates a built-in procedural control for reagent stability. Federal Teaching Hospital, Gombe is a 420 bed health facility and leading tertiary health institution in the North East sub region of the country.

Results

23,688 were tested; 11% (2,626/23866) children. 19% (4536/23,866) were Hepatitis B surface antigen positive; 70.3% (3188/4536) males. 18.9% (496/2,626) of children and 19.8% (4,040/20,262) of adults were hepatitis B surface antigen positive. Peak Hepatitis B surface antigen positivity in children was among adolescents 20.5% (352/1717); and in adults aged 26-45, 21.2% (2559/12,039).

84% (3,821/4,536) of HBSAg positive individuals were tested for envelope antigen. 9.4% (360/ 3821) of hepatitis B surface antigen positive children and adults tested positive for envelope antigen. Dual carriage was highest in infants and young children 56.2% (9/16) and highest in adults ages 19-25years 39.2% (113/288).

Conclusions

There is a high burden of Hepatitis B surface and envelop antigenaemia in adults and children in the sub-region. Hepatitis B surface antigenaemia is highest among young adults. Dual sero-positivity is highest in infants and young children. This high seroprevalence has profound implications for chronic liver disease and hepatocellular carcinoma. Strengthening immunization and appropriate case management are priorities.

ESP16-0150
13. EPIDEMIOLOGY AND PUBLIC HEALTH

INCIDENCE OF VARICELLA PEDIATRIC HOSPITALIZATIONS IN ILE DE FRANCE (2009 – 2012)

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Background

Varicella is a benign highly contagious ubiquitous human disease affecting mainly young children that induce hospitalizations for severe cases. Varicella vaccines, available in France since 2004 are not included in the NIP and vaccination coverage is very low. The aim of this study was to define the incidence of hospitalized varicella in the most populated area in France (about 2.3 millions of children 0 to 14 years old).

Methods

Between September 2009 and August 2012, our network of 41 pediatric wards systematically reported data on children admitted in hospital services for varicella.

Results

783 children were enrolled (<5 years= 89.8%) of whom 2 were vaccinated. Superinfection was reported in 51.9% of cases and 3 patients died. The incidence of hospitalized varicella significantly decreased (2009-2012) particularly in children < 5 years.

	Incidence /100.000			Incidence Rate Ratio (95%CI)		
Age (years)	2009/2010 Year 1	2010/2011 Year 2	2011/2012 Year 3	Year 2 vs Year 1 *p*	Year 3 vs Year 2 *p*	Year 3 vs Year 1 *p*
<5	39.9	32.5	24.7	0.81 [0.69; 0.96] ***0.012***	0.76 [0.63; 0.91] ***0.003***	0.62 [0.52; 0.74] ***<0.001***
5/9	4.3	2.7	2.4	0.63 [0.27; 1.09] *0.098*	0.90 [0.48; 1.67] *0.73*	0.57 [0.32; 1] ***0.046***
10/14	0.8	0.3	0.3	0.33 [0.07; 1.64] *0.178*	0.99 [0,14; 7,02] *1*	0.33 [0.07; 1.62] *0.175*
Total	18.2	12.5	9.6	0.69 [0.59; 0.80] ***<0.001***	0.77 [0.64; 0.91] ***0.003***	0.53 [0.45; 0.62] ***<0.001***

Conclusions

As varicella vaccination coverage is very low in our country, the important and significant decrease of hospitalized varicella incidence (18.2 vs. 9.6/100.000), observed between 2009

and 2012 is probably due to natural epidemiological variation. Morever, these results must be qualified since the incidence was particularly high in the 2009/2010-reference year.
Acknowledgment: This study was funded by GlaxoSmithKline

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0032
13. EPIDEMIOLOGY AND PUBLIC HEALTH

PREMATURE RUPTURE OF MEMBRANES WAS CLOSELY CORRECTED WITH RESPIRATORY DISTRESS SYNDROME IN TERM NEONATES

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Background

Premature rupture of membranes (PROM) is a common clinical complication with an incidence of 20% which adversely influence fetal lung development and even result in respiratory distress syndrome (RDS) in premature infants. However, the correlation between PROM and full-term neonatal RDS remains controversy. This study was assigned to investigate their relationships by retrospective case-control study.

Methods

From Jan. 2010 to Dec. 2014, a total of 1580 full- term newborns with RDS were included in the study group who were administrated in the Department of Neonatology＆NICU, Bayi Children's Hospital Affiliated to Beijing Military General Hospital. At the same periods, 3160 full-term neonates without RDS were assigned as control group. The clinical information including the presence or absence of PROM, gender of the babies, mode of delivery, birth weight, and any conditions suffered by the infants, etc. were recorded to compare their difference between two groups.

Results

(1)The incidence rate ofPROM was 30.1% in RDS patients as higher as compared to those without RDS patients15.7%（χ^2=12.57,p<0.001）.(2)Univariate analysis showed that PROM, selective cesarean section, male, low birth weight, oligohydramnion, meconium staining of amniotic fluid, severe fetal distress and birth asphyxia are the main risk factors of full-term neonatal RDS (p<0.05). (3)The Logistic regression analysis showed that PROM, selective cesarean section, male, low birth weight, gestational glucose abnormoalities, and birth asphyxia was closely correlated with RDS in full-term newborns.

Conclusions

PROM is closely correlated with RDS in full-term neonates, this finding is significance for the clinical management of RDS in term newborns. This work was supported by the Clinical Research Special Fund of Wu Jieping Medical Foundation (320.6750.15072）.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0559
13. EPIDEMIOLOGY AND PUBLIC HEALTH

EPIDEMIOLOGICAL EVALUATION OF MEDITERRANEAN SPOTTED FEVER IN CHILDREN OF THE KARAK PROVINCE IN SOUTH JORDAN

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Background

Introduction: The aim of this study was to describe the epidemiological patterns of Mediterranean spotted fever (MSF) as well as its treatment and outcomes in children in south Jordan.

Methods

Methodology: We conducted a retrospective observational study from June 2013 to December 2015. Data regarding demographics, the clinical presentation, laboratory findings, treatment, and outcomes were collected.

Results

Results: Thirty-five males and 20 females (mean age: 6 years ± 3.6) were included. The incidence was 7.9 cases per 100,000 inhabitants/year; MSF affected 89% of individuals in the summer, 74.5% of those living in a rural area with tent housing, and 100% of those who had contact with animals. All cases presented with fever, and 94.5% had a skin rash. Serological tests were positive in 87.2% of cases, and *Rickettsia conorii* (the Moroccan strain) was present in all positive cases. All cases had thrombocytopenia, but none had leukocytosis. Hyponatremia was present in 71% of cases, and 49%, 61.8%, and 72.7% had an increased urea, alanine transaminase, and aspartate aminotransferase levels, respectively. Doxycycline was administered to all patients with a cure rate of 96.4% and mortality rate of 3.6%.

Conclusions

Conclusions: MSF caused by *R. conorii* (the Moroccan strain) is prevalent in Jordan, and contact with animals is a common route of transmission. Patients' response to doxycycline was excellent. A high index of suspicion, an early diagnosis, and specific treatment considerably decrease mortality. MSF should be considered as a possible cause of febrile disease in those with a rash and in those living in rural areas.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0296
13. EPIDEMIOLOGY AND PUBLIC HEALTH

EPIDEMIOLOGY OF BONE AND JOINT INFECTIONS IN FRENCH GUIANA

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Background

Given the diversity of management for paediatric bone and joint infections in French hospitals, guidelines were issued in 2008 by the “Groupe de Pathologie Infectieuse Pédiatrique”

Studies showed that the most frequent pathogen found in metropolitan France for these infections to be *Kingella kingae.*

In French Guiana (the only French overseas department located in South America), no epidemiologic study regarding which types of pathogens were the most frequently encountered has ever been performed.

The aim of our study was to perform an inventory of bacteria responsible for paediatric bone and joint infections in French Guiana, as well as an inventory of the duration of antibiotic therapy for these infections.

Methods

We retrospectively collected data from all 3 hospitals in French Guiana (Cayenne, Kourou, Saint Laurent du Maroni) for children under 18, admitted for haematogenous bone and joint infection (osteomyelitis, septic arthritis, spondylodiscitis) between January 1, 2010 and December 31, 2015.

Results

76 patients were analysed for this 6-year period (58 boys, 18 girls). The mean age was 8. A pathogen was found in 40,7 % (31/76) of the analysed patients. *Kingella kingae* was found in none of the analysed patients. The main pathogen found was *Staphylococcus aureus* (24/31 patients). Some of these *Staphylococcus aureus* infections, due to Panton Valentine leukocidine secreting strains, were associated to severe outcomes (1 death, 1 hemorragic pericardic effusion requiring urgent surgical intervention). The mean duration of antibiotic therapy was 12,4 days for intravenous antibiotic therapy and 31,4 days for oral antibiotic therapy.

Conclusions

The majority of documented infections in French Guiana are due to *Staphylococcus aureus*, but antibiotic therapy durations are similar to the ones found in metropolitan France.

ESP16-0369
13. EPIDEMIOLOGY AND PUBLIC HEALTH

MOLECULAR CHARACTERIZATION OF NON-VACCINE SEROTYPES 11A, 15 B/C AND 23A OF STREPTOCOCCUS PNEUMONIAE RECOVERED FROM INVASIVE DISEASE OF 1994 TO 2014 IN COLOMBIA

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Background

A total of 192 invasive *Streptococcus pneumoniae* isolates from serotypes 11A, 15B/C and 23A (Not included in the conjugated vaccines) were collected in Colombia between 1994 and 2014 as part of the Network surveillance system for the causative agents of pneumonia and meningitis (SIREVA II).

Methods

Molecular characterization of the isolates was carried out through pulse field gel electrophoresis (PFGE) and selected strains were analyzed by Multilocus sequencing type (MLST).

Results

Serotype 11A showed one clonal group represented by ST62. Serotype 15B/C was composed by three groups associated with Netherlands^{15B}-37 ST199 (28.75%), ST8495 (18.75.5%), and SLV (Single-Locus Variant) of ST193 (21.25%). Isolates from serotype 23A were gathered in three clonal groups where 70.21% of them were closely related with the ST42, 17.02% with Colombia^{23F} ST338, and 6.38% with Netherlands^{15B}-37 ST199.

Conclusions

The two successful clones Colombia^{23F} ST338 andNetherlands^{15B} ST199 found in this study covered more serotypes than the reported previously by other authors including now the serotype 23A, remarking the importance of the capsular switching to spread the successful clones between the non-vaccine serotypes for causing invasive pneumococcal disease.

ESP16-0493
13. EPIDEMIOLOGY AND PUBLIC HEALTH

IMMUNIZATION COVERAGE, IN CHILDREN 12 YEARS OLD, IN WESTERN GREECE

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Background

Immunization coverage in children in Greece has achieved high levels during the previous years. However, recent poor economic situations in the country may have influenced children's admissions to pediatric surgeries, especially for preventive medicine. The main purpose of our study was to investigate the immunization coverage in children who live in Patras.

Methods

There were randomly selected 12 public primary schools in Patras, all in urban areas. All children who were born between 2003 and 2004, and whose parents gave consent, were included in the study. Immunization data were collected through the National pediatric vaccination cards. The sampling took place between September and December 2015.

Results

There were 325 subjects enrolled in the study. The mean age was 12 years and 45.5% were boys. Children were fully vaccinated against Hepatitis B (97.9%), Tetanus, Poliomyelitis, Diphtheria, Pertussis and *Haemophilus Influenzae* (97.3%). Additionally, they were fully vaccinated against Measles, Mumps, Rubella (98.2%), Varicella (80.57%), Hepatitis A (84.7%) and *Meningitidococcus* type C (97.3%). The vaccination coverage was low for *Streptococcus Pneumoniae* (54.2%), *Mycobacterium* (BCG, 28%) and *Meningitidococcus* type B (1.6%).

Conclusions

Immunization coverage in children (12 years old) in Patras remained in high levels. A lower vaccination coverage was observed against *Streptococcus Pneumoniae*. Greek children were almost not vaccinated against *Mycobacterium* and *Meningitidococcus* type B. The reasons of this low vaccination coverage should be explored. We should mention that the Meningitis B vaccine is not yet included in the National Vaccination Program. There is a need for a national strategy plan in order to increase vaccination, especially against *Streptococcus Pneumoniae*, *Mycobacterium* and *Meningitidococcus* (type B).

ESP16-0988
13. EPIDEMIOLOGY AND PUBLIC HEALTH

MEASLES ACTIVITY DURING THE 2011-2015 PERIOD IN SAO PAULO STATE, BRAZIL

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Background

This report describes measles activity in Sao Paulo State (SPS), Brazil, during the 2011 – 2015 period, despite declared measles elimination.

Methods

Measles cases were described by geographic distribution, age group, immunization status, hospitalization, travel history and genotype information.

Results

A total of 1420 suspected and 42 confirmed measles cases (2.9%) were reported during 2011-2015 period, in nine municipalities. Most cases occurred during 2011 (526 suspected, 27 confirmed – 5.1%). The highest proportion of cases was in children under 1 year of age and individuals aged 20 to 24 years (n = 9 (21.4%); n=7 (16.7%), respectively). Therefore, incidence rate was higher among younger age groups (< 1 year: 1.6 cases/ 100,000 inhabitants/ year; 1 year old: 0.4 cases/ 100,000 inhabitants/ year). Less than half of cases were vaccinated (n=16; 40%); 13 of them (81.3%) were not fully vaccinated, having only one dose of Measles Mumps Rubella vaccine (MMR) after one year of age, mainly individuals from 11 to 29 years (n=9; 69.2%). Hospitalization occurred in 11 of cases (26.2 %), mostly among those aged 20 to 24 years (n=3; 27.2%). Measles genotypes were detected in 22 cases (52.4%). Genotypes identified were D4 (n=13), D8 (n=8) and B3 (n=1), while travel history was reported by 10 cases (23.8%) .

Conclusions

Although endemic measles transmission was interrupted around 2000, sporadic cases continue to be identified. Incidence rate, vaccination status, hospitalization and distribution by age group indicated the importance to reach individuals over 11 years of age, who are most needed to update immunization status (MMR second dose) to prevent measles transmission.

ESP16-0306
13. EPIDEMIOLOGY AND PUBLIC HEALTH

GASTROENTERITIS CAUSED BY CAMPYLOBACTER IN CHILDREN: EPIDEMIOLOGY, CLINICAL AND LABORATORY FINDINGS, A COMPARISON WITH OTHER PATHOGENS THAT CAUSE A SIMILAR DISEASE

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Background

Bacterial gastroenteritis is a common disease in children. The clinical symptoms include abdominal pain, restlessness, vomiting, diarrhea, bloody stools and dehydration. *Campylobacter jejuni* is one of the main causative pathgens. The purpose of the present study is to check if *campylobacter jejuni* is the leading pathogen of gastroenteritis with bloody stools and to compare the clinical and laboratory findings to other pathogens that cause a similar disease.

Methods

A retrospective study on children hospitalized with acute gastroenteritis with bloody stool and positive stool culture between 2003-2012.

Results

Positive stoolcultures were found in 622 patients, 266(43%) females and 356 (57%) males. 367(59%) Arabic origin and 255(41%) Jewish origin. *Campylobacter* is the leading pathogen (53.3%), followed by *shigella* (24.4%) and *salmonella* (21.2%). The median age of the children in the *campylobacter* group is 17 months, 63 months in the *shigella* group and 12 months in the salmonella group. We found a statistical difference in age between *campylobacter* and *shigella* groups (P<0.001) and between *shigella* and *salmonella* (p<0.001). In the *campylobacter* group; *campylobacter jejuni* was isolated in 288/332(86.7%) patients, in the *shigella* group; *shigella sonnei* was isolated in 145/158(91.7%) and in the *salmonella* group all the isolates were *salmonella enterica*. *Campylobacte*r bacteremia was found in two patients. Children with *campylobacter* recovered with macrolides. The *shigella* and *salmonella* group were highly sensitive to ceftriaxone and ciprofloxacin.

Conclusions

Campylobacter jejuni is the leading pathogen in children hospitalized with bacterial gastroenteritis, followed by *shigella* and *salmonella*. Children in the *shigella* were older than patients in the other groups. Bacteremia is rare complication. Macrolide is the drug of choice for *campylobacter,* ceftriaxone and ciprofloxacin are the best empiric treatment for *shigella* and *salmonella*.

ESP16-0092
13. EPIDEMIOLOGY AND PUBLIC HEALTH

PREVALENCE OF HEPATIS C VIRUS INFECTION AMONG ASYMPTOMATIC PAKISTANI CHILDREN

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Background

Hepatitis C infection is alarmingly high in Pakistan, reaching almost 7%.So this study was carried out to find the incidence in our children.

Methods

This study was conducted at Pediatrics Medicine Department of Akhtar Saeed Trust Hospital,Lahore.It was performed on 1358 successive asymptomatic patients both inpatients as well as outpatients. It was a descriptive cross-sectional study.Sampling was done by non-probability purposive technique. Consecutive patients of all ages of pediatrics with mean age of eight years were taken. Anti-HCV kits were used to screen all blood specimens. Rapid chromatography immunoassay for qualitative detection of antibodies for hepatitis C was the screening technique. Those found positive on screening test were confirmed by ELISA. SPSS version 16.0 was applied for statistical analysis. Percentages were calculated directly for HCV. Statistical significance was established at a level of $P < 0.01$ and confidence interval was taken at 99%.

Results

During this study, blood specimens of 1358 participants were screened for C.Female participants were 50% and males 50% of the studied population.After screening, 0.3% (4/1358) were found to be sero-positive anti-HCV.

Conclusions

The level of the recorded prevalance values calls for the completion of programs expected at detecting clusters or population areas at risk.Ali and collegues showed 2.1% prevalence in children in Pakistan..[5]Anyhow, further studies are needed at the national level - with depiction from across the country to determine the actual disease burden in the pediatric population of Pakistan.There is need to edify public through a well structured infection control programme , scattering awareness and teaching of infection control events. Larger population based studies are needed to confirm the results.

Systematic Review Registration (Please input N/A if not registered)

n/a

ESP16-0830
13. EPIDEMIOLOGY AND PUBLIC HEALTH

PREVALENCE OF VARICELLA ZOSTER VIRUS IGG ANTIBODIES AND DETERMINANTS OF SEROPOSITIVITY IN CHILDREN AND ADOLESCENTS IN THE PRE-VACCINE ERA, GERMANY

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Background

Primary varicella-zoster virus (VZV) infection results in chickenpox. Since 2004 routine vaccination of children (11–14 months) is recommended in Germany. Evaluation of the vaccination strategy is supported by sero-epidemiological data before and after implementation of a routine vaccination.
Objectives: Determination of age-specific prevalence of anti-VZV IgG-antibodies in the pre-vaccine era and identification of factors which are associated with seropositivity.

Methods

Serum samples of 13,433 varicella-unvaccinated children aged 1-17 years of the population-based German Health Interview and Examination Survey for Children and Adolescents (KiGGS; conducted 2003-2006) were tested for anti-VZV-IgG by EUROIMMUN-ELISA. Equivocal results were retested by fluorescent antibody to membrane antigen test (FAMA).

Statistical analyses used a weighting factor adjusting the study population to the German population. Seroprevalence is reported as percentages (%) with a 95% confidence interval (CI). Odds ratios (OR) were computed by multivariate logistic regression to determine the association between socio-demographic factors and seropositivity.

Results

Overall seropositivity rate was 80.6% (95% CI 79.4-81.2%). Seropositivity rates differed significantly between age-groups up to the age of six years, but not by gender. About 95% of adolescents had anti-VZV IgG-antibodies. Multivariate analyses showed that beside age, older siblings and early start of day care were main factors increasing seropositivity rate in preschoolers; migration background reduced the chance of seropositivity in school-children (OR: 0,65; 0,43-0,99) and adolescents (OR 0,62; 0,4-0,97).

Conclusions

This study delivers baseline data to monitor the impact of the routine varicella vaccination strategy in Germany for a follow-up with seroprevalence data from the post-vaccine era.

During the pre-vaccine era most children contracted VZV-infection by the age of six. Identified risk groups for reduced seropositivity, such as school-children with migration background, should be targeted for catch-up vaccination.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0255
13. EPIDEMIOLOGY AND PUBLIC HEALTH

CURRENT PROBLEMS OF VACCINATION-PREVENTABLE DISEASES IN SLOVAKIA FOR THE YEARS 2000 TO 2014

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Background

Vaccination has a positive impact on the epidemiological situation in Slovakia. The obligatory vaccination of children in Slovakia is historically traditional. Vaccination against 12 diseases was gradually established from year 1876 to 2009. Nowadays, children are vaccinated against 10 diseases. Aim of our study was a retrospective analysis of occurrence of the vaccination preventable diseases and of the vaccination coverage.

Methods

We compare the incidence of diseases during the last 15 years (between 2000 and 2014). Data were obtained from Epidemiological Information system of the Slovak Republic, data about vaccination from the annual administrative monitoring and data about tuberculosis incidence from the National registry of patients diagnosed with tuberculosis. We also processed the changes of legislative actions in Slovakia about establishing regular vaccination of children.

Results

The elimination of measles, polio, diphtheria and tetanus (zero morbidity in a long term) was declared. Comparing years 2004 and 2014 the incidence was decreased for tuberculosis (20.6 and 13.10 per 100,000 inhabitants), rubella (0.20 and 0.00), hepatitis B (3.05 and 1.57) and Haemophilus influenzae type b (0.30 and 0.06); was increased for pertussis (0.80 and 20.73), mumps (0.59 and 28.78) and pneumococcal disease (0.04 and 0.66). In 2014, the boundary of 90% of vaccinated children was not reached in 16.7% of paediatric counties.

Conclusions

In Slovakia were achieved excellent results for the vaccination-preventable diseases. The decrease of vaccination coverage in recent years has local reasons, such as refusal of vaccination, antivaccination-activities, irresponsible attitude of Romani parents towards vaccination or their migration, and more. Nowadays, the threat is also posed by the external factors – arrival of the immigrants to the European Union.

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ESP16-1094
13. EPIDEMIOLOGY AND PUBLIC HEALTH

ROTAVIRUS GENOTYPES CIRCULATING IN GREECE DURING THE POST VACCINATION ERA (2011-14)

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Background

Rotavirus (RV) is the commonest cause of viral gastroenteritis in children <5 years old. In 2007 two RV vaccines (Rotarix and Rotateq) were licensed in Greece. Aim of our study was to describe the diversity of RV genotypes circulating in Greece and evaluate the impact of limited vaccine uptake in the natural fluctuation of the virus.

Methods

Faecal samples from children <5 years old who visited emergency units of 12 Pediatric Hospitals with acute gastroenteritis between September 2011-August 2014. Samples were tested for RV Group A antigen with a rapid immunochromatography kit. Positive samples were further G and P typed through multi-nested PCR and sequencing using specific primers for the VP7 and VP4 genes respectively.

Results

A total of 1157 samples were genotyped; male outnumbered female (55%). Mean age of children was 29 months and 69% belonged to children ≤3 years old. Seasonal peak of RV presented between December and March, as 57% of the samples were collected during these months. Predominant types were G4P[8] (48,2%), G2P[4] (23,8%), G1P[8] (14,8%), G3P[8]

(2,4%), G9P[8] (3,2%), G12P[8] (1,2%); G4P[8] was the most predominant genotype in all seasons except for the 2012/13 that G1P[8] was the most frequent. Mixed and uncommon infections were account for 3,5% and 2,9% respectively. Although genotypes were not associated with the gender or the age of the children, differed geographically and temporally ($p<0,001$).

Conclusions

The post vaccine distribution of RV genotypes does not follow a specific pattern as a possible impact of the use of the two RV vaccines in Greece. Continuous post-vaccine surveillance is essential for monitoring the current molecular epidemiology of RV and assessing the possible genetic evolution of RV strains as an effect of vaccine implementation.

ESP16-0102
13. EPIDEMIOLOGY AND PUBLIC HEALTH

HPV-VACCINATION COVERAGE IN FLANDERS 5 YEARS AFTER LAUNCHING THE VACCINATION PROGRAMME FOR YOUNG GIRLS

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Background

In September 2010 HPV-vaccination for young girls was added to the vaccination programme of Flanders. Vaccines are made available free of charge to vaccinating school health services, general practitioners and paediatricians. They are supposed to register all vaccinations in a central registry linked to the vaccine ordering system in Vaccinnet. The first 4 school years the 4-valent vaccine was used in a 3-dose schedule. Since September 2014 the 2-valent vaccine is used in a 2-dose schedule.

Methods

We want to estimate the HPV-vaccination coverage as follow-up of the vaccination programme. To do so, all available HPV-vaccination information was extracted from the vaccination database for all girls born in the age groups involved. Data of the target age groups for HPV-vaccination for the consecutive years were analysed. Vaccination coverage was estimated based upon these registrations and target groups.

Results

In the different consecutive years, the registered vaccination data in girls show a participation degree to the vaccination programme of over 85%, with a vaccination coverage for full vaccination of 82%. There was little variation over the consecutive years. These numbers should be considered as a minimal coverage as registration isn't always complete. About 95% of HPV-vaccinations were registered by school health services for each of the vaccination moments.

Conclusions

General vaccination of young girls in the first year of secondary school is well accepted in Flanders. A stable participation degree over years of over 85% and about 82% coverage for complete vaccination are observed.The possibilities of offering HPV-vaccination in a systematic and organised way by school health services and the availability of vaccines free of charge for all vaccinators contribute to reach and maintain a relatively high HPV-vaccination coverage in the vaccination programme.

ESP16-1107
13. EPIDEMIOLOGY AND PUBLIC HEALTH

MOLECULAR METHODS IN THE SURVEILLANCE OF INVASIVE MENINGOCOCCAL DISEASE IN THE CZECH REPUBLIC

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Title of Case(s)

The invasive meningococcal diseases (IMD)

Objectives

The National Reference Laboratory for Meningococcal Infections (NRL) has been conducting enhanced surveillance of invasive meningococcal disease (IMD) in the Czech Republic (CR) since 1993.

Background

The National Reference Laboratory for Meningococcal Infections (NRL) has been conducting enhanced surveillance of IMD in the Czech Republic (CR) since 1993. Neisseria meningitidis isolates from IMD cases are referred to the NRL to be characterized by serogrouping, PorA and FetA sequencing and MLST. Non-culture PCR detection and typing of N. meningitidis directly from clinical specimens have been used to enable the diagnosis in culture-negative IMD cases and deaths. The NRL has recently added a whole-genome sequencing method to the molecular IMD surveillance tools.

Case Presentation Summary

Within the surveillance program, 49 cases of IMD were reported in the CR in 2015 (preliminary data). The incidence of 0.5/100 000 population is similar to the figure of the previous year. Of the 49 IMD cases, two were fatal, with one death caused by serogroup B and the other by serogroup W. The most common serogroup to cause IMD in 2015 was B (67.4 %), followed by serogroup C (20.4 %) and serogroup W (4.1 %). One case was caused by serogroup Y. All IMD isolates from 2015 were examined by MLST. The most frequent clonal complex was cc 41/44 which is typical for serogroup B, followed by cc 32, cc 198, and cc 11. In the light of the current epidemiological situation in the Czech Republic where the incidence of IMD is low (0.4 - 1.0/100 000 in the last decade), the importance of individual protection and vaccination of risk groups is pointed out. The aim of the vaccination recommendation is to provide long-lasting immunity against a broad spectrum ofN. meningitidis serogroups.

Learning Points/Discussion

It is essential to have implemented high quality laboratory diagnosis of IMD in this surveillance, which is a source of valid epidemiological data and serves as a basis for effective vaccination strategy in the country.

Supported by Ministry of Health of the Czech Republic, grant nr. 15-34887A.

ESP16-0492
13. EPIDEMIOLOGY AND PUBLIC HEALTH

EFFECTS OF 7 YEARS OF IMMUNIZATION WITH HIGHER-VALENT PNEUMOCOCCAL CONJUGATE VACCINES IN GERMAN CHILDREN.

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Background

A general recommendation for vaccination with pneumococcal conjugate vaccine (PCV) was issued for German children ≤2 years in 2006. In 2009, two higher-valent PCVs (PCV10, PCV13) were licensed in Germany. Here, we present data on invasive pneumococcal disease (IPD) -cases sent in for serotyping in the ten years following the start of PCV-vaccination.

Methods

Pneumococcal isolates recovered from children with IPD were serotyped at the GNRCS using the Neufeld-Quellung-reaction.

Results

From July 2014 toJune 2015, 84 IPD isolates recovered from children <2 years were sent in, of which only 15 had PCV13 serotypes. This represents a reduction of 45% compared to 2005/2006 (before vaccination introduction) and a reduction of 33% since the introduction of higher-valent vaccination. Among the PCV13-non-PCV7 serotypes, reductions were observed for serotypes 1 (-78%), 3 (-63%), 6A (-100%), 7F (-94%) and 19A (-75%). Serotype 5 is very rare in Germany. Among the remaining eight PCV13 cases in children <2 years reported in 2014/2015, six children were not vaccinated and 1 was incompletely vaccinated. Among the non-vaccine serotypes, 10A, 15A/B/C and 24F were most prevalent. Compared to 2009/2010, among children 2-4 years and 5-16 years reductions were observed for serotype 1 (-78% and -80%) and serotype 7F (-100%, -70%), whereas cases of serotypes 5, 6A and 19A were rare in these age groups. Serotype 3 cases have increased among 2-4 year old children from 2 to 5 cases, but decreased from 7 to 1 case in 5-15 year olds.

Conclusions

Almost seven years after the introduction of higher-valent vaccines, PCV13 serotypes have almost disappeared among children. Currently, serotypes 10A, 15A/B/C and 24F are the most prevalent serotypes among children <16 years of age in Germany.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0206
13. EPIDEMIOLOGY AND PUBLIC HEALTH

TIMELINESS OF ROUTINE IMMUNIZATION IN FRENCH CHILDREN < 2 YEARS

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Background

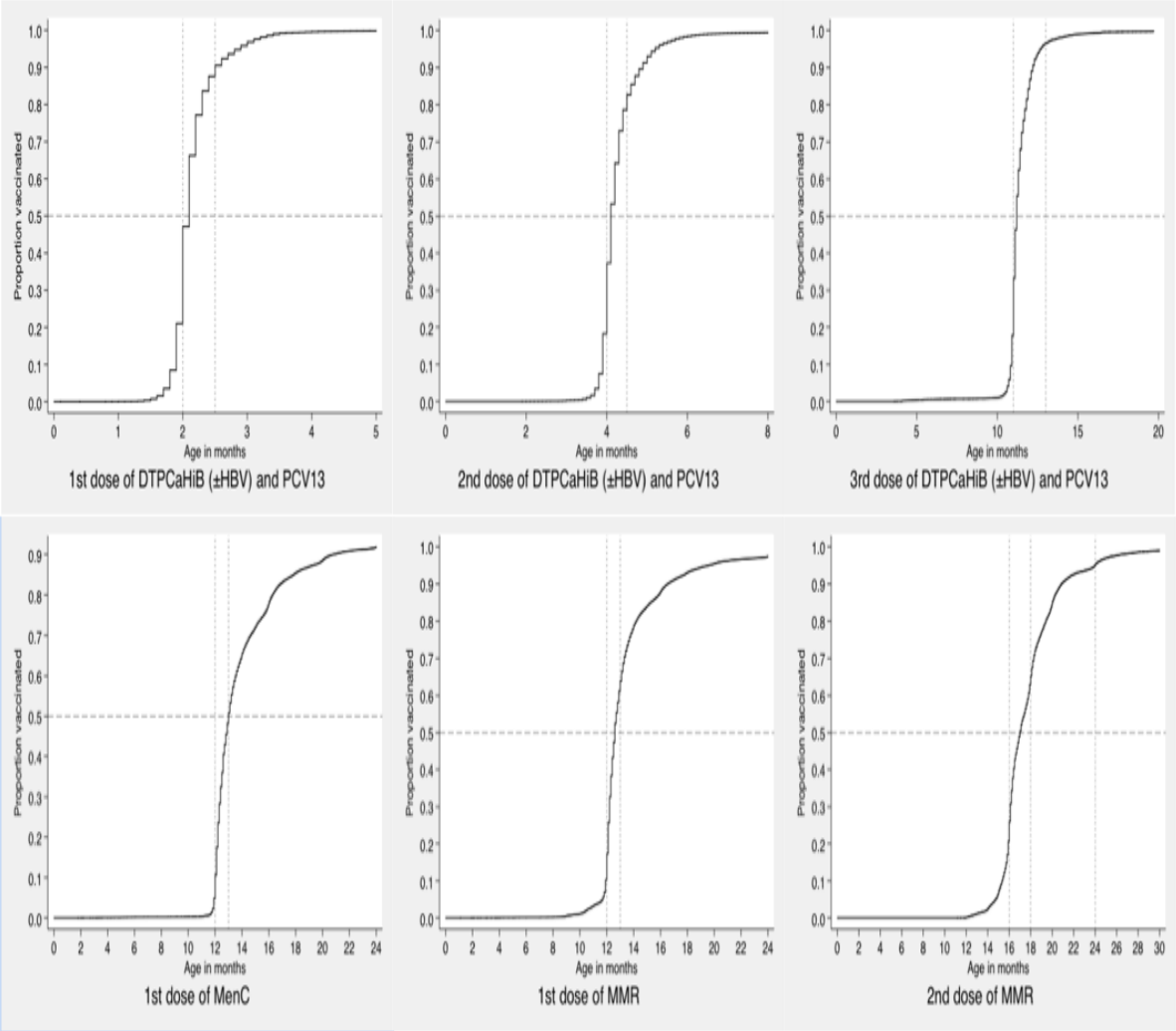
Since 2013, the recommendations of the French vaccination schedule for children <2 years are: 2+1 schedule at 2, 4 and 11 months (mo) for DTCaPHib (±HBV) and PCV13; the first dose of MMR at 12 mo with the single dose of MenC; and the 2nd dose of MMR between 16-18 mo.

Methods

To analyze the timeliness of childhood vaccination, we extracted during 6 months retrospective and prospective data from 2013 to 2015, directly from the computers of 92 pediatricians, members of AFPA and using Infansoft® software. Delayed immunization was defined as more than 14 days after the recommended age for primary series of DTCaPHib (±HBV) and PCV13, 2 mo for boosters, 1 mo for MMR/MenC, and 6 mo for the 2nd dose of MMR. We used the Kaplan-Meier method to estimate the age at immunization.

Results

Data on 119,900 immunization doses given to 23,286 children < 2 years were analysed. 89% of children started DTCaPHib (±HBV) and PCV13 immunization by 2.5 mo of age, 83% received the 2nd dose by 4.5 mo and 96% the booster before 13 mo. MMR and MenC were administered by 13 mo of age for 64% and 51% of children, respectively. The 2nd dose of MMR was administered by 24 mo for 95% of children.



Conclusions

This large study shows that the proportion of children vaccinated with delay was only substantial for Men C and first dose of MMR vaccines.
Acknowledgment: Study funded by an unrestricted grant from Sanofi Pasteur MSD

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0215
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

SEROPREVALENCE OF BORDETELLA PERTUSSIS IN SCHOOL AGE CHILDREN IN LIBYA

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Background

Background and aim:

In Libya, no pertussis booster doses are administered to children after 18 months of age. In light of recent evidence of waning of vaccine-induced immunity to pertussis, this study aimed at characterising pertussis immunity in vaccinated school-entry children (> 5 to ≤ 7 years) in Tripoli, Libya. For this purpose, we measured the prevalence of antibodies to *Bordetella pertussis* toxin (PT) (IgA and IgG) and analysed the distribution of this interference according to demographic, socio-economic characteristics in the study sample.

Methods

Materials and methods:

This was a cross sectional study undertaken in Tripoli, in February 2015.Children of school-entry age (> 5 to ≤ 7 years) were recruited on convenience basis at vaccination centers.Sera were tested for antibodies to PT by commercial ELISA*SAVYON SeroPertussis*™kits. Cut-off values and interpretation of the results are shown in Table I.

Results

Results:

Samples from 791children (421 males and 370 females, mean age 6.50(IQR 6.28-6.78) were tested. All (100%) of the participants had received 4 doses of wP-containing vaccine in the first 2 years of life. The overall prevalence of recent and non-recent pertussis infection were 0.76 % and 2.53 %, respectively. The proportion of children with undetectable level of IgG was 67.8 %. Multivariate regression analysis between socio-demographic variables and IgG levels

showed no significant relationship (p>

Table I. Cut-off values for anti-PT antibodies		
Antibody	**Value (IU/mL)**	**Result**
Anti-PT IgG	< 40	Negative
	≥ 40 to < 100	Intermediate
	≥ 100	Positive
Anti-PT IgA	< 12	Negative
	≥ 12	Positive

0.05).

Conclusions

Conclusion:

The findings of this study showed circulation of *B. pertussis* among vaccinated children by school-entry age. Since 67.8 % of children had undetectable levels of IgG, suggesting a possible increased risk of the disease, we recommend an additional booster dose of pertussis vaccines a logical approach for disease prevention in the targeted age group and improved control of *B.pertussis* circulation in Libya.

ESP16-0436
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

ASSESSMENT OF KNOWLEDGE OF THE CAUSES AND PREVENTION OF NEONATAL TETANUS AMONG FEMALE UNDERGRADUATES OF THE POLYTECHNIC, ILE- IFE, SOUTH WEST, NIGERIA.

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Background

Background: Neonatal tetanus is an important cause of avoidable morbidity and mortality. The elimination of neonatal tetanus is an attainable goal. It may be achieved by combining two approaches increasing the immunization coverage of women of child-bearing age, especially pregnant women, with tetanus toxoid. This study was carried out to determine the overall knowledge of the disease and attitude of women to receiving the vaccine.

Methods

Methods: Three hundred and eighty females of the reproductive age group in a tertiary institution in South West, Nigeria were randomly recruited using semi-structured interviewer administered questionnaire designed to elicit knowledge of risk factors for neonatal tetanus, uptake of the tetanus toxoid vaccine and attitude towards receiving vaccine among these women. A multistage sampling technique was used in administering the questionnaire.

Results

Results: Results showed that respondents have a fair knowledge (46.3%) of the risk factors for neonatal tetanus with 74% being aware that it can result in death. Socioeconomic class had a significance with the level of knowledge as women of the upper economic class had better knowledge (p= 0.00001). There's significant relationship between knowledge of the risk factors for neonatal tetanus and uptake of the vaccine (p=0.00001). Also, a significant relationship was found between the marital status and the uptake of the vaccine (p=0.001)..

Conclusions

Conclusion: The study showed that although knowledge of risk factors for neonatal tetanus was fair but the uptake of the vaccine was negligible. Also, attitude was noted to be negative in more than half of the respondents. We recommend that women of reproductive age group, pregnant or not, should be educated about the risk factors and tetanus toxoid vaccine which is a very effective method of preventing neonatal tetanus.

ESP16-0065
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

FACTORS TO INCREASE INFLUENZA VACCINATION ACCEPTENCE AND COVERAGE RATE AMONG PEDIATRICIANS IN STATE OF QATAR

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Background

Influenza is a highly infectious but preventable viral illness. Influenza vaccine remain cornerstone of prevention,WHO encourages annual vaccinations for all children and youth ≥6 months of age and those who have chronic illness at risk for the development of complications.Vaccinating pediatricians will reduce their risk of getting flu and could potentially prevent illness in patients;their positive attitudes play a central role in educating parents and support decision-making to increase vaccine coverage in children's.AIM of our study is to identify several factors to enhance seasonal influenza vaccine acceptance among pediatricians

Methods

cross sectional survey was conducted among pediatricians working at different locations in the department such as inpatients ward, intensive care unit, neonatal intensive care unit and emergency department at Hamad Medical Corporation the main tertiary teaching hospital in Qatar,it includes details demographics, attitudes, uptake of influenza vaccine in current year and factors influencing vaccine acceptance

Results

A total of 63 pediatricians from different department participated in this survey.(78%)of participants received sessional flu vaccination.Flu vaccination uptake was observed to be(58%)among physicians working in high-risk area;PICU, NICU and Pediatrics Emergency compared to(42%)on inpatients ward. In order to promote immunization acceptance and coverage rate among pediatricians,use of evidence-based statement to support vaccine effectiveness ranked the highest(42%),followed by(23% provides free on site vaccination,(20%)participating in multidisciplinary educational campaign and(10%)leadership support and being a role model ,lastly(5%)increase access to vaccine

Conclusions

Personal experience of seasonal influenza vaccination, knowledge, vaccine effectiveness and safety plays an important role in physician’s attitude towards immunization.Our finding showed that vaccine coverage among pediatricians working in a hospital setting close to the international target of 80% in a healthcare facilities.Our study described several practical intervention to enhance flu vaccine acceptance and achieve higher coverage rate

ESP16-0384
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

IMPACT OF MENINGOCOCCAL C CONJUGATE VACCINATION IN INFANTS IN BRAZIL WITH NO CATCH-UP OR BOOSTER DOSE IN ADOLESCENTS: EVIDENCE OF HERD PROTECTION

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Background

BACKGROUND:

Routine infant immunization with meningococcal C conjugate (MCC) vaccine began in Brazil in November 2010, administered at 3, 5 and 12 months of age with no catch-up or booster dose for older age-groups. Annual coverage rates have been above 95% since 2011. We assessed the overall impact of MCC vaccination on incidence rates of invasive meningococcal disease (IMD) after 4 years of vaccination introduction.

Methods

METHODS:

We performed a record linkage between the National Reference Laboratory for meningococcal disease, and the National Information System for Notifiable Diseases for the years 2008-2014. An interrupted time-series analysis was conducted to estimate rates of IMD in the post-vaccination period, based on rates from the pre-vaccination period, adjusting for seasonality and secular trends. The outcomes were IMD rates, confirmed IMD cases (CMD) rates, and serogroup-C MD (SCMD) rates. Confirmed cases due to other serogroups were assessed for comparison with SCMD.

Results

RESULTS:

A total of 18,136 cases of IMD were analyzed. At the pre-vaccination period the highest incidence rates were observed for infants aged 3-11 months, with no secondary peak among teenagers or young adults. High relative reductions in SCMD were observed for the vaccinated age-groups 3-11 months *(*80%; 95%CI:61-99*),* 12-23 months *(*92%; 95%CI:78-107*),* and 2-4 years *(*66%; 95%CI:60-72*).* Relative reductions of 25% (95%CI:18-32) and 20% (95%CI:15-25) were also observed for the unvaccinated individuals aged 5-9 years and 10-39 years, respectively. Overall, 1,181 SCMD cases per 100,000 have been averted.

Conclusions

CONCLUSIONS:

MCC vaccination of infants was able to induce herd protection among unvaccinated individuals after 4 years of MCC vaccination in Brazil. Continuous monitoring of SCMD rates is essential to evaluate the sustainability of these findings.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0699
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

IMMUNE RESPONSE OF TWO DOSES OF HAEMOPHILUS INFLUENZAE TYPE B CONJUGATE VACCINE IN VACCINE NAIVE CHILDREN WITH HIV (2-15 YEARS)

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Background

Children living with HIV are at higher risk for *Haemophilus influenzae* type b (Hib) diseases. The Hib conjugate vaccines (HibCV) are effective and recommended for all children with HIV infection. HibCV is soon being introduced as a part of primary immunization series in India. Data on catch up dosing schedule for those HIV infected children missing the primary series are inadequate. Aim of this study is to look at the baseline immunity to Hib, and immune response following two doses of HibCV in HIV infected Indian children.

Methods

We conducted a cohort study to look at impact of HibCV in families affected by HIV in West Bengal India from 2012-2014. As a part of study HIV infected children (2-15 years), not having prior Hib immunization, received two doses of the HibCV. Serum anti Hib PRP IgG antibodies were measured at baseline and two months post immunization.

Results

125 HIV infected children were vaccinated. 40% of children contributing serum for analysis were on antiretroviral therapy (ART), and 26% had viral load >100,000 copies/mL. Median age at ART initiation was 7 years. Prior to vaccination, the geometric mean concentration (GMC) of serum anti-Hib PRP antibody was 0.25 µg/mL which had a 10.6 fold increase post 2 doses ($p<0.0001$, GMC:2.65 µg/mL). 76% of HIV infected children exceeded the recommended threshold of 1 µg/mL post vaccination. Immune response was adequate in children with viral loads >100,000 copies/mL. Moderate or severe immune suppression, Trimethoprim/sulfamethoxazole prophylaxis lowered post vaccine antibody levels.

Conclusions

A two dose schedule may be more useful among HIV infected older children, having delayed ART access, compared to the currently recommended single dose.

Funding : ICMR, New Delhi

Clinical Trial Registration (Please input N/A if not registered)

Outcomes reported are part of CTRI/2012/03/002515; CTRI/2013/04/003535

ESP16-0714
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

POTENTIAL RISK FACTORS FOR VACCINE FAILURES IN HIV INFECTED INDIAN CHILDREN (2-15 YEARS) VACCINATED WITH HIB CONJUGATE VACCINES AS CATCH-UP

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Background

Haemophilus influenzae type b conjugate vaccines (HibCV) are proven to decrease both Hib disease and carriage in HIV infected individuals. The threshold for antibody response to prevent Hib carriage in HIV infected individuals is unknown. Analysis of potential factors for nasopharyngeal (NP) colonization with Hib in post vaccine cohorts can elucidate risk factors contributing to vaccine failures. The current study has two objectives: (1) To identify level of anti-Hib antibody optimum to protect Hib NP colonization in HIV infected Children; (2) risk factors of Hib colonization in HIV infected children who received 2 doses of HibCV as catch-up.

Methods

We conducted a cohort study in HIV infected children 2-15 years of age. All children received two doses of the HibCV as catch-up. NP swabs were collected at 2, 4, 16 and 18 months post vaccination with 2 doses. Swabs were also collected from accompanying parent. Serum anti-Hib-PRP-IgG antibodies were measured two months post immunization.

Results

125 HIV infected children received HibCV two doses. A total 915 NP-swabs were collected. Concurrent Hib colonization of parents, coexisting pneumococcal colonization in child, more than one child per room in the house, and severely immune compromised (based on age specific CD4 counts) were associated with higher Hib colonization post immunization. Anti-Hib-PRP-IgG level ≥3.3 µg/mL was protective from Hib colonization. This cut off has 83% specificity and 59% sensitivity in predicting absence of hib colonization in post vaccines NP swab samples.

Conclusions

Timely access to anti-retro viral therapy is likely to improve CD4 counts and hence reduce post vaccine failures. A higher Anti-Hib-antibody level post vaccine (≥3.3 µg/mL) is likely to protection from Hib colonization.

Primary Funding : ICMR, New Delhi

Clinical Trial Registration (Please input N/A if not registered)

Outcomes reported are part of CTRI/2012/03/002515; CTRI/2013/04/003535

ESP16-0241
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

DEVELOPMENT OF A NEW VACCINE AGAINST THE RECENT PREDOMINANT SEROTYPES OF STREPTOCOCCUS PNEUMONIAE IN EGYPT

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Background

Streptococcus pneumoniae is one of the major causes of morbidity and mortality worldwide particularly in developing countries. There is a dearth of information regarding the prevalent serotypes in Egypt in recent years. Most of the vaccines used in the present day are formulated against certain serotypes which might not represent the current prevalence of the disease. We aim to determine the most prevalent serotypes of *S. pneumoniae* in Egypt to design a vaccine that would include the serotypes that are currently spread. In addition, we examine the antibiotic susceptibility patterns of these dominant serotypes and their virulence characters to follow the evolution of such potent pathogen.

Methods

A total of 100 clinical specimens were collected, in Cairo/ Egypt, in the past 2 years, representing cases caused by *S. pneumonia*e. Conventional and molecular identification methods were both applied to confirm the identification of *S. pneumoniae*. The antimicrobial susceptibility patterns were assessed against various classes of antibiotics. Capsular polysaccharides were purified from the most predominate serotypes, prepared in a conjugated form with BSA and tested in animal models. The response in the form of production of antibodies was measured by ELISA and challenge test.

Results

The most prevalent serotypes were found to be 6A/B and 19F. Isolates exhibited high rates of resistance to various classes of antibiotics. Both the virulence factors autolysin (*lytA*) and pneumococcal surface antigen A (*psaA*) genes were more specific than pneumolysin (*ply*) gene for *S. pneumoniae* identification. High titers of antibodies were detected in animals immunized with the conjugated capsular polysaccharides prepared from the predominant serotypes.

Conclusions

This study demonstrates the importance of constantly monitoring the prevalent serotypes in any region to modulate the components of the used vaccines.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0444
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

USE OF A FULLY LIQUID, READY-TO-USE INVESTIGATIONAL HEXAVALENT VACCINE IN A MIXED HEXA/PENTA/HEXA PRIMARY SERIES SCHEDULE

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Background

Concomitant administration of vaccines simplifies delivery. DTaP5-IPV-Hib-HepB is an investigational, fully-liquid, combination vaccine against 6 diseases. This study evaluated the immune response to all antigens included in this investigational hexavalent vaccine when used according to a mixed hexa/penta/hexa primary series schedule.

Methods

Phase III, open-label, multi-centre study (PRI02C) in Spain. 385 infants (who received one dose of hepatitis B vaccine at birth) received mixed schedule including DTaP5-IPV-HB-Hib (PRP-OMP conjugate) at 2 and 6 months of age, DTaP5-IPV-Hib (Pediacel, PRP-T conjugate) at 4 months, MCC vaccine (NeisVac-C) at 2 and 4 months and routine vaccination with Prevenar 13 and RotaTeq. One month post-dose 3 of the mixed schedule, acceptability of Hepatitis B and Hib response was assessed and antibody response to all hexavalent antigens described. Acceptability of MCC response was assessed one month post-dose 2 of MCC vaccine. Safety profile was described.

Results

Primary objective: Acceptability of HBs and Hib (PRP) Antigen Responses One Month Post-Dose 3 of the Mixed Schedule – (PR5I Per Protocol Set - N=370)					
Antigen	Endpoint	n	Point estimate (95%CI)	Lower bound limit for acceptability	Conclusion: acceptability criterion
HBs	% with titre ≥10 mIU/mL	369	365 (98.9%) [97.2;99.7]	90%	Met
PRP	% with titre ≥0.15 µg/mL	365	365 (100.0%) [99.0;100.0]	80%	Met
N: Number of subjects vaccinated, n: number of subjects, CI: Confidence interval. Response rate is considered as acceptable if the lower bound of the 95% CI is greater than the pre-specified acceptability threshold					

Secondary objective: Hexavalent Antigen Responses One Month Post-dose 3 of the Mixed Schedule (PR5I Per Protocol Set - N=370)				
Antigen	Endpoint	n	Observed response	[95% CI]
Diphtheria	% with titre ≥0.01 IU/mL	359	359 (100.0%)	[99.0;100.0]
Tetanus	% with titre ≥0.01 IU/mL	350	350 (100.0%)	[99.0;100.0]
Pertussis				
PT	GMT (EU/mL)	349	107.46	[101.55;113.71]
FHA	GMT (EU/mL)	349	67.09	[62.38;72.15]
PRN	GMT (EU/mL)	349	56.46	[51.60;61.78]
FIM 2&3	GMT (EU/mL)	349	360.99	[332.58;391.82]
Poliovirus Type 1	% with titre ≥1:8 (dil)	356	356 (100.0%)	[99.0;100.0]
Poliovirus Type 2	% with titre ≥1:8 (dil)	356	356 (100.0%)	[99.0;100.0]
Poliovirus Type 3	% with titre ≥1:8 (dil)	356	356 (100.0%)	[99.0;100.0]
N: Number of subjects vaccinated, n = number of subjects included in the analysis, CI: confidence interval				

Secondary objective: MCC Antigen Responses Post-Dose 2 of MCC Vaccine (MCC Per Protocol Set - N=375)			
MCC	n	Point estimate	(95% CI)
% with titre ≥1: 8 (dil)	375	372 (99.2%)	[97.7;99.8]
N: Number of subjects vaccinated, n: number of subjects included in the analysis. CI: Confidence interval.			

The mixed schedule was generally safe and well tolerated. No related SAE was reported.

Conclusions

One month post-dose 3 of the mixed primary series schedule (Hexa/Penta/Hexa) including PRP-OMP/PRP-T/PRP-OMP, acceptability of response rates against Hib and hepatitis B were demonstrated and robust immune response against all other hexavalent antigens observed. A high proportion of subjects was seroprotected post-dose 2 of MCC vaccine. Vaccines were well tolerated.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov identifier NCT01839188, EudraCT Number: 2012-004221-25

ESP16-0401
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

NEW POSSIBILITIES OF PREVENTING PNEUMOCOCCAL INFECTION IN RUSSIA

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Background

A purpose of the study was to estimate significance of pneumococcal infection in the country and the first results of vaccinal prevention from it.

Methods

Statistical data on morbidity and vaccinal prevention coverage as well as publications on this problem in Russia were used.

Results

In Russia more than 2.5 million persons have suffered from pneumonia. Pneumococcus causes nearly 60% of all pneumonias. Mortality from pneumonia is especially high among children of the first year of life (37 per 100,000), and also among the persons aged 55 or older (to 78.5:100 thousand). In children during the first five years of life pneumococcal meningitis is 8 per 100,000, the mortality rate is 18.4%. Significant underestimation (more than by 20 times) of acute *otitis* media morbidity has been observed at routine registration. In Russia 29% of strains of S. peumoniae have decreased sensitivity or are resistant to penicillin, 26% of strains are resistant to macrolides, 50% of strains - to co-trimoxazole. At the end of 2014 introduced vaccination of children at the age of 2 and 4 months, revaccination at the age of 1.5 and non-immunized children at the age of 2-5, adults from the risk groups including the persons to be called up to military service. For vaccination of young children a 13-valent pneumococcal conjugate vaccine (PCV13) is used, and PCV13 and a 23-valent polysaccharide vaccine (PSV23) are used for children at the age of 2-18 and adults.

Conclusions

Owing to introduction of pneumococcal vaccine only in 2014 in Russia it became possible to decrease the number of community-acquired pneumonia cases by 17.9% in children under the age of 14. The program economic effect can make about 40 billion rubles in the near future.

ESP16-0577
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

THE INTERACTION BETWEEN BREAST MILK AND RESPONSE TO VACCINATION IN INFANTS: A REVIEW OF THE LITERATURE

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Background and Objective

Human breast milk is ideal for infants, providing both a source of nutrition and protection from infection. Protection has traditionally been understood as resulting from passive transfer of maternal antibody, primarily IgA, and bactericidal components, but there has been increasing interest in the effect of breastfeeding in activating the infant's own immune system. The objective of this review is to explore the literature examining the relationship between breastfeeding and infant vaccination in infants less than 12 months.

Methods

We searched the Medline and Embase databases in January 2016 for the periods1946-2015 and 1974-2015 respectively. We used the Medical Subject Headings (MeSH) terms: 'infant' AND 'breastfeeding' AND 'vaccination' and also searched using keywords. All searches were limited to English language.

Relevant abstracts were reviewed in January 2016 and selected according to the inclusion and exclusion criteria. Potentially relevant references were obtained and reviewed according to the same criteria.

Learning Points Discussion

There is increasing evidence that breast milk is bioactive and affects infants' response to vaccination.

The nature of the interaction between breastfeeding and vaccination depends on method of administration. There is reason to hypothesise that breastfeeding might interfere with the action of some enteral vaccines, but the results of studies investigating this have been mixed.

There is most literature about oral rotavirus vaccination, where there are longstanding concerns that breast milk might interfere with its activity. This is particularly important in low income settings, where efficacy has been repeatedly shown to be lower than in high income countries, and where the burden of morbidity lies.

It is important to gather information about feeding method when conducting vaccines studies to better understand the relationship between breast milk and vaccine response.

ESP16-0160
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

PROGNOSIS OF VACCINATION EFFECTIVENESS IN DIMINISHING OF PNEUMOCOCCUS NASOPHARYNGEAL CARRIER STATE IN CHILDREN UP TO 5 YEARS OLD IN UKRAINE

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Background

Pneumonia takes 3-rd place among causes of children mortality in Ukraine. Usually, pneumococcal infection begins from carrier state. Contemporary implemented vaccines usually have antigens against 10-13 pneumococci serotypes. There are no data about serotype spectrum of pneumococci circulating in Ukrainian children population.

Methods

Cultural and PCR methods. Positive samples (297 isolates) were typed by multiplex PCR method, for amplification primers for 15 serotypes of S.pneumonia were used, namely 1, 3, 4, 5, 6A, 6B, 6C, 7F, 9V, 14, 18C, 19A, 19F, 20, 23F (13 are included in vaccine contents). In prospective observational study 900 healthy children from 6 month to 5 years old from 46 Ukrainian settlements took part.

Results

Pneumococcal carrier state was established by cultural method in 20.3% of children. Using PCR method, revealing of pneumococci increased by 30.1% and became 50.4 % (95%DI: 47.4-53.4). Pneumococcal carrier state depended from children social activity. In children's communities carrier state was found in up to 95.6% of samples. Among received samples 88.9% (264 isolates) were capsulated, and from the latter ones 14 serotypes were identified. Serotypes 19F (26.1%) and 14 (11.4%) prevailed, almost similarly often 6A (9.1%), 6B (9.1%) were found, 23F (5.7%), others had incidence 3%, 1% and less than 1%. In children's communities more homogeneous spectrum of pneumococci serotypes was found: 19F (63.0%), 6A/B (25.9%). In general, serotypes which are included in contents of 13-component vaccine, were present in 65.5% of children in Ukrainian population with nasopharyngeal carrier state, and 92.6% of children from children's communities.

Conclusions

One may prognosticate high effectiveness of vaccination in prophylaxis of pneumococcal carrier state in children of Ukraine, especially in children's communities.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0159
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

MEDICO-ECONOMIC IMPACT OF PCV13 ON COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN SEEN AT THE PEDIATRIC EMERGENCY DEPARTMENTS OR HOSPITALIZED

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Background

The PCV13 vaccination was implemented in France in 2010 with a high coverage (>92%). This study was designed to analyze its impact on hospital stays and pediatric emergency departments (PEDs) visits for community-acquired pneumonia (CAP) and the related costs to the National Sickness Fund.

Methods

The cost of the PEDs visits, hospitalizations and follow-ups after discharge were estimated pre- and post-PCV13, using the data of a CAP study performed by the Pediatric Infectious Diseases Group. Billing data were collected in a representative center and then applied to all patients.

Results

From 2009 to 2013, 6,592 consecutive children (1 month to 15 years) with CAP were enrolled in 7 hospitals. Between 2009 and 2013, the number of CAP with a C reactive protein (CRP) level >120 mg/L and all CAP decreased by 48% and 37% respectively. Related savings were respectively €0.9 M for CAP with a CRP>120 mg/L and €1.5 M for all CAP over the 3 years-period compared to the pre-PCV13 period. The national extrapolation to the 109 hospitals with PEDs in France, showed a savings estimation of €13.5 M for CRP>120 mg/L cases and €23.1 M for all CAP cases; savings represented 88,000 to 150,000 PCV doses per year, for 800,000 annual births.

Conclusions

The study suggested a strong impact of PCV13 vaccination on the number of admissions or PEDs visits for children with CAP, which resulted in substantial savings. Savings could be more important if episodes taken care of in an ambulatory setting were included.

Acknowledgment: study funded by an unrestricted grant from Pfizer

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0145
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

EFFECTIVENESS OF UNIVERSAL SINGLE DOSE VARICELLA VACCINE ON CAUSE OF HOSPITALIZATIONS IN TURKEY (VARICOMP STUDY 2008-2015)

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Background

VARICOMP study is an ongoing study and aims to evaluate pediatric varicella-related hospitalization in Turkey since October 2008. Single dose varicella vaccine at 12 month of age was introduced to the National Immunization Program in February 2013 in Turkey. The aim of this study was to compare the clinical findings between pre- and post-vaccine era.

Methods

Medical records of 3266 children requiring hospitalization due to varicella from 30 health care centers in 14 cities have been evaluated from October 2008- October 2015.

Results

Mean age at admission was slightly older during post vaccine era (52.8±50.6 vs. 48.6±42.8 months, $p<0.05$). Hospitalization rate of children with underlying conditions was lower during the post-vaccine era ($p<0.01$). Breakthrough infection rate was similar. Cause of varicella related hospitalization's percentage (fever, poor feeding/dehydratation, hematological complications, secondary bacterial infections, respiratory complications, cerebellitis, encephalitis) were similar between pre and post-vaccine era. Only the presence of seizures (especially febrile seizures) at admission were significantly lower during the post vaccine era ($p<0.001$). Children requiring intensive care unit stay and mortality were low during the pre and post-vaccine era and no changes have been observed.

Conclusions

After 2.5 years of routine single dose immunization, we observed significant decrease for the incidence of varicella related hospitalization among children aged 1-5 years. We did not observed herd protection for other age groups, however hospitalization rate of children with underlying conditions decreased. We observed decreased rate of febrile seizures during the post-vaccine era, mainly due to routinely vaccinated population are at higher risk age for febrile seizure. Our routine hospital based surveillance until 2018, could help us to evaluate the potential effect of single dose vaccine or requiring booster dose of varicella vaccine.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0269
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

EMPYEMA ASSOCIATED WITH COMMUNITY ACQUIRED PNEUMONIA IN LUXEMBOURG CHILDREN: OCCURRENCE OVER A 14 YEAR PERIOD (2001-2014) AFTER PCV IMPLEMENTATION

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Background

In Luxembourg there is excellent pneumococcal vaccination coverage (95.4% in 2012) and no data are available on the impact of immunisation on the incidence of complicated pulmonary disease in children.

Methods

Data were retrospectively collected from records of hospitalised children aged ≤15 years with empyema between 1/1/2001 and 31/12/2014 in our centre. Data were collected from 3 periods: A) (2001-2003) before PCV (Pneumococcal Conjugate Vaccine) implementation; B) (2004-2010) period were children were universally vaccinated with PCV7 and C) (2011-2014) with PCV 13.

Results

91 children were identified: 12 during period A, 48 during period B and 31 during period C. The incidence of hospital admissions with a primary diagnosis of empyema were 4.76/100000, 8.02/100000 and 8.61/100000 for period A, B and C respectively. The median age on admission was 48 months (32, 43 and 58 months for period A, B and C). 57% were boys. The mean duration of fever before admission was 4.7 days. Microbiological diagnosis was obtained for 21% of the patients. Additional treatment to antibiotics was applied in 69 patients: 22 had initially chest tube drainage including 5 with fibrinolysis, 21 had needle thoracocentesis and 40 had VATS (Video Assisted Thoracoscopic Surgery). The median duration of fever after admission was 96 hours (0-384). The median length of hospital stay was 12 days (3-30), patients treated with VATS stayed a median of 11 days (5-30), with fibrinolysis 17 days (13-30) (p 0.0052).

Conclusions

The incidence of empyema increased after PCV7 implementation and stayed high 3 years after PCV13 implementatio**n.** There was a shift to older patients during the study period. Patients treated with VATS had a shorter hospitalisation stay compared to patients treated with fibrinolysis.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0725
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

IMPACT OF THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON THE INCIDENCE OF PNEUMOCOCCAL MENINGITIS IN CHILDREN

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Background

The impact of the 13-valent pneumococcal conjugate vaccine (PCV13) on the incidence of pneumococcal meningitis (PM) in children in unknown.

Methods

To determine this impact, a descriptive multicentre retrospective cohort study was conducted from 2008 to 2013 in northern France. All laboratory-confirmed PM in children less than 18 years of age in all hospitals of the area with paediatric units were included. Two independent databases were used for exhaustive identification of cases: medical plus laboratory records at each hospital and discharge codes. The corrected incidence of PM was determined by a capture-recapture analysis with these two databases.

Results

Sixty-two cases were found over the 6 years period. A decrease of the PM corrected incidence was observed in the global population (p=0.07), significant only for children younger than two, from 11.9/100 000 in 2008 in 1.9/100 000 in 2013 (6.4 fold-decrease, 95% confidence interval: 1.4-41, p=0.01) between year 2008 and year 2013. When comparing the pre and post-PCV13 periods, this decrease was still statistically significant for children younger than two (7.32/100 000 [4.39-10.25] to 2.78/100 000 [0.96-4.60]; p=0.01). Only three cases (5%) of PM

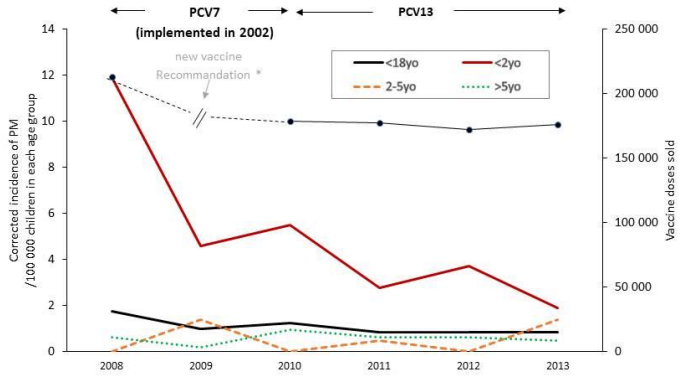

Figure I: Trends in the corrected incidence of pneumococcal meningitis in children younger than 18 according to age and vaccine doses sold in northern France from 2008 to 2013.

PCV13: 13 valences-pneumococcal conjugate vaccine; yo: years-old; PM: pneumococcal meningitis
** : in 2009, the vaccine recommendation changed from 3 doses at 2, 3 and 4 months and a booster at 12 months to 2 doses at 2 and 4 months only and a booster at 12 months, explained the decrease of vaccine doses sold.*
Data of vaccine doses sold not accessible for 2009.

caused by vaccine serotypes could have been prevented.

Conclusions

After the introduction of the PCV13, a decrease in the incidence of PM cases in children in northern France was observed.

ESP16-0030
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

PHYSICAL IMMOBILIZATION OF 60 KDA CHAPERONIN LINKED LIPASE FROM PSEUDOMONAS AERUGINOSA BN-1

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Background

Abstract: The 60 kDa chaperone linked lipase from Pseudomonas aeruginosa was subjected to physical adsorption on silica 60 and acrylicbeads. It was found that higher enzyme loading was achieved on silica gel than acrylic bead. The half life of immobilized enzyme was greater compared to the free enzyme. The adsorption of the enzyme onto a solid phase also resulted in increased thermo and solvent stability. It was observed that soluble enzyme showed maximum stability at 70°C while immobilized enzyme showed stability up to 80°C for 45 minutes. The stability of immobilized enzyme increased up to 48 hours from 24 hours against different organic solvent at 1.0M concentration. It was noted that enzyme immobilized on acrylic beads have greater reusability compared to silica immobilized enzymeKeywords: Pseudomonas aeruginosa BN-1, 60 kDa Chaperonin linked lipase, immobilized lipase.

Methods

n/a

Results

n/a

Conclusions

. n/a

ESP16-1097
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

LACK OF HIGH VACCINE COVERAGE OVER NINE YEARS LIMITS IMPACT ON ROTAVIRUS ACUTE GASTROENTERITIS (RVAG) INCIDENCE IN PORTUGAL

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Background

Two rotavirus vaccines have been available in Portugal on the private market since May 2006 with estimated coverage rising from 16 to 44% between 2007 and 2014. The aim of this study is to monitor trends in RVAG presenting to the emergency service (ES) and Short Stay Unit (SSU) of a paediatric hospital in central Portugal.

Methods

1st January to 30th June, from 2006 to 2014, all children ≤36M, attending the ES or admitted to the SSU, with AG (³ 2 watery or looser than normal stools within a 24 hour period with or without vomiting) providing a stool sample were tested for RV using an immunochromatographic rapid test.

Results

9899 AG cases were observed and 3189 (32%) tested for RV. There was a downward trend but no clear cut decline in numbers of cases of AG or RVAG nor in the average age of cases. Lack of trends in the proportion of cases admitted to the SSU suggests no change in severity of cases seen. Although seasonality differed between years - in 2010 and 2013 two annual peaks were seen, the second in June in both cases – again there was no progressive trend towards delayed epidemics.

Conclusions

We have shown in a case control study, that both RV vaccines are very effective in preventing RVAG in immunized children in this population. Despite this, annual epidemics continue to occur with little obvious change. These epidemiological findings underline the need for high coverage and resulting indirect effects for RV vaccine effectiveness.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0821
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

COST-EFFECTIVENESS ANALYSIS OF PNEUMOCOCCAL VACCINATION USING THE OVERALL EFFECTIVENESS APPROACH

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Background

Diseases caused by *Streptococcus pneumoniae* represent a major public health problem. The aim of this study was to compare the estimated health benefits, cost and cost-effectiveness of childhood immunization with pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV) versus no vaccination, 7-valent pneumococcal conjugate vaccine (PCV-7) and 13-valent pneumococcal conjugate vaccine (PCV-13), using the concept of overall vaccine effectiveness (OVE), in the Italian population.

Methods

A Markov model was adapted to simulate the impact of infant vaccination on epidemiological and economic burden of pneumococcal diseases (invasive pneumococcal diseases (IPD), pneumonia and acute otitis media (AOM)) from the National Health Service perspective.

In the recent literature, there is increasing evidence regarding vaccination effectiveness expressed in terms of overall IPD incidence reduction which is an outcome of high interest to policy makers because of the uncertainty surrounding herd protection and serotype replacement. For this reason, an advisory board of Italian experts chose to use OVE rather than serotype-specific effectiveness data.

Results

Compared to no vaccination and PCV-7, PHiD-CV was found cost-effective (incremental cost-effectiveness ratio of 28,855€/QALY and 12,500€/QALY, respectively) according to conventional thresholds.

Comparing PHiD-CV versus PCV-13, the effectiveness of these vaccines against IPD and pneumonia was estimated to be similar, while the two strategies differ in their effect on AOM. The reduced AOM incidence is expected to be associated with some 300 incremental QALYs and savings >4M€ for a newborn cohort followed over 18 years, yielding to dominance of PHiD-CV.

Conclusions

In conclusion, results indicate that at an equal level of protection against IPD and pneumonia, PHiD-CV may offer additional advantages over PCV-13 in terms of AOM prevention and allow for economic savings contributing to the sustainability of vaccination programs.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0923
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

PERTUSSIS ANTIBODY LEVELS OF MOTHERS AND THEIR INFANTS AT FIRST AND SIXTH MONTHS OF AGE

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Background

The belief that pertussis is a disease limited to childhood years is far from truth. The aim of this study was to measure the pertussis antibody levels in women and their infants at the first and the sixth month of their lives. This prospective, multi-central study encompassed 209 mothers and their infants from one private and three public hospitals in Turkey.

Methods

Samples were collected via venopunction and were studied by pertussis enzyme-linked immunosorbant assay (IgG anti-PT ELISA). For parameters without a normal distribution Mann Whitney U test was used. Qualitative data comparisons were made by Pearson chi-square test, Yates Continuity Correction test, Fisher's exact test, Fisher –Freeman Halton test and finally Mc Nemar test. Safety interval was at 95%, significance $p<0.05$.

Results

The proportion of seropositive mothers was 49.8%. Within their first month of life, only 32.1% of the babies had positive titers and this rate had increased to 43.3% after two doses of vaccination at 6 months of age. Almost 89.5% of the babies whose mothers had negative pertussis titers also had negative titers.

Conclusions

Our findings led us to think that cocoon vaccine strategy for pertussis is important for newborns in our society.

Clinical Trial Registration (Please input N/A if not registered)

Granted by the Scientific Research Unit of Istanbul University (Project No:35513)

ESP16-0682
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

EFFECT OF SOCIODEMOGRAPHIC DETERMINANTS AND SOCIO-ECONOMIC STATUS ON POLIOMYELITIS IMMUNIZATION AMONG UNDER-FIVE CHILDREN IN PAKISTAN

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Background

Pakistan is among those countries where poliomyelitis (polio) is still categorized as an endemic viral infection. However, in rural areas of Punjab province of Pakistan, little is known about the determinants of polio and its prevalence in under-five children. That's why, this study sought to examine the sociodemographic factors that determine polio among under-five children in Punjab, Pakistan.

Methods

This study used secondary data drawn from the 2014 Punjab Demographic and Health Survey. Multivariate analysis based on binary logistic regression models and multiple linear regression techniques were applied to determine factors associated with child health outcomes and the determinants of polio prevalence. Hosmer-Lemeshow Goodness-Of-Fit with Akaike Information Criterion were used to determine factors effecting education rate and polio vaccination rate.

Results

The results revealed that region of residence, socio-economic status, educational background, and basic healthcare arrangement were the key predictors of polio infection among under-five children in Pakistan for the one-year period preceding the study. Higher socio-economic status was directly associated with a higher rate of poliomyelitis vaccination for children under 5 years of age.

Conclusions

Polio vaccination rates for children less than 5 years were higher in socio economically stable regions than the rest districts. Also, the coverage of polio vaccination was low and less children from lower socio-economic regions received these vaccines than the higher socio-economic regions. It is therefore imperative that special education on prevention of polio should be intensified by the National Polio Control Program in all the regions.

ESP16-1013
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

IMMUNOGENICITY AND SAFETY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN CHILDREN AGED 6 TO 17 YEARS IN INDIA: AN OPEN-LABEL TRIAL

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Background

Pneumococcal diseases are a significant cause of morbidity and mortality in young children, but may also affect older children and adolescents with underlying conditions. The 13-valent pneumococcal conjugate vaccine (PCV13) recently received approval for this age group in the United States and European Union based on safety and immunogenicity data from a US study in 6- to 17-year-olds. To support an age extension of the PCV13 indication in India to this age group, an open-label, multicentre clinical trial (ClinicalTrials.gov: NCT02034877) was conducted at three sites in India.

Methods

A single dose of PCV13 was administered intramuscularly to 200 healthy children and adolescents who had not been previously vaccinated with a pneumococcal vaccine. Blood samples were collected before and one month after vaccination for measurement of functional antibody levels by serotype specific anti-pneumococcal opsonophagocytic activity (OPA) assays. Safety was assessed for one month after vaccination.

Results

Of the 200 participants, the mean age was 9.7 years and 46.5% were male. PCV13 elicited robust immune responses against all 13 pneumococcal serotypes, as reflected by the magnitude of the OPA geometric mean fold rise (GMFR) in functional antibody levels from before to one month after vaccination (Table). The immune responses were generally similar to those observed in a US study population aged 6 to 17 years. No adverse events were

reported.

Table: GMFR of OPA GMTs before and one month after PCV13 vaccination (n=153–199)			
Serotype	**Pre-vaccination GMT**	**Post-vaccination GMT**	**GMFR (95% CI)**
1	10	170	16.3 (13.26, 19.92)
3	18	118	6.4 (5.23, 7.80)
4	234	7616	32.6 (21.59, 49.08)
5	19	287	15.3 (12.15, 19.26)
6A	470	8980	19.1 (13.77, 26.48)
6B	260	6466	24.9 (17.19, 35.94)
7F	742	5246	7.1 (5.52, 9.05)
9V	2140	7058	3.3 (2.65, 4.10)
14	1366	7471	5.5 (4.16, 7.19)
18C	211	8765	41.5 (26.82, 64.25)
19A	63	1965	31.2 (23.38, 41.74)
19F	265	3536	13.3 (9.87, 17.99)
23F	83	4434	53.3 (36.17, 78.40)

CI=confidence interval; GMFR=geometric mean fold rise; GMT=geometric mean titer; OPA=opsonophagocytic activity; PCV13=13-valent pneumococcal conjugate vaccine

Conclusions

PCV13 is immunogenic and safe when administered to children and adolescents aged 6 to 17 years in India. PCV13 has the potential to protect against vaccine-type pneumococcal disease. On behalf of the B1851140 study team. Funded by Pfizer Inc.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov: NCT02034877

ESP16-0332
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

SAFETY AND IMMUNOGENICITY OF A CELL CULTURE-DERIVED INACTIVATED TRIVALENT INFLUENZA VACCINE (NBP 607) IN HEALTHY KOREAN CHILDREN FROM 6 MONTHS TO 18 YEARS OF AGE

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Background

Although a number of cell culture–derived influenza vaccines have been approved for use in adults, there are a few clinical trials of cell culture–derived seasonal influenza vaccines for children, especially young children.

Methods

We conducted a randomized, double-blind phase III clinical trial to evaluate the safety and immunogenicity of cell culture-derived inactivated subunit trivalent influenza vaccine (NBP607, SK Chemicals, Seongnam, Korea) in healthy children from 6 months to 18 years of age. Subjects were randomized to receive either NBP607 or control TIV vaccine. Antibody levels were measured by hemaglutination inhibition assay using cell-derived antigens. Solicited adverse events were assessed for 7 days after each injection. Serious adverse events were collected for 6 months post-vaccination.

Results

A total of 374 participants completed the study. No deaths, vaccine-related SAEs, or withdrawals due to adverse events were reported. The solicited adverse events reported were generally of mild intensity. Overall, NBP607 met the immunogenicity criteria of Committee for Medicinal Products for Human Use for the three influenza strains. Between the NBP607 and control groups immunogenicity endpoints were comparable. Participants younger than 3 years of age had lower immunologic responses against influenza B virus in both NBP607 and control group. In subjects aged 9 or more, NBP607 met all three regulatory criteria for the A/H1N1 and B strains except seroconversion rate for the A/H3N2 strains.

Conclusions

NBP607 is well-tolerated and has favorable immunogenicity in children aged 6 months to 18 years.

Clinical Trial Registration (Please input N/A if not registered)

registered

ESP16-0357
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

FIRST ROTAVIRUS SEASON EXPERIENCE AFTER IMPLEMENTING THE PENTAVALENT BOVINE-DERIVED ROTAVIRUS VACCINE INTO THE NATIONAL IMMUNIZATION SCHEDULE IN ESTONIA

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Background

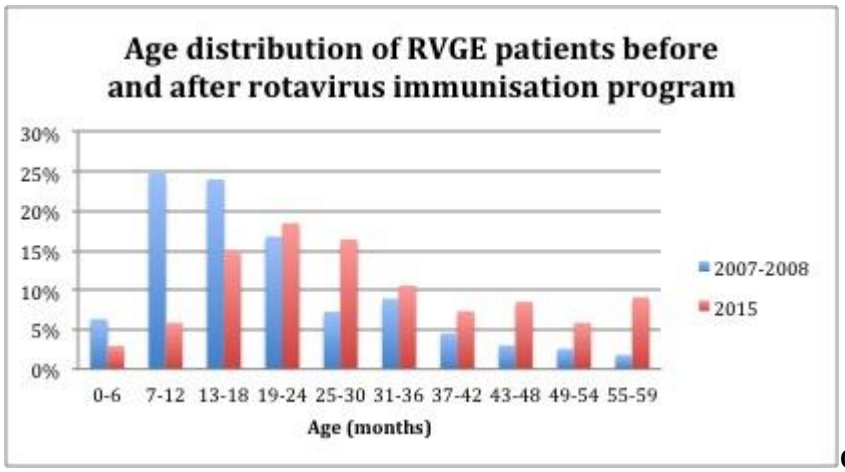
In Estonia rotavirus gastroenteritis (RVGE) is the most common cause for hospitalization among children aged <5 years. Rotavirus (RV) vaccines have been available for self-purchase in Estonia since 2007. In July 2014, the pentavalent bovine-derived rotavirus vaccine (Rotateq®) was implemented in the national immunization schedule. Vaccine coverage with 3 doses in the first year was 76.4%. We aimed to compare hospitalized RVGE cases in the first RV season following introduction of national vaccination program to those in the pre-vaccine era 2007-2008.

Methods

All children aged 0-18 years hospitalized with acute gastroenteritis (AGE) at any of the seven largest Estonian hospitals (~80% of pediatric hospitalizations in Estonia) during 01.02.2015 to 31.10.2015 were eligible for the study. Demographical data, hydration status according to WHO criteria, severity of disease according to Vesikari and Clark scales, and stool rotavirus status were recorded in an electronic study database.

Results

1,070 children were hospitalized with AGE and 38.6% (n=413) were confirmed as RVGE;82.6% (n=341) were aged <60 months. Vaccine coverage was 17%[12/70] among cases in the vaccine-eligible age group and 5% (N=17) in <60 month-olds. The 2015 RV season was of the same duration and RVGE hospitalization rates were similar when compared to pre-vaccine seasons. However, only 24% of hospitalized RVGE cases in the first post-vaccine RV season were aged <18 months compared to 55% in the pre-vaccine era. No significant differences in severity of RVGE were observed between two periods but disease severity scores demonstrated major differences in severity interpretation.



Conclusions

During the first post-vaccine season, hospitalization rates for RVGE did not change but RVGE patients were older compared to the pre-vaccine era, most likely reflecting a reduction in hospitalized cases in the vaccine-eligible cohort of infants.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0272
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

IMMUNOGENICITY AND SAFETY OF THE INACTIVATED HEPATITIS A VACCINE IN CHILDREN WITH PFAPA SYNDROME: A PROSPECTIVE CONTROLLED OBSERVATIONAL COHORT STUDY

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Background

To compare the immunogenicity and safety of vaccination against Hepatitis A virus (HAV) between PFAPA patients and healthy controls who have not been previously exposed to HAV.

Methods

Prospective controlled study including PFAPA patients and haelthy controls who received two doses of the vaccine 6 months apart. Immunogenicity was expressed as seropositivity rates and mean HAV-IgG concentrations measured at 0, 1, 7 and 18 months. Safety was defined as incidence of adverse events and the effect of vaccination on PFAPA symptoms.

Results

104 participants completed the study; demographic characteristics and time interval between the two vaccine doses were similar in both groups. All participants were seronegative and seroconverted at 1,7 and 18 months. At month 1, 92.9% of patients and 77.6% of the controls attained seroprotection, while rates increased to 100% and 96.1% at 7 months. Gender, disease duration and use of steroids had no impact on seroprotection rates and mean anti-HAV antibody titers. Overall, vaccines were well tolerated. Mild adverse events were similar in both groups.

Parameters	PFAPA group	Control group	P value
Study sample	28	76	0.87+
Age(years) (mean +/-SD)	4.4+/-2.3	4.75+/-2.7	0.8+
Gender	12(43%) females	35(45%) females	0.96*
I			
Disease duration (years)(mean +/-SD)	2.1+/-1.5	-	
Serprotection rate at 1 month	92.9%	77.6%	0.07*
Seroprotection rate at 7 months	100%	96.1%	0.2*
Seroprotection rate at 18 months	100%	95%	0.2*
Disease flare	3(14.2%)	NA	
Adverse events systemic local	6(17%) 4(12%) 2(6%)	15(21%) 10(14%) 5(7%)	0.1*
Mean IgG titers 1 month(mIU/ml)	110	96	0.3+

Mean IgG titers 7 months(mIU/ml)	223	218	0.8+
Mean IgG titers 18 months(mIU/ml)	275	248	0.2+

* Pearson's chi square test; + student t-test

Conclusions

Two doses of the inactivated HAV vaccine are safe and effective in children with PFAPA.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1019
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

ASSESSMENT OF POSTVACCINAL IMMUNITY AGAINST HEPATITIS B VIRUS (HBV) IN CHILDREN AND ADOLESCENTS RECEIVING IMMUNOSUPPRESSIVE THERAPY

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Background

The need for a booster dose of Hepatitis B vaccine has been subject to scientific debate. There is no need to administer booster doses of HBV vaccine to healthy and previously vaccinated individuals. The booster dose should be planned for immunocompromised patients, based on serological monitoring. The aim of the study was to determine the long-term protection measuring the anamnestic response after administration of a one booster dose in children receiving immunosuppressive therapy.

Methods

Fifty-four immunosuppressed children, vaccinated against HBV in neonatal period, aged from 3 to 17 years (38 children suffering from juvenile idiopathic arthritis – JIA and 16 children suffering from autoimmune hepatitis - AIH) were enrolled in the study. The control group consisted of 120 healthy children. Patients and children with anti-HBs <10 IU/l were given one booster dose of HBV vaccine. The response to booster was assessed 4-6 weeks later.

Results

Anti-HBs <10 IU/l were found in 15/38 (39.5%) children with JIA and in 7/16 (43.8%) of patients with AIH, compared to 23/120 (19.1%) healthy patients ($p<0.05$). There was no significant correlation between the time from the primary vaccination schedule and the concentration of anti-HBs assessed initially in any group. As compared with healthy controls, JIA and AIH were associated with increased risk for low anti-HBs (<10 IU/l; (OR=2.9; [95% CI: 1.42-5.92]; P=0.003). In 100% of patients the response to booster dose, i.e. anti-HBs concentration above 10 IU/l was observed.

Conclusions

In the group of immunocompromised patients, low anti-HBs concentrations (<10 IU/l) of antibodies occur more frequent than in healthy children. The response to the booster dose of HBV vaccine in this group of patients is good and similar to the healthy population.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0058
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

LOW EFFECTIVENESS OF MEASLES VACCINATION IN A SETTING WITH LOW ROUTINE IMMUNIZATION COVERAGE

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Background

Measles vaccination is routinely administered at 9 months of age according to the World Health Organization's expanded programme on immunization schedule. It has a lower efficacy when administered at this age because of existence of maternally derived antibodies against measles virus. The virus has a high infectiousness and causes outbreaks in areas of low immunization.

Methods

A case control study was carried out to determine the vaccine effectiveness. The case files of children with a provisional diagnosis of measles were the cases. Those fitting the case definition of measles in Usmanu Danfodio University Teaching Hospital, Sokoto. Nigeria in the last 5 years. Age-matched controls admitted around the same period were selected and the Odds ratio (OR) of vaccination among cases and controls was calculated with the vaccine effectiveness being 1-OR.

Results

Odds of vaccination among cases against controls was 0.3. Thus the vaccine effectiveness was found to be 70%. Probably because routine coverage for the period ranged from 45 to 60% for measles antigen. There is also a large pool of unimmunized despite periodic vaccination campaigns in 2008 and in 2013.

Conclusions

Low measles vaccine effectiveness was found when administered routinely at 9 months in a context with low routine immunization coverage and high number of unimmunized.

ESP16-0038
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

CHANGES IN BACTEREMIA IN A JAPANESE UNIVERSITY HOSPITAL AFTER INTRODUCTION OF VACCINES FOR HAEMOPHILUS INFLUENZAE TYPE B AND STREPTOCOCCUS PNEUMONIAE

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Background

Bacteremia with *Streptococcus pneumoniae* or *Haemophilus influenzae type b* (*Hib*) was a concern in non-compromised children under 3 years of age before vaccines for *Streptococcus pneumoniae* and *Hib* were introduced. In Japan, these vaccinations have been publicly funded in most areas since February 2011. Before introduction of these vaccines, occult bacteremia required consideration in children under 36 months of age with fever without source.

Methods

A total of 10,487 blood culture specimens were examined from 3,916 children who were admitted to the Department of Pediatrics, Juntendo University Urayasu Hospital, Chiba, Japan and underwent blood cultures from January 2006 to December 2014. Results for blood culture-positive children were compared before and after introduction of *Hib* vaccine and *Streptococcus pneumoniae* vaccine, based on a retrospective analysis of a bacterial laboratory database.

Results

A total of 94 patients had significant bacteria isolated from blood culture. Based on annual changes in the number of blood culture-positive patients aged 1 month or older, the number of *Streptococcus pneumoniae*-positive patients significantly decreased after 2010, while the number of *Hib*-positive patients reached a peak in 2008 and subsequently decreased. The major cause of fever without source in patients aged 1 month or older was *Streptococcus pneumoniae* until 2010, but subsequently changed to other serotypes or bacteria that were unrelated to the vaccines.

Conclusions

Introduction of *Hib* vaccine and *Streptococcus pneumoniae* vaccine significantly decreased both the number of cases of bacteremia in children and the incidence of invasive infections caused by *Hib* and *Streptococcus pneumoniae*. However, serotype replacement is a growing concern in Japan. Diagnostic standards for occult bacteremia should be revised based on the history of vaccination.

ESP16-0318
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

THE RESPONSE TO PREVENAR IN PAEDIATRIC ACUTE LYMPHOCYTIC LEUKEMIA AND ACUTE MYELOID LEUKEMIA PATIENTS RECEIVING BONE MARROW TRANSPLANTATION (BMT) IS VARIABLE

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Service hématologie et immunologie pédiatrique, Lyon, France
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Background

Post bone marrow transplantation (BMT), protection against *pneumococcus* is achieved through revaccination with Prevenar. In this study, we report the variability in response to Prevenar and identify factors that may influence this response.

Methods

Pre and post vaccination serum samples were obtained from 14 acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML) patients who had received BMT (7 females, 7 males; median age 9 years (range 1-15)). All patients received intravenous immunoglobulin IgG (IVIG) until immune reconstitution and prior to 3 doses of Prevenar 13. Response was assessed using the VaccZyme PCP IgG EIA kit (The Binding Site, Birmingham, UK).

Results

There were two groups identified in this study, those with a >100mg/L post vaccination response (8/14 median 270 mg/L; range 111-270) and those who had a lower titre response (6/14 median 51 mg/L; range 32-95; $p<0.0019$). These groups were also separated by the magnitude of response with those achieving greater than 100mg/L having a median fold increase of 5 fold (range 4-14) v 2 fold (range 0.6-3; $p<0.03$)

Factors that influence the Prevenar response included duration of IVIG treatment, a longer time to vaccination and post vaccination sample collection.**Conclusions**

The response to Prevenar is variable in ALL and AML patients receiving BMT. Only 8/14 produced >100 mg/L antibodies post vaccination. There are several factors that influence the Prevenar response. Consideration needs to be given to measuring the concentration of post vaccination antibodies after BMT.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0404
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

IMPACT OF TEN-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV10) AGAINST TYMPANOSTOMY TUBE PLACEMENTS AMONG VACCINE-ELIGIBLE CHILDREN IN FINLAND

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Background

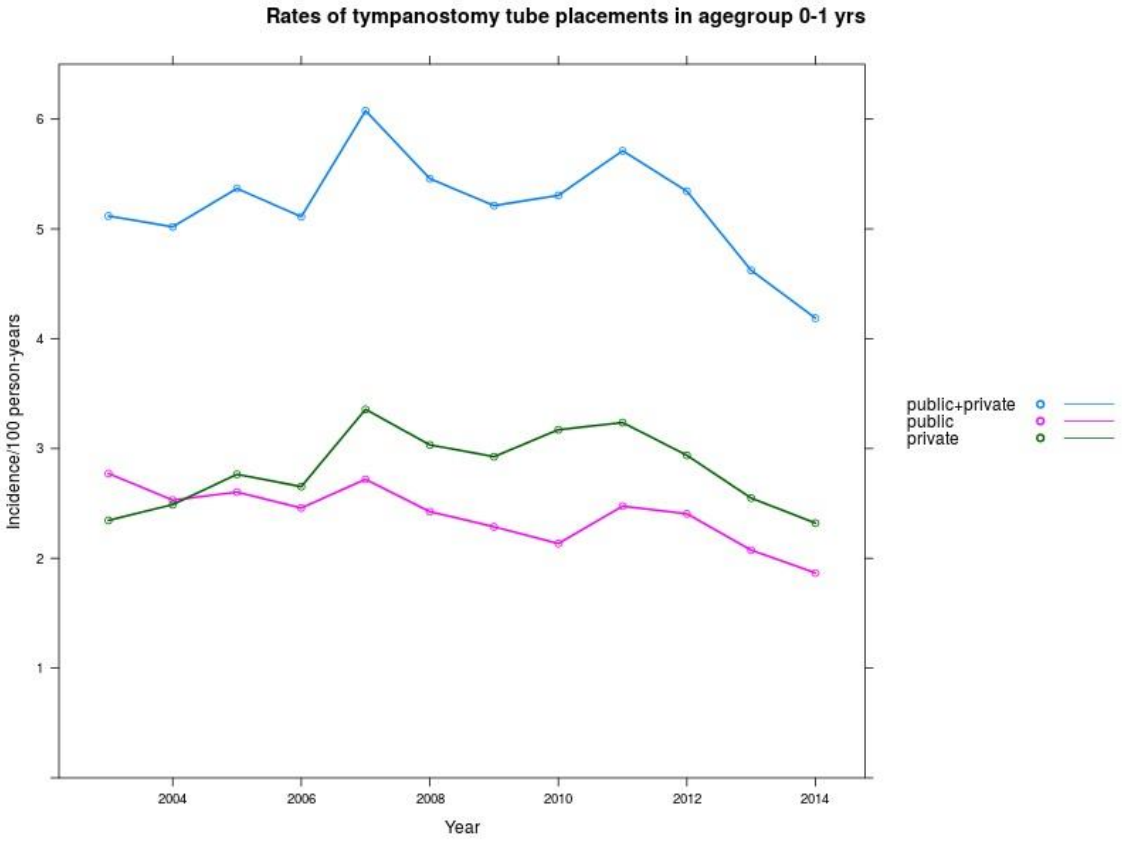
Tympanostomy tube placement (TTP) is one of the most common surgical procedures in children in many high-income countries. The ten-valent pneumococcal conjugate vaccine (PCV10) reduced TTP in the FinIP clinical trial setting. We evaluated the impact after introduction of PCV10 in in the Finnish National Vaccination Programme (NVP) in September 2010 using a 2+1 schedule.

Methods

The target cohort eligible for NVP (children born 06/2010-09/2014) was compared with a season and age-matched (age 3-54 months) reference cohort (born 06/2004-09/2008) before NVP introduction. Period 01/2009-08/2010 was excluded because of the nation-wide PCV10 trial (FinIP). Vaccine uptake was estimated to be 92% in 2012. Data on all TTP procedures were obtained from National Care register and Social Insurance Institution reimbursement register and included both public hospital and private office procedures.

Results

The incidence of overall TPP was quite constant until 2010 with an increase in 2011 followed by a gradual decrease in 2012 through 2014 (Figure). The rate of any TTP was 5.4/100 person-years in the reference cohort and 4.6/100 person-years in the target cohort. The relative rate reduction was 15% (95%CI 14-17) and the absolute rate reduction 0.8/100 person-years.



Conclusions

This study provides evidence for the impact of PCV10 against tympanostomy tube placement during a routine vaccination program setting. The absolute rate reduction was 16-fold compared with reduction in culture-confirmed IPD. This is important from public health perspective.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0447
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

IMPLEMANTATION OF MULTIVALENT VACCINE IN BITOLA, REPUBLIC OF MACEDONIA

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[2]University "St. Kliment Ohridski" Bitola- Republic of Macedonia., Higher Medical School- Bitola, Bitola, FYR Macedonia
[3]PHO "Dr. Angelovska-Dr. Timovski"- Skopje- Republic of Macedonia., Primary health care, Skopje, FYR Macedonia

Background

Active immunization in our country is compulsory. Polyvalent vaccine was implemented for the first time in august 2015. The purpose of the study is to evaluate the comprising of preschool children till 5 years with polyvalent vaccine in Municipality of Bitola and to determine the first results of the vaccination.

Methods

In retrospective epidemiological study the vaccination data were analyzed in the period of 04 08.2015 to 31.12.2015.

Results

The study was conducted in the Health Centre in Bitola, in the Office for preventive health care for children aged 0-6 years. A total number of 1376 children (92.41%), from 1489 planned, were vaccinated with polyvalent vaccine. From them 724 children were vaccinated with hexavalent and 652 with pentavalent vaccine, 1078 children from the city and 298 from the country side. There were side effects in three cases vaccinated with pentavalent vaccine (fever, anxiety, pain, and swelling). In one case after vaccinating with hexavalent vaccine a rash appeared on the body and on the head of the child, which withdrew in a few hours. For all effects, reports for post vaccine reactions were duly submitted to the Expert team at the Child disease clinic in Skopje.

Conclusions

In Macedonia the implementation of multivalent vaccines was successfully launched in August 2015. Side effects of the vaccine are minimal, the benefits for the parents are reduced number of visits to the doctor, less stressful conditions and side effects and increase vaccine coverage**.**

Clinical Trial Registration (Please input N/A if not registered)

N\A

ESP16-0231
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

OPTIMIZING PRIMARY VACCINATION SCHEDULE FOR PREMATURE INFANTS: STUDY DESIGN AND RATIONALE

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Background

Introduction – The National Immunization Program (NIP) aims to protect all individuals and the population at large against the target diseases. The current "one size fits all" NIP schedule may not provide optimal protection to the approximately 15 000 preterm infants born annually in the Netherlands. Optimal timing and dosing for this group is currently unknown. Immunogenicity studies in preterm infants and clinical testing of alternative vaccination schedules is critical to optimize their protection against vaccine preventable diseases.

Methods

Study design – This study is a prospective observational study which aims to include 300 preterm infants divided in 3 GA groups (< 28, 28-32 and 32-36 weeks). Follow up is until infants reach 12 months of age.

Results

Objective– The primary objectives of this study are:

1. To determine immunogenicity of the vaccines administeredaccording to the current Dutch NIP schedule (DTaP-IPV-Hib-HepB and PCV10) at 2,3, 4 and 11 months of age in preterm infants and with rotavirus vaccine.

2. To unravel the mechanism of immaturehost responses and interaction with gestational age (GA).

3. To propose alternative, better-adapted, vaccinationschedules with respect to number and timing of doses for preterm infants, basedon the immunogenicity findings.

Conclusions

Study endpoints – The primary study endpoints are seroconversion rates in preterm infants and absolute antibody levels against the regular NIP vaccine components and rotavirus vaccine at 5 and 12 months of age. Secondary endpoints are levels of maternal antibodies at 6 weeks of age and its association with vaccine response at 5 months, parameters of cellular immunity at 12 months, tolerability and vaccine side effects and timelines of NIP vaccines.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0233
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

RISK-GROUP INFANT VACCINATION AGAINST ROTAVIRUS - IMPLEMENTATION AND PHASE IV EFFECTIVENESS STUDY: STUDY DESIGN AND RATIONALE

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Background

Introduction - Infants with underlying medical conditions, prematurity and low birth weight are at increased risk of severe rotavirus (RV) gastroenteritis, RV related complications and mortality. Prevention against RV gastroenteritis is therefore urgently needed for high-risk infants. Yet, there is no RV vaccination program in the Netherlands, but the vaccine is available on the private market. Furthermore, there is a lack of data on RV vaccine performance among the special populations of high-risk infants. Data on vaccine effectiveness are needed to improve vaccination guidelines pertaining to high-risk infants.

Methods

Study design and population – The study is designed as a step-wedged implementation project with before-after observational cohort analysis to determine the effects of RV vaccination of high-risk infants. The eligible population includes high-risk infants with at least one high-risk condition (i.e., gestational age <36 weeks, birth weight < 2500 grams or a qualifying diagnosis of a severe congenital malformation) and receiving care at a participating hospital. The intended sample size is 1800 infants. Follow-up is for occurrence of all cause and rotavirus gastroenteritis until age of 18 months.

Results

*Study endpoints – V*accine effectiveness against severe RV gastroenteritis among high-risk infants up to 18 months of age comparing pre-vaccination to post-vaccination cohort. In addition, RV vaccine coverage rates, timeliness of vaccination, impact of the RV vaccination program in reducing RV related hospitalizations among high-risk infants are studied. Secondary endpoints are RV epidemiology and RV immunogenicity.

Conclusions

This project will pilot a RV vaccination program for high-risk infants implemented in secondary and tertiary pediatric care and will determine RV vaccine effectiveness among high-risk infants.

Clinical Trial Registration (Please input N/A if not registered)

NTR5361

ESP16-0354
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

ADMISSION DUE TO ROTAVIRUS GASTROENTERITIS IN PREVIOUSLY IMMUNIZED INFANTS

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Background

To describe the epidemiological characteristics, clinical presentation and evolution of children previously immunized with Rotateq, admitted for Rotavirus gastroenteritis, in comparison to their non-immunized peers.

Methods

Retrospective analysis of children hospitalized for gastroenteritis due to Rotavirus in a tertiary care hospital in Madrid, between January/2014 and March/2015. Clinical presentation and evolution of previously immunized patients were compared to non-vaccinated chidren. Complete immunization was defined as administration of 3 doses of RotaTeq® separated at least one month, started between 6 and 12 weeks of age, and completed before 32 weeks and at least 8 weeks before admission.

Results

76 patients were admitted for Rotavirus-confirmed gastroenteritis; 6 properly vaccinated, 66 non-vaccinated and 4 with an incomplete vaccination schedule (excluded from the analysis). The median age was 19.5 months [14.2-28.2] for the immunized children vs 8.7 [3.6-16.7] (P=0.03) in the unvaccinated group. Four patients were male (66%) vs 32 (52%).
Three previously immunized children (50%) had clinical signs of dehydration at admission, compared to 66.67 % of non-vaccinated children (P=0.4). In 4 vaccinated (67%) vs 39 (64%) unvaccinated children, mild metabolic acidosis (P=0.6) was documented. Epidemiological risk factors were documented in two (40%) vaccinated vs. 32% (P=0.5) of non-immunized children.The average stay was 2.5 days [2-3] vs 4 days [2.5-5] (P=0.2). Two vaccinated patients (33%) and 17 (28%) unvaccinated presented complications (P=0.5); mainly water-electrolyte disturbances, clinical sepsis and nosocomial infection. One patient had febrile seizures.

Conclusions

Immunization against Rotavirus does not guarantee protection from sever illness. Children admitted due to a severe Rotavirus gastroenteritis were observed at least one year after immunization, suggesting loose of protection over time. Average stay was shorter although non-significantly, probably due to the limited sample size.

ESP16-0739
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

THE TOLERANCE OF PNEUMOCOCCAL VACCINE IN CHILDREN

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Background

Unfortunately problem of pneumococcal infection in children stays actually in Belarus. Opportunities of vaccinoprophylaxis against pneumococcal infection are limited in children younger 2 years. It connects with using for immunization polysaccharide vaccine which has contradictories for vaccination children less 2 years.

Methods

We carried out analysis of development of postvaccinal reactions and complications after using pneumococcal polysaccharide vaccine (Pneumo-23). There were 114 patients (63% were children 2-5 years, 24% - 6-16 years and 13% - older 16 years) under our supervision.

Results

In 25 % cases vaccination was made against pneumococcal infections and others - hemophilic infection, influenza, and hepatitis A, in 75% - only against pneumococcal infections.

We did not have any complications after using pneumococcal vaccine. In 30 % cases we registered development of postvaccinal reactions in our children (66% - were in children from 2 to 5 years).

The estimation of postvaccinal reactions was based on acknowledged criteria - the general (severe, medium and light) and local reactions (severe, medium and light): local reactions (light, medium) - 66%, local + general reactions (light) – 34%.

Conclusions

The tolerance of pneumococcal vaccine is good with rarely development of reactions and absence of complications.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0138
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

A COHORT STUDY OF THE OUTCOMES OF PRETERM INFANTS BORN TO HEPATITIS B CARRIER MOTHERS USING CURRENT IMMUNIZATION GUIDELINES

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Background

The Advisory Committee on Immunisation Practices (ACIP)recommends a 4-dose vaccination schedule for preterm low birth weight infants (< 2kg) and a 3-dose vaccination schedule for preterm infants (≥ 2kg) born to Hepatitis B carrier mothers (HBsAg positive). However, data remains limited on its efficacy. We describe our experience with this recommended schedule for these high risk infants.

Methods

A cohort of preterm neonates (gestation < 37 weeks) born to hepatitis B carrier mothers were recruited over 6 years from the National University Hospital and KK Women's and Children's Hospital. Neonates with birth weight (BW) < 2kg were given a 4-dose vaccination schedule; at birth, on reaching 2kg, a month after the second dose and 6 months after the second dose. The larger preterms (≥ 2kg) were given the 3-dose vaccination schedule; at birth, 1 and 6 months of chronological age. All were given hepatitis B immunoglobulin at birth. Vaccine response was determined by testing for the anti-hepatitis B s antibody (anti-HBs) and hepatitis B s antigen (HBsAg) at 9 months of chronological age.

Results

Twenty-four preterm low BW neonates were recruited. The median (range) age was 35^{+4} (27^{+3}-36^{+5}) weeks' gestation and the median (range) BW was 2.37 (1.31-3.21) kg; 4 were < 2kg and 1 was < 1.5kg. All 23 surviving preterm infants were tested negative for HBsAg at 9 months of age. Twenty-two infants (95.6%) achieved immune anti-HBs antibody titres (15->1000 IU/L). All 4 neonates with BW < 2kg achieved levels more than 500 IU/L.

Conclusions

The current ACIP recommended vaccination schedule results in adequate antibody titres in preterm and low BW infants of HBsAg positive mothers.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0339
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

EFFECTIVENESS OF PNEUMOCOCCAL CONJUGATE VACCINES (PCV7, PCV10 AND PCV13) AGAINST INVASIVE PNEUMOCOCCAL DISEASE AMONG CHILDREN UNDER TWO YEARS OF AGE IN GERMANY

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Background

A general recommendation for vaccination with pneumococcal conjugate vaccine (PCV) with a 3+1 schedule was issued for German children ≤2 years in 2006. As of 2009, PCV7 was replaced by higher-valent PCVs, mostly PCV13. We calculated vaccine effectiveness (VE) of PCVs using the indirect cohort method.

Methods

Pneumococcal isolates from children with IPD were serotyped at the GNRCS using the Neufeld-Quellung reaction. VE was estimated by comparing the odds of vaccination among IPD cases due to vaccine serotypes with the odds of vaccination among IPD cases cases due to non-vaccine serotypes.

Results

For PCV7, VE against all 7 serotypes was 84% (95% CI: 70-91) for at least one dose and 98% (86-99.8) after three primary doses. For PCV13, VE was 90% (82-94) for at least one dose, 89% (75-95) post primary, and 93% (64-99) post booster. For the additional serotypes included in PCV13, VE was 88% (78-93), 84% (64-93) and 92% (61-98) respectively. VE (at least one dose) for serotype 1 was 91% (53 – 99), serotype 3: 73% (8 – 92), 7F: 98% (88 – 99.8), 19A: 79% (55 – 90). During the analysis period, no cases with serotype 5 were reported, and serotype 6A cases were not reported among vaccinated children. Vaccination rates increased from 27.4% in 2006-2007 to 80.0% in 2014-2015, but there was considerable delay in administration of doses. Over 90% of vaccine serotype cases were in non- or incompletely- vaccinated children.

Conclusions

Our data show high VE for all included serotypes. A disturbing finding is the considerable delay in administration of vaccine doses. About 90% of the remaining vaccine type IPD cases in children <2 years could have been prevented by timely vaccination.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0755
14. S - VACCINE IMMUNOGENICITY, EFFICACY, EFFECTIVENESS

POST EXPOSURE PROPHYLAXIS (PEP) WITH INTRAVENOUS IGG (IVIG) PREVENTS INFANTS FROM MEASLES

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Title of Case(s)

Post Exposure Prophylaxis (PEP) with intravenous IgG (IVIG) prevents from measles in twelve infants younger than 6 months of age

Background

Measles are highly contagious and may lead to severe complications in non-vaccinated individuals. As global herd-immunity remains a yet unreached goal active vaccination offers the best protection against measles. However vaccination is not recommended for infants younger than 6 months and infants are usually vaccinated not before the 10th month of age. Non-vaccinated infants exposed to measles are at particular high risk for severe, potentially lethal, complications of the disease.

Although measles-exposed infants younger than 6 months of age are at highest risk to develop severe complications published evidence for post-exposure prophylaxis (PEP) against measles is rare. Recommendations of PEP against measles are based on the intravenous application of pooled IgG-products (IGIV). However neither the optimal dose of IGIV, nor the acceptable time-gap between exposure to measles and PEP by IGIV are clear.

Case Presentation Summary

In the latest outbreak in Berlin (2014/2015) 1359 individuals developed measles and the incidence of measles was highest in infants (3554/ Mio). We administered polyvalent IgG (IGIV) at a dose of at least 0,4g/kg bodyweight intravenously in eleven infants with proven exposure to measles and one infant with highly likely exposure to measles younger than 6 months of age. On average the infants in this case series received IGIV four days post exposure. One infant recieved IGIV ten days post exposure. None of these developed measles.

Learning Points/Discussion

Our observations strongly reinforce intravenously administered IgG (IGIV) as post-exposure prophylaxis (PEP) against measles. We further suggest that IGIV at a dose of at least 0.4 g/ kg bodyweight should be given regardless of the time-gap after exposure.

ESP16-0510
15. S - VACCINE SAFETY

SAFETY OF THE IMMUNIZATION STRATEGIES (INFLUENZA/TDAP) FOR PROTECTION OF THE NEWBORN BY MATERNAL IMMUNIZATION.

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Background

Babies too young to be vaccinated are susceptible of preventable diseases as influenza or pertussis. Immunization of pregnant women can protect them and their infants. Monitoring and evaluating the safety of immunizations in pregnancy are a highlight point in order to implement and maintain these immunization strategies. Influenza vaccination is recommended in this target group in Valencia Region (*Comunidad Valenciana* – CV) since years ago, the Tdap vaccination strategy since 1st January 2015.

The aim of the study was to analyze adverse events following immunization (AEFI) related to influenza and Tdap vaccination in pregnant women reported in CV from 2012 to 2015.

Methods

Reports of AEFI registered in the Vaccination Information System (SIV) of CV were analyzed. Sociodemographic variables (age, risk group) and those related with the adverse events (type of event and system organ class) were included in the study.

Results

A range of 3,297 to 10,825 influenza doses were administered in pregnant women from 2012/13 to 2015/16 influenza season and 2 AEFI were reported during the study period (1 in 2014/15, rate 17 per 100,000 and 1 in 2015/16, rate 9 per 100,000). 35,907 doses of Tdap were administered in 2015 and 11 AEFI (3 per 100,000). General disorders and administration site conditions were the most common adverse events for Tdap vaccine (94%).

Conclusions

Influenza and Tdap immunization strategies in pregnancy are safe. Continued safety monitoring of vaccines is essential.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0979
15. S - VACCINE SAFETY

TRANSIENT HEPATITIS B SURFACE ANTIGENEMIA DUE TO RECOMBINANT HEPATITIS B VACCINE

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Title of Case(s)

TRANSIENT HEPATITIS B SURFACE ANTIGENEMIA DUE TO RECOMBINANT HEPATITIS B VACCINE-EUVAX B® IN A NEWBORN WITH HYPOPLASTIC LEFT HEART SYNDROME

Background

Hepatitis B is one of the most serious kind of hepatitis and a grand health problem of the world. Hepatitis B vaccines became available after early 1980s. Transient Hepatitits B surface antigenemia (HbsAg) after hepatitis B vaccination is first described in adults in 1990s and both monovalent and multivalent vaccines may cause transient HbsAg antigenemia. Herein we present a newborn with HbsAg seropositivity due to EuvaxB® vaccine.

Case Presentation Summary

A term baby-girl weighing 2940 gr was born to a 37 year-old multiparous mother after 39 weeks pregnancy. The patient was diagnosed with hypoplastic left heart syndrome prenatally according to ultrasonography. She was accepted to the neonatal intensive care unit after delivery. Hepatitis B vaccine (EuvaxB®) was administrated at the first hour after birth. Cardiac surgery was planned after cardiologic evaluation. On the second day, serum HbsAg was positive. The antigen was detected twice- in case of false-positivity- with macroELISA assay. Her liver enzymes were normal. Her mother's HbsAg was negative. On the other day HbsAg returned negative with the same method.

Learning Points/Discussion

Serum HbsAg positivity indicates acute or chronic hepatitis. But transient HbsAg antigenemia may also occur due to HBV vaccine. The incidence of transient HbsAg antigenemia after hepatitis B vaccine is uncertain. Vaccine related seropositivity develops 24 to 72 hours after vaccination and lasts approximately 8 or 9 days. The longest period of seropositivity afer vaccination is 21 days. Vaccine related transient HbsAg antigenemia should be kept in mind so that unnecessary and overdiagnostic process can be avoided.

ESP16-0876
15. S - VACCINE SAFETY

LOCAL HYPERTRICHOSIS AND PRURITUS FOLLOWING MENINGOCOCCAL C VACCINATION IN A YOUNG GIRL

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Title of Case(s)

LOCAL HYPERTRICHOSIS AND PRURITUS FOLLOWING MENINGOCOCCAL C VACCINATION IN A YOUNG GIRL

Background

Redness, swelling and induration are typical local reactions classified as adverse events following immunization (AEFI). Here, we report a case with a rare local adverse event following meningococcal group C conjugate (MCV) vaccination.

Case Presentation Summary

In accordance with the Swiss immunization schedule, a 5 year old girl had received MCV intramuscularly (right thigh) at age 21 months. A few days later redness and swelling around the injection site developed with formation of a subcutaneous nodule. The girl was also complaining about pruritus with intense daily scratching at the former injection site. The nodule disappeared after a few months, but the pruritus persisted and a blue skin discoloration 4 x 3 cm in size appeared along with hypertrichosis. Treatment with topical steroids did not resolve the symptoms and the girl was admitted to our immunization clinic for further evaluation.

Learning Points/Discussion

Hypertrichosis following immunization with various vaccines at various sites has been described in the literature, but only in very few cases. Pathophysiologic explanations for this phenomenon include a direct cause due to subcutaneous inflammation or indirectly due to repeated rubbing of the skin. We started local treatment with adhesive tape to protect the skin from further irritation and expect rapid termination of the pruritus followed by gradual regression of the hypertrichosis. A follow-up visit is scheduled and findings will be reported at the conference.

ESP16-0045
15. S - VACCINE SAFETY

COMPLICATIONS FOLLOWING BACILLUS CALMETTE-GUERIN VACCINATION IN CHILDREN UNDER THE AGE OF 18 MONTHS: AN IRANIAN MULTI-CENTER STUDY

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Background

Background: We aimed to identify the frequency and correlates of complications following Bacillus Calmette-Guérin (BCG) vaccination in children who referred to primary health care centers in Tehran for their vaccination program.

Methods

We enrolled 14044 children up to the age of 18 months who have received their BCG vaccine and presented to primary health care centers in Tehran for their routine vaccination program other than BCG. We investigated the occurrence of BCG complications through history taking from the parents and physical examination by the study physician. Based on our findings, complications were categorized into four major groups: local, regional, remote, and generalized and the frequency of these complications were compared between male and females.

Results

A total of 573 patients had experienced at least one complication following BCG vaccination. The most common complication was local side effect that was observed in 304 (2.1%) children. Lymph node involvement was the second common side effect as detected in 272 (1.9%) children. Lymph node involvement was more observed in males ($P<0.001$), and axillary lymph nodes were the most common site of involvement overall. There was a significant relationship between the age and the presence of local side effects and lymph node involvement (OR=0.96, P=0.001; and OR=1.16, $P<0.001$, respectively).

Conclusions

we found local adverse reactions as the most common complication following BCG vaccination and age was an independent predictor for the development of this adverse reaction.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0959
15. S - VACCINE SAFETY

HISTORICAL SERIES OF MILD ADVERSE REACTIONS FROM VACCINES

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Background

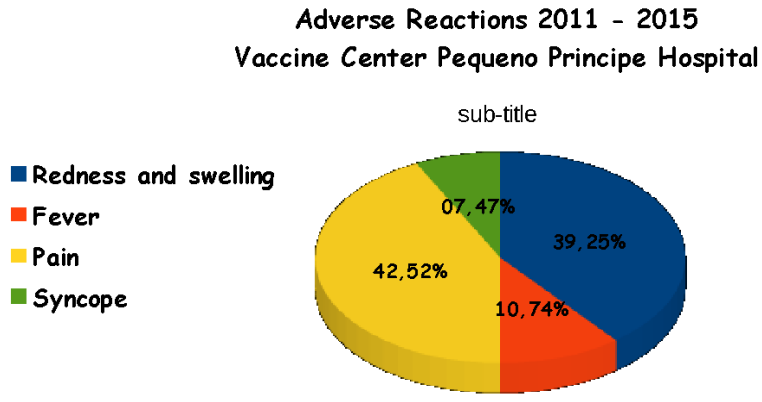
Any vaccine can cause side effects or adverse reactions(AR) however**,** the most are tolerable, with low clinical significance and are self -limited. This study confirms this concept and reiforced the security of vaccines.Misconceptions and false contraindications to immunization can discourage parents of children and adolescents to following their vaccination schedules. The aim of this study is to describe its experience,for a referral center of vaccines, in south of Brazil.

Methods

vaccine reaction forms were analysed from January 2011 until December 2015, from **Vaccine Center of Pequeno Principe Hospital,** Curitiba - PR, Brazil. Data of the most frequent vaccines used were included.

Results

Between January/2011 to December/2015, we made 36300 doses of the following vaccines: Pneumo 23 *(MSD / SP)*,Cervarix (GSK),Pertacel (DTPa) (SP) Meningitis C (NVT/PFZ),Menveo (GSK),Infanrix (GSK),Gardasil (MSD),Prevenar (PFIZER)and were observed 214 AR (0.59%), which were:39,25%(84) redness and swelling, 10.74%(23)fever, 42.52%(91) local pain, 7,47%(16) syncope 4.90% . The AR was more associated with the following vaccines: Pneumococcal conjugate vaccine 13-valent (21,42%) , Menveo (20.23%), meningococcal C conjugate vaccine (20.23%).



Conclusions

Most AR observed was mild and well tolerated. The lower AR rate of 0.59% and the no serious ARs confirms the security of vaccines and the importance to correct indication and adherence to the vaccines.

ESP16-0685
15. S - VACCINE SAFETY

EFFECTIVENESS OF PHARMACISTS-LED PROVIDER-FOCUSED INTERVENTIONS TO IMPROVE HPV VACCINATION RATES IN ADULTS IN MALAYSIA

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Background

Human papillomavirus (HPV) vaccination is universally recommended for adolescents, yet vaccination rates remain low worldwide.

Methods

A pharmacists-led provider-focused interventional study that included repeated contacts, education, individualized feedback, and strong quality improvement incentives to raise HPV vaccination rates at three qualified community health centers in Malaysia was conducted. The effectiveness of the intervention, rates of initiation of vaccination, and completion of the HPV vaccination among teenagers (girls and boys, ages 11–25 years) were compared by means of two follow-ups.

Results

We divided the sample size into two groups, intervention group 250 patients and 250 subjects in control group. We conducted multivariable logistic regression accounting for clustering by practice. Patients in interventional study group significantly increased HPV vaccine initiation during the active intervention period relative as compared to control group (girls OR 1.4, boys OR 12.1; $p < 0.001$ for both). Boys at intervention group were also more likely to continue to initiate vaccination during the post-intervention or maintenance period (OR 7.9; $p < 0.01$). Girls and boys at intervention practices were also likely to complete their next needed HPV vaccination doses than those in control group (girls OR 1.3, boys OR 21; $p < 0.04$ for both).

Conclusions

Provider-focused interventions including repeated contacts, education, individualized feed-back, and strong quality improvement incentives have the potential to produce sustained improvements in HPV vaccination rates.

ESP16-0957
15. S - VACCINE SAFETY

SAFETY AND TOLERABILITY OF A 2015/2016 TRIVALENT INACTIVATED SPLIT-VIRION INFLUENZA VACCINE IN ELITE ATHLETES

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Background

he risk-benefit analysis in elite athletes differs from that of the general population – while prevention of infections is crucial, minor vaccination adverse effects can interfere with training schedules and arouse anxiety. The objective of our study was to evaluate the safety and tolerability of inactivated trivalent 2015/2016 Northern Hemisphere formulation influenza vaccine in elite athletes.

Methods

We enrolled 117 healthy Polish elite athletes of different disciplines (i.a. swimmers, runners, triathletes, basketball players), including 49 women, aged 18-39 years (mean 25). Patients received one dose of 0.5 ml (45 µg) TIV intramuscularly. All subjects were examined with post-vaccination diary (days 0-7) including local reactions, headache, muscle pains, fever and ability to train. Adverse event (AE) data were collected including fever (temperature: ≥ 37.5°C axilla), serious AEs, and new-onset chronic illnesses up to 90 days after the vaccination.

Results

At least one AE was reported by 73.5% of athletes. Local AEs were more common among than general AEs (66.7%, vs 39.3%). Neither serious, unexpected AEs, nor new-onset chronic illness were observed. Reported local reaction were: pain at injection site (55%), redness (30%), induration (22%), edema (17%) and bruising (5%). General complains were: headache (23.9%), malaise (14%), muscle aches (11%), shivering (6%) and fever (0.9%). Fourteen vaccinees reported training inconvenience due to the vaccination but only 7 modified their schedules (mainly on the vaccination day and the day after).

Conclusions

Elite athletes tolerate inactivated trivalent influenza vaccine well but immunization may interfere with training schedule on the vaccination day and the day after. We suggest the

influenza vaccination should be performed on training-off days, and non-dominant arm vaccination site.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0777
16. S - EPIDEMIOLOGICAL MODELLING FOR IMMUNISATION

INFLUENCE OF PNEUMOCCAL VACCINATION ON THE INCIDENTION OF OTITIS MEDIA IN THE PAEDIATRIC OFFICE IN ZAGREB, CROATIA

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Background

Streptoccocus Pneumoniae is the most common infection in the preschool children, especially those attending the kindergarten. Otitis media, in the preschool age is very common diagnosis.
There is not obligatory vaccination against Streptoccocus Pneumnoniae in Croatia, only for patients with chronic disease. Some of patients could be vaccinated individually.
The purpose of the paper was to show how the vaccination against Streptoccocus Pneumoniae could prevent the onset of Otitis media in population of preschool children.

Methods

There were three generation retrospectively observed, generation 2012. year 191 children, 2013. year 170 children, and 2014. year. 174 children. All together 535 children.

The standard tests were provided.

Results

In every generation the children who are vaccinated (against Pneumoccocic disease) were observed (33 children 2012, 29 children 2013 and 26 children 2014. all together 88 children), and diagnosis Otitis media in this population was detected. As a control there were the all other children from this generation with or without dg. Otitis media.

Conclusions

There were statistically less diagnoses Otitis media in vaccinated children (against Pneumoccocic disease).

There is a need for vaccination against Pneumoccoc disease especially for the children who are attending kindergarten.

ESP16-0090
16. S - EPIDEMIOLOGICAL MODELLING FOR IMMUNISATION

PREVALENCE, SEROGROUP DISTRIBUTION AND RISK FACTORS OF MENINGOCOCCAL CARRIAGE IN ADOLESCENTS AND YOUNG ADULTS IN TURKEY

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Background

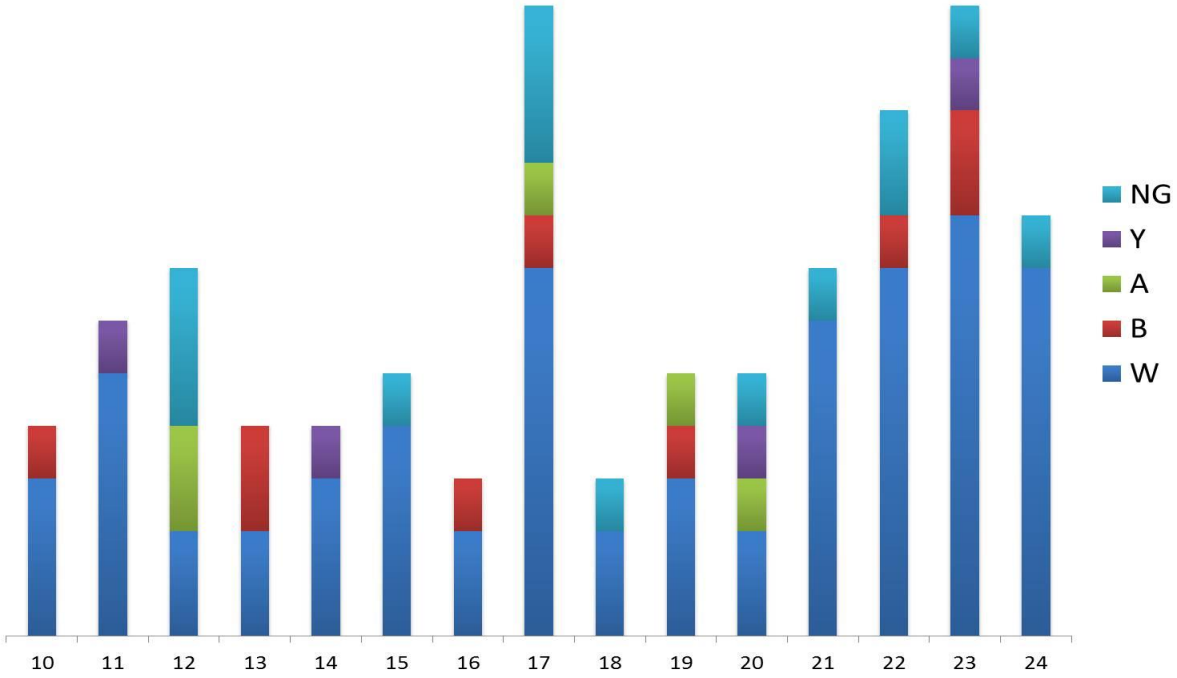
Serogroepidemiology of invasive meningococcal disease (IMD) varies considerably by countries' geographical area and immunization programmes, is continuously changing. Meningococcal carriage data is crucial for assessment of IMD epidemiology and design of potential vaccination strategies. Meningococcal seroepidemiology in Turkey differs from other countries and there is a lack of data on meningococcal carriage that represent the whole country

Methods

The aim of this multicenter study was to evaluate the prevalence of *Neisseria meningitidis* (Nm) carriage, serogroup distribution and related risk factors) of 1518 adolescents and young adults aged between 10-24 years. Presence of Nm DNA and serogroup analysis was performed using polymerase chain reaction.

Results

The overall meningococcal carriage rate was 6.3%(n=96) and 66% was serogrup W. No serogroup C cases were detected. Carriage rates of Nm by age are shown in Figure 1. The highest carriage rate was detected in 17 year-old children (11 %). Carriage rate was higher among the participants who have had household contacts with a history of Hajj/Umrah pilgrimage and was also higher among the participants who lived in a dormitory or student house ($p<0.01$ for both).



Conclusions

Nasopharyngeal carriage rate in Turkey was similar to the rate detected in other countries.The most prevalent serogroup was serogroup W. According to previous studies there no adolescence peak in the incidence of IMD in Turkey however meningococcal carriage reaches peak level by the age 17 and the highest carriage rate was found between 21-24 year olds. Adolescents and young adults carriers seems a potential reservoir for the disease and further immunization strategies including adolescent immunization might play a role for the control of meningococcal disease.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1017
16. S - EPIDEMIOLOGICAL MODELLING FOR IMMUNISATION

EFFECTIVENESS AND COST-EFFECTIVENESS OF DECENNIAL PERTUSSIS BOOSTERS FOR ADULTS

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Background

With evidence of vaccine-induced waning immunity, repeated adult pertussis vaccination may be necessary to contain the spread of pertussis. Our objective is to estimate the effectiveness and cost-effectiveness of a decennial adult acellular pertussis booster program compared to the one-time only program for adults in Ontario, Canada using a mathematical model.

Methods

A stochastic, individual-based model has been created to perform a dynamic cost-effectiveness analysis from the healthcare payer's perspective. The cost of the vaccine and vaccine administration, costs of diagnostic testing and treatment of pertussis, and costs and risks associated with vaccine-related adverse events are incorporated into the model. Health-related quality of life has also been integrated to reflect the impact of different health states on overall well being. Parameters have been obtained from the literature or will be estimated using calibration against Ontario pertussis incidence. A probabilistic sensitivity analysis will be used to examine the relative impact of these parameters.

Results

Pertussis incidence, hospitalizations, and mortality will be examined under both the one-time and decennial adult pertussis vaccination strategies. The quality-adjusted life years gained with each strategy will also be calculated to estimate the incremental cost-effectiveness ratio. The intervention will be considered cost-effective if it is found to be below $50,000 per quality-adjusted life year. Results are in progress but will be ready for presentation in May.

Conclusions

The evaluations of the relative cost-effectiveness of plausible competing strategies for pertussis immunization will allow Canadian public health decisions makers to institute policies, based on the best available data, that minimize the impact of pertussis at a reasonable cost.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0858
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

EVALUATING THE USE OF GENERAL PRACTICE DATA TO MEASURE CHILDHOOD ROTAVIRUS VACCINE COVERAGE, ENGLAND, 2014-2015

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Background

The UK introduced rotavirus vaccine in 2013. To rapidly assess vaccine coverage, Public Health England introduced a temporary automated collection using GP data from 95% of English practices. Since 2015, rotavirus vaccine coverage data has also been available from child health information systems (CHISs, including non GP-registered individuals). We compared rotavirus vaccine coverage estimates from GP and CHIS data to evaluate GP data as a source for vaccine coverage estimates.

Methods

Local authorities (LAs) in England with rotavirus coverage data available from both sources were included. We compared the 2-dose rotavirus vaccine coverage data for children born between 1 April 2014 and 30 September 2014 evaluated at 25 weeks of age from GP systems, and 12 months of age from CHISs, using binomial regression. We calculated the proportion of LAs with significantly (α=0.05) different estimates in the two datasets.

Results

Of 152 LAs, 71(47%) had coverage data from both CHIS and GP systems for the whole study period. There was no difference in rotavirus vaccine coverage estimates in CHIS and GP systems (88%, 95%CI 86.6-89.4 vs 86.8%, 95%CI 83.3-90.2, p=0.25). Of 71 included LAs, 33 (46.5%) had different estimates in CHIS and GP systems. Of these, 12 (36%) were in London and an additional 7 (21%) in major urban centres (North West, West Midlands).

Conclusions

In England in 2014-2015, GP data could be used to accurately estimate national rotavirus vaccine coverage. Compared with CHIS data-derived coverage, GP data-derived coverage assessed vaccination status at a younger age, resulting in discrepancies at local level, particularly in urban areas with high population mobility. Using GP data to monitor recently vaccinated cohorts allows rapid estimation of national vaccine coverage, but requires caution when interpreting local estimates.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0749
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

PARENTAL IMMUNISATION NEEDS AND ATTITUDES (PINA) SURVEY IN PAEDIATRIC HOSPITAL CLINICS (PINA-H) AND COMMUNITY MATERNAL AND CHILD HEALTH CENTRES (PINA-C) IN MELBOURNE, AUSTRALIA

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Background

While 92% of Australian children are fully immunised by 24 months of age, 1.7% of parents register vaccine exemption on grounds of personal belief and a further proportion choose to select out or delay vaccines. We aimed to determine parents' (i) level of vaccination concerns; (ii) specific vaccine related concerns; (iii) use of, trust in and satisfaction with vaccine resources and Health Care Providers (HCPs) and (iv) the relationship between socio-economic status (SES) and vaccination status.

Methods

Parents of children under five years attending General Paediatric Clinics in a Tertiary Paediatric Hospital (PINA-H) and children under 19 months attending Community Maternal Child Health Centres (PINA-C) in Victoria, Australia were recruited. Surveys were completed on iPads and vaccination status was obtained from the Australian Childhood Immunisation Register.

Results

Between September 2014 and May 2015, 303 (76%) parents completed the PINA-H and 311 (81%) the PINA-C surveys. Despite high levels of overall support for vaccination (98%) nearly half of parents (43%) reported some vaccine concerns. Specific concerns included too many vaccines in the first two years (25%); concerns about vaccine ingredients (22%); allergies (18%) autism (11%) or their child's immune system being more sensitive than most (28%) or weakened by vaccines (17%). HCPs were considered the most useful and most trusted sources for vaccine information. Nearly a quarter of parents (22%) reported insufficient knowledge to make good decisions about vaccination. There was no evidence of a relationship between SES and the child's vaccination status.

Conclusions

Despite high support for vaccines, nearly half of parents have some concerns regarding vaccination. Given some parents' lack of decision-making confidence and high levels of trust in HCPs, strategies to address vaccine concerns in the consultation room are needed.

ESP16-0423
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

ANALYSIS OF MANDATORY VACCINE COVERAGE AND VACCINE HESITANCY IN FERRARA, ITALY (YEARS 2011-2014)

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Background

Vaccination is a key preventive intervention. Recently published reports show that in Italy in 2014 the coverage rate for mandatory vaccinations fell for the first time below 95%, the minimum threshold to ensure herd immunity.

Due to the concern for the emerging data, the Department of Public Health in Ferrara analyzed immunization data of mandatory vaccinations in years 2011-2014 to monitor the trend of vaccine coverage and vaccine hesitancy.

Methods

Data about coverage rate for mandatory vaccinations (polio, diphtheria, tetanus, hepatitis B) in the years 2011-2014 were evaluated, considering resident newborns who received at least 3 doses at 24 month. For 2014 the obtained data were compared with national ones.

Reasons of non-vaccination were also investigated and splitted in four categories: objectors, transferred, untraceables, others (exemptions or missing informations).**Results**

The cohort of the newborn in the studied period was equal to 10.924 subjects.

Table 1 shows data about coverage for mandatory vaccine at 24 months of age.

	Ferrara				Italy
	2011	2012	2013	2014	2014
Polio	97,6%	97,2%	97,5%	96,3%	94,7%
Diphteria	97,5%	97,2%	97,5%	96,3%	94,7%
Tetanus	97,5%	97,5%	97,6%	96,3%	94,8%
Hepatitis B	97,5%	97,2%	97,4%	96,2%	94,6%
Mandatory vaccinations	97,5%	97,2%	97,3%	96,2%	94,7%

320 newborns result to be unimmunized, with the following distribution: 107 parental objection, 103 transferred, 53 untraceable, 57 others.

The percentage of vaccine hesitancy, stable around 0.5% from 2011 to 2013, increased to 2.3% in 2014.

Conclusions

These data confirm a decreasing trend of vaccine coverage, even if at a lower rate than the national one. The coverage rate remained above 95% for all mandatory vaccinations. Vaccine hesitancy is the first cause of missed vaccination and its rate increased widely very recently.

ESP16-0213
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

POST-PARTUM VACCINATION PROMOTION INTERVENTION USING MOTIVATIONAL INTERVIEWING TECHNICS IMPROVES VACCINATION COVERAGE DURING INFANCY

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Background

Delays in vaccinations at 2, 4 and 6 months are associated with a higher probability for delay in age-appropriate vaccination during childhood. The aim of this study was to assess the long-term effectiveness of an information session targeting immunization that was performed during postpartum hospitalization on vaccination coverage (VC) in children.

Methods

An individual educational information session, administered according to motivational interviewing technics and regarding immunization of infants at 2, 4 and 6 months, was proposed (experimental group) or not (control group) during post-partum stay at the maternity. Immunization data were obtained through the Eastern Townships Public Health registry at 3, 5, 7, 13, 19 and 24 months of age. Logistic regressions with repeated measures were conducted to assess intervention's impact on the whole vaccination during infancy. Relative risks (RR) were estimated and a multivariate model was realized

Results

Respectively, 1140 and 1249 families were included in the experimental and control groups. A significant increase in vaccination coverage of 3.2, 4.9, 7.3, 6.7, 10.6 and 5.1% was observed at 3, 5, 7, 13, 19 and 24 months of age. Children from experimental group had 9% more chance to have a complete vaccine status between 3 and 24 months compared to children from control group (RR (95% CI): 1.09 (1.05-1.13), p<0.001). Children who had complete vaccine status at 3 months were more likely to have a complete vaccine status at 24 months of age (82.3 vs 48.1%, RR (95% CI): 2.72 (2.28-3.24), p<0.001). After adjustment, estimated RR of the intervention's impact is 1.05 (1.02-1.07), p<0,001.

Conclusions

This new vaccination promotion strategy based on motivational interviewing technics improves the first vaccinations but also enhances the entire infancy vaccination schedule.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0829
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

PROMOTING VACCINATION AT BIRTH WITH MOTIVATIONNAL INTERVIEWING SESSION IMPROVES VACCINATION INTENTION AND REDUCE VACCINATION HESITANCY

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Background

Many countries are dealing with growing numbers of individuals who are delaying or refusing recommended vaccinations for themselves or their children. This has created a need for approaches and strategies to address vaccine hesitancy. The aim of this study was to assess the effectiveness of an information intervention delivered during postpartum hospitalization to enhance vaccination intention and reduce vaccine hesitancy in parents.

Methods

A randomized controlled trial was conducted in 4 maternity wards in Quebec (Sherbrooke, Québec, Montreal (Ste-Justine and McGill University). Between September 2014 and December 2015 an individual information intervention on infants immunization based on motivational interviewing technique was delivered to parents (intervention group) or not (control group). A questionnaire based on the Health Belief Model and Opel's tool to measure vaccine hesitancy was administered to all participants in the intervention group before and after the intervention. Parents' intention to have their infants vaccinated and parents' vaccine hesitancy score were calculated.

Results

1223 families were included in the experimental group. Before intervention, global vaccination intention was 78% and was significantly different between each maternity wards (74%, 77%, 84%, 79%, p=0.02). A significant increase in vaccination intention was observed in each sites after the intervention (74% vs 89%, 77% vs 85%, 84% vs 95%, 79% vs 93%) with a global increase of vaccination intention of 12% (78% vs 90%, p <0.0001). A significant decrease in Opel's vaccine hesitancy score was also observed before and after the intervention in each maternity ward (28% vs 16%, 29% vs 24%, 27% vs 20%, 24% vs 13%) with a global decrease of 33% (p<0.0001).

Conclusions

An information intervention based on motivational interviewing technique delivered at birth is effective to improve vaccination intention and address vaccine hesitancy.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0463
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

VARICELLA-ZOSTER VIRUS INFECTION IN BIRTH COHORTS INCLUDED IN THE VARICELLA VACCINATION PROGRAM. NAVARRA, SPAIN

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Background

Navarre, Spain, initiated universal chickenpox vaccination in 2007, for children born since 2006. A catch up was performed for children born in 2004 and 2005.

We aim to asses the prevalence in the 2014 population of a previous chickenpox and herpes zoster (HZ) episode in the cohorts included in the varicella vaccination program, in vaccinated (breakthrough varicella) and non-vaccinated.

Methods

From the 2014 Population database of people covered by the Health Service of Navarre, we selected the cohorts in which chickenpox vaccination had been offered (born between 2004 and 2013), and we measured the vaccination coverage, and the prevalence of previous chickenpox and HZ according the vaccination status.

Results

Population: 66,669 inhabitants (inh.). Any-dose vaccinated: 87%. 2-dose vaccinated: 70%

Prevalence of a previous episode of chickenpox:

- in all the cohorts: 59.46 cases per 1000 inh.

- in non-vaccinated subjects: 354.70 cases per 1000 inh.

- in vaccinated subjects: 15.29 cases per 1000 inh. (36.72 in 1-dose vaccinated and 10.19 per 1000 inh. in 2-dose vaccinated)

Prevalence of a previous episode of HZ:

- in all the cohorts: 6.13 cases per 1000 inh.

- in non-vaccinated subjects: 26.28 cases per 1000 inh.

- in vaccinated subjects: 3.12 cases per 1000 inh.

- in vaccinated subjects with history of breakthrough varicella: 25.93 cases per 1000 inh.

- in vaccinated subjects with no history of previous chickenpox: 2.77 cases per 1000 inh.

Conclusions

- Breakthrough varicella was 3.60-fold higher in 1-dose vaccinated.

- HZ was 8.42-fold higher in non-vaccinated than in varicella vaccinated.

- In vaccinated, HZ was 9.37-fold higher in those who reported a previous varicella breakthrough episode than those with no history of previous chickenpox.

ESP16-1027
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

VACCINE ADVOCACY - THE BRIDGE BETWEEN DISEASE AND HEALTH

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Background

Vaccine advocacy - the bridge between disease and health

Among the great threats for mankind in the last decades we find antibiotic resistance, low vaccination coverage and public mistrust in health care provider's decisions. All three are strongly interconnected. If vaccination coverage against HPV (human papilloma virus) will be low, we will register a high rate of cervical cancer, widespread forms of condyloma acuminata, HPV infected new born babies. Non-protected women will be at risk of high mortality. The poverty gives rise to diseases, suffering, deaths.

Purpose: sharing vaccine advocacy's experience with GP's team from other countries in finding optimal solutions for raising rate of HPV vaccination coverage.

Methods

Vaccination remains indisputably the most cost-effective measure that we can preserve the life and health of dearests. Evidence based medicine and continuing education of population, remains the best lawyer for this purpose. Life and science has demonstrated the superiority of prevention versus treatment.

First of all immunization prevents and protects your child. Secondly, it protects your family and then the community where you live. The concept of freedom must be well understood. The aspect means taking the whole responsibility and accepting social norms, in order to see life as an evolving process and not as an involute one.

Results

An applicable National Immunization Program (NIP), having permanent vaccines supplies for complete schedule, compliance with this program to the feminine population, an optimal vaccine coverage, remain some major targets for Romania , targets that can contribute for maintaining the long-term health of our children.

Conclusions

Participants will exchange their experience and ideas to improve the vaccine coverage against HPV and for searching and finding new methods of implemented the prevention program for cervical cancer in their countries.

ESP16-0741
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

WHAT DO MOTHERS OF BOYS KNOW ABOUT THE VACCINE AGAINST HPV IN PORTUGAL AND WILLINGNESS TO VACCINATE

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Background

In 2008 the quadrivalent vaccine against HPV was included in the national immunization program (PNV) for girls aged 13 years. The Immunization Committee from the Portuguese Pediatric Society (SPP) recommends individual consideration of the vaccine to boys. The perception from the population to vaccination is a relevant issue to design campaigns and to improve literacy about health preventive measures. The main objective was to quantify the level of knowledge and awareness of HPV vaccination in males.

Methods

An online interview of 407 Portuguese mothers of boys (6-18 years), based on a questionnaire designed with 25 questions designed by GfK Metris, a market research company, and validated by SPP was performed using the system *Computer Assisted Web Interviewing*. The interviews took place in May 2015 with a total duration of 15 minutes.

Results

85% had heard about HPV and 70% were aware of an available HPV vaccine. Only 19% knew that this vaccine could be used in boys. Almost 75% would favor the vaccination of their sons. 4% of those who are against assume to be so due to lack of information. Less than 1% were formally against. 44% would support vaccination in the context of private practice. A similar percentage would follow the opinion of the pediatrician; only 10% are against it. A majority agrees with the inclusion of boys in PNV.

Conclusions

Only few of the surveyed mothers admitted to know about the possibility of administration of the vaccine against HPV to boys and assume a favorable position concerning the possibility of vaccinating their boys against HPV. The pediatrician advice was found to be decisive in vaccine related issues.

ESP16-0567
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

EFFECT OF BACILLE CALMETTE GUERIN (BCG) SHORTAGE ON IMMUNISATION PRACTICE IN EUROPE – A PTBNET STUDY

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Background

Universal or selective BCG immunisation is part of TB prevention in most European countries. Current reports indicate an ongoing BCG shortage, that may influence immunisation practice. This study aimed to determine current availability of BCG across Europe, and describe the impact of existing shortages.

Methods

Web-based survey among the pediatric-tuberculosis-network- European-trials-group (ptbnet) members, conducted between May and October 2015.

Results

Twenty individuals from 13 European countries participated (Table). BCG was routinely used in 11 countries, comprising BCG-Denmark SSI 1331 (10/11;91%) and BCG-Russia Bulbio Sofia (1/11;9%). BCG was imported by a single distributor (6/11;55%), a government agency or the department of health (4/11;36%), or was produced nationally (1/11;9%). Eight countries reported an ongoing BCG shortage (8/11;73%), and one country reported a shortage that resolved in 2014 (Table). Two countries experiencing a shortage were stockpiling BCG. Reported consequences of the shortage were: BCG not given as completely unavailable (2/8;25%); BCG given: whenever available (1/8;13%), only in certain regions of the country (1/8;13%), to selected high-risk individuals (2/8;25%), by cohorting vaccinees on specific days to maximise the use of multi-dose vials (3/8;38%). Two countries were considering a change of manufacturer/supplier (2/8;25%).

Table

	n	%
Participants	20	100
Paediatric hospital	16	80
General hospital	3	15
Outpatient TB specialised clinic	1	5
Countries	13	100
Not routinely using BCG (Austria, Germany)	2	10
Reporting no current shortage (Bulgaria, Slovenia, Croatia*)	3	15
Reporting current shortage (Belgium, Finland, Greece, Italy, Spain, Sweden, Switzerland, United Kingdom)	8	75

* reported a previous shortage

Conclusions

In this survey, BCG shortage was reported in eight countries, leading to adapted immunisation practice. However, as BCG-Denmark SSI 1331 is the most commonly used BCG vaccine in Europe, the shortage likely affects further countries. If supply shortages continue, it is likely that a significant proportion of infants and children in Europe will not be immunised and/or the BCG strain used will be changed. To achieve consistently high BCG immunisation coverage, better collaboration between national health agencies and vaccine manufacturers is crucial.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0430
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

ASSESSING THE CONTEXTUAL AND SOCIAL DETERMINATS OF HEALTHCARE WORKERS (HCWs) ON SEASONAL FLU VACCINATION IN A TERTIARY PEDIATRIC HOSPITAL IN GREECE

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Background

Influenza vaccination rates remain low internationally among HCWs who are an important priority group for vaccination. Greece, like other European countries, reports low rates but there is little data on the barriers and facilitators of influenza vaccine in the healthcare setting. This study assessed HCWs' knowledge and perceptions about seasonal flu vaccination in a tertiary pediatric hospital in Athens, Greece.

Methods

A cross-sectional anonymous survey of HCWs was conducted to assess HCWs attitudes toward influenza vaccination in the hospital as well as knowledge and perceptions about the influenza vaccine. The survey instrument also identified the most commonly cited facilitators and barriers to HCW receipt of the seasonal influenza vaccine. Descriptive statistics and associations between specific factors were conducted using SPSS v.20.

Results

352 participants (106 doctors,145 nurses,and 101 other hospital staff) responded to the survey (response rate around 65%). Overall, 64% of participants had not been vaccinated in the previous 3 years. Non-vaccination rates were significantly higher among nurses(75.7%) and cleaning/food service workers(72.7%), compared to doctors(40%) ($P<0.001$). The most commonly cited reasons for non-vaccination were concerns regarding vaccine side effects(40.1%) and ineffectiveness(26.6%). Only 14.2% of the respondents received influenza vaccine annually, although 88.2% reported difficulties obtaining the vaccine at the hospital. Only 26.6% strongly disagree with a mandatory administrative directive for vaccination.

Conclusions

We identified both knowledge and perception barriers as well as logistical difficulties that might undermine HCW influenza vaccination in the hospital setting, although a majority agreed with mandatory directives for vaccination. Additional qualitative studies will help better characterize modifiable barriers to vaccination. These findings may inform the development of interventions to improve HCW influenza vaccination in hospitals in Greece.

ESP16-0786
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

UPTAKE AND PARENTAL ACCEPTABILITY OF CHILDHOOD VACCINES AMONG HONG KONG INFANTS AND TODDLERS

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Background

Active immunisation is an effective strategy for preventing childhood infectious diseases. A number of existing and new vaccines are not included in the Government Vaccination Programme (GVP) of Hong Kong. This study investigated the uptake of such vaccines in Chinese infants and toddlers and acceptability among their parents.

Methods

This study recruited Chinese parents who had children aged 6-30 months. They completed an online self-administered questionnaire on uptake of vaccines included under GVP in Hong Kong (http://www.fhs.gov.hk/english/main_ser/child_health/child_health_recommend.html) and five non-GVP vaccines (rotavirus, influenza, meningococcus, *Haemophilus influenza* type b [Hib] and hepatitis A). Parents gave reasons for not accepting the latter vaccines if their children did not receive them.

Results

588 parents with children aged 1.2 ± 0.4 years participated. 314 (53.4%) of these children were males. 570 (96.9%) children received vaccines according to GVP. The uptake rates for rotavirus, influenza, meningococcus, Hib and hepatitis A vaccines were 423 (71.9%), 108 (18.4%), 161 (27.4%), 252 (42.9%) and 189 (32.1%). Breastfeeding ever was associated with higher uptake of rotavirus vaccine ($P = 0.003$) but not the other four vaccines ($P > 0.14$). The most common reasons for non-uptake were high cost for rotavirus vaccine (35.8%), worry about safety for influenza vaccine (46.6%), lack of knowledge about disease for meningococcus (37.7%) and Hib (48.8%) vaccines, and unawareness of vaccine availability for hepatitis A vaccine (31.8%).

Conclusions

The compliance with GVP is high among Chinese infants and toddlers whereas there is variable uptake of vaccines not covered by GVP. Breastfeeding influences rotavirus vaccine uptake. This survey also identifies some barriers for parents to accept non-GVP vaccines.

ESP16-0894
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

BEHAVIORAL INOCULATION? AN EFFECTIVE COMMUNICATION STRATEGY TO INDUCE RESISTANCE TOWARDS NEGATIVE INTERNET MESSAGES ABOUT THE HPV VACCINATION?

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Background

This study investigated whether the communication strategy “inoculation” can strengthen Dutch parents’ attitudes towards the HPV vaccination in order to make them more resistant to negative HPV messages on the Internet. With inoculation parents are exposed to weak arguments against attitudes favouring HPV vaccination, including refutation of these arguments.

Methods

In 2014/2015 an online two-phase experiment was carried out among 390 parents of 12/13 year old girls. Phase 1 consisted of a baseline measurement of two outcome variables attitude extremity (how positive or negative parents are towards HPV vaccination) and attitude certainty (how certain parents are about their attitude towards HPV vaccination), and other psychological measures. Next, participants were randomly assigned to 1) inoculation message communicating arguments used on anti-vaccination websites, 2) receiving HPV brochure used to inform parents and daughters, 3) control group who did not receive HPV-related information. Phase 2 started seven days after participants completed phase 1. The participants read a persuasive attack in the form of a vaccine-critical internet message and filled out the follow-up measurement.

Results

No statistical differences were found between the three conditions for attitude extremity and attitude certainty when adjusting for baseline and/or covariates. Participants who received HPV brochure reported highest extremity and certainty attitudes followed by participants in the inoculation condition. Participants in the inoculation and control condition reported more extreme negative attitudes at post-test compared to pre-test.

Conclusions

In this study behavioural inoculation was ineffective in inducing resistance to persuasion on the topic of HPV-vaccination. Additionally, the results suggest that the persuasive attack was responsible for the negative attitude change among parents. More attention needs to be paid to strategic communication interventions that induce resistance towards negative HPV messages.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0995
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

THE INTENTION OF DUTCH GENERAL PRACTITIONERS TO OFFER VACCINATION AGAINST HERPES ZOSTER, PNEUMOCOCCAL DISEASE AND PERTUSSIS TO THE ELDERLY

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Background

In the Netherlands, the only vaccination routinely offered by General Practitioners (GPs) to the elderly within a national program is influenza vaccination. Vaccines against herpes zoster, pneumococcal disease and pertussis are available, but rarely used. The aim of this cross-sectional study was to assess the predictors of GPs' intention to vaccinate people aged 60 years and older against other infectious diseases than influenza given their possible role in offering these vaccines.

Methods

All Dutch GPs were invited to fill in an online questionnaire about factors that influence their willingness to vaccinate the elderly, practical considerations of adding more vaccines to the national program, demographics and characteristics of their patient population.

Results

Prediction analysis showed that the intention of GPs (N=732) to offer additional vaccination is mainly predicted by their attitude, and whether they think that the GP is suitable to administer additional vaccinations (R^2=.60). The attitude of GPs was mainly predicted by the preference to offer vaccination on the basis of co-morbidities instead of age, and the perceived severity and prevalence of the different diseases (R^2= .39).

Conclusions

In order to ensure a positive attitude of GPs towards offering additional vaccinations to the elderly, they need to have evidence-based information about severity and prevalence of the diseases as well as about advising vaccination based on age or based on high-risk groups.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0738
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

CHANGE IN THE PNEUMOCOCCAL VACCINATION SCHEDULE IN BRAZIL FROM 3+1 TO 2+1: DO WE NEED A BETTER ASSESSMENT OF BOOSTER VACCINATION COVERAGE?

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Background and Objective

Brazil introduced a pneumococcal conjugate vaccine (PCV) in its National Immunization Programme (NIP) in 2010 using a 3+1 schedule (ages 2/4/6 months, booster at 12-15 months, catch-up in <24-month-olds). Subsequently, reductions in invasive pneumococcal disease, pneumonia, otitis and carriage were observed. In January-2016 a 2+1 schedule was adopted (ages 2/4 months, booster preferably at 12 months, up to 4 years). As a booster contributes to maximal PCV effectiveness, particularly for some serotypes, it is important to evaluate booster vaccination coverage (BC), especially at this time of schedule change in Brazil.

Methods

We reviewed the literature and national reports to obtain BC data from Brazil and other Latin American countries that have switched from a 3+1 to a 2+1 PCV schedule.

Learning Points Discussion

Information on BC in Brazil in the literature is limitedand concerns have been raised about heterogeneity and incomplete vaccination. Administrative coverage estimates from the Brazilian NIP vaccination register showed BC greater than the targeted coverage of 95% in 10 of the 27 states in 2013. BC was <80% in 5 states (Table). Preliminary 2015 data reported by the Immunization Program of the health department of the city of Recife showed that ~24% fewer children received a booster dose compared to dose 1. The caveats associated with deriving coverage estimates from administrative data (e.g. complexities in estimating target population denominators) and the sub-optimal BC in some states highlight that Brazil may benefit from a community-based survey to acquire accurate PCV coverage estimates, and to assess homogeneity across states and municipalities, and timeliness of booster vaccination. These factors are vital to guaranteeing protection of children against pneumococcal diseases.

Table: Vaccination coverage for the booster dose in Brazil, by state (2013 complete data)

State	Booster coverage (%)
Acre	56.1
Roraima	74.3
Amazonas	76.1
Pará	76.5
Amapá	78.3
Maranhão	81.0
Rio de Janeiro	85.8
Alagoas	86.6
Tocantins	88.9
Mato Grosso	90.0
Rio Grande do Sul	90.1
Bahia	90.5
Rio Grande do Norte	90.9
Paraíba	91.0
Piauí	92.5
Pernambuco	92.9
Rondônia	93.1
Other 10 states	95.5–108.0

Source: administrative coverage estimates from the Brazilian National Immunization Programme vaccination register, available at http://tabnet.datasus.gov.br/cgi/tabcgi.exe?pni/cnv/cpniuf.def
Booster coverage defined as number of administered booster doses divided by estimated target population of 1 year of age

Funding: GlaxoSmithKline Biologicals SA

ESP16-0179
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

AUDIT OF HEPATITIS B TESTING AND VACCINATION IN CHILDREN LIVING IN HEPATITIS B POSITIVE HOUSEHOLDS

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Background

Public Health England recommends vaccinating children against hepatitis B when they live in hepatitis B positive households.
At risk children are not always identified at birth and for those that are vaccinated, hepatitis status is not always checked at one year.
This could lead to infected children not being identified in a timely manner.
Public Health England has recently introduced Dried Blood Spot (DBS) testing for infants.
This audit includes the use DBS for older children not yet tested.

Methods

Our laboratory supplied a list of positive hepatitis B results over a 14-month period.
Through our patient administration system we identified children with the same surname and living at the same address.
We then ascertained whether their hepatitis B status was known – if not GPs were asked to confirm hepatitis B contact and send relevant test results.
If untested, DBS kits were sent to GPs to aid this process.

Results

Over a 14-month period there were 888 HBsAg positive results.
As a result of the audit, 77 children have been tested by by GP or in hospital outpatients.
For other children identified, 97 dried blood post testing kits have been sent to GPs.
Completion of the audit will be reviewing the results of DBS and recommending wider roll out if successful.

Conclusions

This was a time-consuming method of identifying at-risk children.
It has highlighted inadequacies in current systems as it identified several children who had not been vaccinated or tested.
The audit recommends that at-risk children should be identified by the team caring for the infected adult and the GP advised to test and immunise at-risk children.
Dried blood spot testing is a simple way of the testing children and particularly useful in primary care.

ESP16-0040
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

THE IMPACT OF AN URBAN BASED PAEDIATRIC IMMUNIZATION PROGRAMME IN KENYA: WELL BABY CLINIC PROGRAMME

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Background

The provision of childhood vaccinations remains a global challenge in the most vulnerable, most disadvantaged and remote populations, and below the target levels.Towards this, Gertrude's Children's Hospital, Kenya launched an expanded immunization programme. This study was designed to evaluate the impact of the Well Baby Clinic immunization programme, which was launched to provide immunization services to children at all points of contact with healthcare workers.

Methods

This was a retrospective study. Hospital records covering immunization were reviewed at all Well Baby Immunization clinic sites for the period between the years 2007 and 2012. The immunization programme was piloted in 2007 and the programme has since scaled up to eleven clinics, networked through a Wide-Area-Network. The target population is children under the age of ten years, residing in slum areas in Nairobi and its outskirts. To increase efficiency, information management and allow for increased coverage, the hospital adopted Information Technology by way of a Hospital Management Information System.

Results

The immunization programme has had a transformational impact on children living in Nairobi and its environs. In 2008, 29,847 children were immunized; 2009, 45,442; 2010, 60,532; 2011, 62,676 and, in 2012, 69,385. Cumulatively, from the onset of the project in 2007 to May 2012, there was a 132% increase in the number of children immunized at the hospital's and outreach clinics. Furthermore, reduced waiting times, from two-three hours to less than thirty minutes and customer feedback surveys conducted established patient satisfaction levels over 95%, leading to increased referral of patients.

Conclusions

These efforts are in line with the WHO Expanded Programme of Immunization and United Nations Millennium Development Goals to ensure that children in all countries benefit from life-saving immunizations.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0174
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

DETERMINANTS OF DELAYED UPTAKE OF IMMUNIZATION REGIMENS: IMPORTANT LESSONS FOR FUTURE TB TRIALS IN WESTERN KENYA

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Background

Immunization remains one of the most cost effective and efficient ways of preventing childhood diseases all over the world. Delayed uptake of immunization regimen puts the children at a risk of contracting vaccine preventable diseases like tuberculosis. We sought to investigate the determinants of delays in uptake of immunization regimens among children between 1 and 4 years living within Boro Division, Siaya County

Methods

Descriptive cross sectional study design employing quantitative methods was used. The target population was mothers of children between 1-4 years who have lived in Boro division, Siaya County in the past one year. Simple random sampling technique was used to come up with a proportional sample size per location of 382 from a target population of 6800 mothers/caretakers. Data was analyzed using Statistical Package for Social Scientists (SPSS) for Windows version 12.0.

Results

The results showed 17% of children did not complete immunization at 1 year. Being divorced ($p=0.0023$), spouse negative attitude towards immunization ($p < 0.0001$), believing in African Religious Churches ($P=0.0001$), having no source of income ($p = 0.0395$), lack of formal education by the mothers ($p < 0.0001$), and lack of formal education by the spouses ($p=0.0402$) were significantly associated with delays in uptake of immunization regimens. However, perception and attitude variables had no significant association with delay in uptake of the immunizations regimen

Conclusions

The uptake of immunization among children in this division is very high, and above the national and provincial averages. However, there are delays in the uptake of immunization regimen and therefore compliance to the immunization schedule is not very good. This therefore puts the children in danger since they don't get the vaccinations as required by the national immunization program

ESP16-0293
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

WHICH HEALTH CARE PROVIDERS PROVIDE IMMUNISATION INFORMATION TO FUTURE PARENTS?

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Background

New Zealand has a maternity care system where pregnant women transition from their GP to a variety of lead maternity carers (LMC). Different LMC types may vary in their provision of information about infant immunisation. Our objective was to describe the relationship between type of healthcare utilised during pregnancy and the receipt of information about infant immunisation.

Methods

We utilised a large, diverse and nationally generalisable cohort of women surveyed during pregnancy. Women were asked if they had received information that would encourage or discourage them to immunise their child once s/he was born. Women described their relationship and interactions during their pregnancy with health care providers.

Associations were described between health care contacts and the receipt of information about immunisation with analyses adjusted for maternal demographics. Associations were reported using adjusted odds ratio (OR) and 95% confidence intervals (CI).

Results

Information about immunisation was received by 2697/6164 (47%) of the pregnant women. After adjustment for maternal demographics and other health care contacts, the odds of a pregnant women receiving immunisation information were increased if they had seen their GP (OR=1.18, 95%CI 1.03-1.35) or a complementary health care provider (OR=1.40, 95%CI 1.21-1.63) during pregnancy. In comparison with women whose maternity care was provided by an independent midwife, the odds of receiving information were increased if maternity care was shared between an LMC and GP (OR=1.32, 95%CI 1.02-1.71) and decreased if this was provided by an obstetrician (OR=0.77, 95%CI 0.63-0.95).

Conclusions

Receipt of information about immunisation during pregnancy varies with type of LMC. Independent of LMC type, women who also access care from their GP or a complementary health care provider are more likely to receive information about their future child's immunisation.

ESP16-1045
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

IMPORTANCE OF THE REGULAR IMMUNIZATION FOR THE ERADICATION OF INFECTIOUS DISEASES IN CHILDREN

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Title of Case(s)

Importance of the regular immunization for the eradication of infectious diseases in children

Background

Immunization has proved to be a supreme method to eradicate children's infectious diseases worldwide. The impact of immunization over the reduction and eradication of infectious diseases and the impact of the anti - vaccine media campaign. Comparative data reports of infectious disease and immunization reports for a period of 5 years (2006-2010) have been used referred to a 5-year period (2011-2015). Analytic, descriptive and comparative method have been used for the processing.

Case Presentation Summary

Out of 1095 children (2006-2010) aged 0 to 6 years, 98% were vaccinated in accordance to the immunization program. In the period of five years, five cases of Measles, one case of Rubella, seven cases of mumps and 451 cases of varicella.

Of the total 1055 children (2011-2015) aged 0 to 6 years, 96% were vaccinated in accordance to the immunization program.In this period four cases of Measles, one case of Rubella, six cases of mumps and 437 cases of varicella had been registered.

The results clearly display a number of significant varicella cases against which no immunization has been conducted, while kids' rash fevers have been recorded only sporadically. Other childhood diseases such as poliomyelitis, tetanus and pertussis are considered to have been eradicated in Macedonia.

The excessive anti- vaccine media campaign has caused a slight decrease in the percentage of regularly vaccinated children

Learning Points/Discussion

The results clearly show the benefit of the successfully conducted immunization which saved significant resources not only to treat diseases but also to deal with their consequences. There is a need for a continuous education of the parents carried out by the pediatricians and related to the benefits of the regular immunization

ESP16-0219
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

SURVEY OF HEALTH CARE PROVIDERS' PERCEPTIONS OF VACCINE PRODUCT MONOGRAPH SAFETY LANGUAGE AND IMPACT ON USE OF VACCINES IN PREGNANCY

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Background

In certain circumstances, WHO recommends maternal immunization to prevent serious infection in pregnant women, newborns, or both groups. Despite these recommendations, global adoption of maternal immunization has been limited. One potential barrier to these programs may be perceptions that product monograph information statements regarding safety and use in pregnancy contradict recommendations for vaccine use. Our objective was to determine the effect of precautionary statements in product monographs on healthcare providers' perceptions of the safety and anticipated use of vaccines in pregnancy.

Methods

Healthcare providers from low, middle, and high income countries were recruited at two global maternal health conferences and from among participants in teaching programs in Ethiopia, Ghana, Uganda, and Laos. Subjects completed an eight-item online survey capturing their perceptions of the safety of recommended vaccines after reading product monograph information. The analysis was descriptive.

Results

141 participants were recruited from 49 countries in six WHO regions. They included obstetricians (80%), midwives (9%), family physicians (4%), and others (7%). 79% of respondents prescribed or administered immunizations and 52% read product monographs "often" or "occasionally". When provided with examples of influenza vaccine product monographs (e.g., "*safety and effectiveness…* [in pregnancy] *is not established"*, use *"only if clearly needed*"), 38% of respondents perceived the vaccine as moderately or very unsafe, 18% would not recommend the vaccine despite national guidelines, and 75% reported that this language would affect how they counseled patients.

Conclusions

The regulatory language used in product monographs regarding safety and use of vaccines in pregnancy can be misinterpreted by maternal healthcare providers as opposing current immunization recommendations. Efforts are needed to clarify labelling information regarding use of vaccines in pregnant women.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0257
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

VACCINATION COVERAGE IN CHILDREN WITH CHRONIC DISEASES

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Background

Vaccines are important to prevent life-threatening infectious diseases in healthy children and especially in children with chronic diseases who are at increased risk of complications and hospitalizations when they contract an infectious disease. We aimed to measure the vaccination coverage and possible influencing factors in children with cystic fibrosis, diabetes type 1, allergies or congenital heart disease in a university hospital in Flanders, Belgium.

Methods

Vaccination status was assessed retrospectively by questionnaire from the parents of 382 patients aged 2-16 years. Vaccination data were copied from relevant documents and verified against the Flemish vaccination register. Missing data were retrieved from the general practitioner where possible. Reasons for non-vaccination as well as disease specific and socio-demographic data were recorded.

Results

Vaccination rates were significantly lower compared to the overall population of Flemish children (table).

Table: Vaccination coverage of children with chronic diseases compared to healthy children in Flanders.

Vaccine	Allergies	Congenital heart disease	Diabetes	Cystic Fibrosis	**All**	Healthy Flemish children
Hexavalent	75.6%	57.6%	55.6%	61.5%	**61.5%**	93.1%
Pneumo	84.4%	83.7%	93.8%	71.4%	**83.2%**	96.5%
MMR	80.8%	61.2%	84.0%	73.7%	**76.0%**	90.6%

MenC	87.3%	80.2%	84.8%	82.9%	**83.8%**	93.1%
Rota	76.7%	71.1%	83.3%	61.1%	**72.4%**	92.2%
DTap booster	95.4%	80.0%	84.4%	74.2%	**83.3%**	90.8%
HPV	33.3%	73.7%	76.9%	42.9%	**69.1%**	83.5%

Factors influencing vaccination coverage negatively were in descending order of importance: the child's age, family structure, severity of disease, number of children in the family, origin of the (grand)parents, age at diagnosis, whereas higher income and parental education had a positive influence on vaccination coverage.

Conclusions

Children with chronic diseases are more likely to have missed vaccinations. We suggest to monitor the vaccination status in these children more strictly.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0719
17. S - VACCINE PROGRAMMES, HESITANCY, COMMUNICATION AND SOCIAL MEDIA

COCOONING STRATEGY AND VACCINATION STATUS OF CHILDREN CONTACTS OF HAEMODIALYSED AND RENAL TRANSPLANT PATIENTS

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Background

End-stage renal disease (ESRD) and renal transplant patients are particularly vulnerable to vaccine-preventable infections. However, they are often undervaccinated due to safety concerns. Cocooning strategy, aiming to protect through immunization of close contacts, has been recommended but not yet officially adopted for ESRD/transplant population. In this survey we evaluated the vaccination status of children living with ESRD/renal transplant patients to investigate the premises for implementation of cocooning strategy.

Methods

An interview-based survey was conducted on haemodialysed/renal transplant patients on regular follow-up. The vaccination status of patients and their children household contacts was recorded through questionnaire and children's vaccination records.

Results

Data were obtained from 24 patients (12 transplants and 12 haemodialysed) and 52 children contacts. Only 7/24 and 8/24 patients were appropriately vaccinated for influenza or pneumococcus respectively, only 2 were vaccinated with tetanus-diphtheria-acellular pertussis (Tdap) as adults and none for herpes zoster. Vaccination rates of the 52 children contacts, aged 0.16-17 years (median 8 years), were high for most recommended vaccines (diphtheria-tetanus-acellular pertussis, hepatitis B, measles-mumps-rubella, 100%; varicella-zoster 87.5%; pneumococcal 71.2%; hepatitis A 86.5%). Influenza rate was very low (7.7%) and booster Tdap rate was only 61%. Most patients and families were unaware of vaccination guidelines for ESRD/transplant patients and the particular interest of annual influenza vaccination for their family.

Conclusions

In the study area, ESRD/transplant population has very low vaccination rates in contrast with their adequately vaccinated children contacts. Protection of ESRD patients thus substantially depends on vaccination of young family contacts. Cocooning policies could improve the influenza and booster Tdap rates among children and adolescents in the family.

ESP16-0556
18. S - HOST-PATHOGEN INTERACTIONS – INFECTIOUS DISEASES PATHOGENESIS

THE SEVERITY OF INVASIVE GROUP A STREPTOCOCCAL INFECTION, A RISK FACTOR FOR INFLAMMATORY MANIFESTATION

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Background

Group A streptococci (GAS) are classically responsible for a number of suppurativeinfections and non-suppurative sequelae. In the past two decades, invasive GAS infections (IGASI) increased both in frequency and severity. GAS infection is known to provoke post infectious inflammatory process as seen in acute rheumatoid fever and multifocal inflammatory post-streptococcal reactions. The main objective of this study is to describe the presentation of non infectious inflammatory symptoms (NIIS) in the course of invasive GAS infection.

Methods

In this retrospective study, we included children aged 0-18 years hospitalized in MontpellierUniversity Hospital between 01/01/2003 and 31/12/2012 for IGASI. We defined NIIS as fever and/or inflammatory reactions (arthritis, orchitis) seen after 36 hours of remission and without evidence of infectious agent. We divided our cohort in 2 groups: with and without NIIS. Genotyping of SGA was performed when available.

Results

49 patients were included: 16 (32,7%) in the NIIS group and 33 (67,3%) in the group withoutNIIS. The NIIS were associated with pleurisy (p<0,0006), scarlet fever (p=0,002) and the presence of at least one sign of septic shock (OR=5,40 ; p=0,025). For biological presentation NIIS was associated with C-reactive protein>200mg/l (OR=5,37 ; p=0,016), and procalcitonin >5ng/ml (OR=4,60 ; p=0,023). There is no association between the genotype and NIIS.

Conclusions

For IGAS, NIIS are not limited to rheumatic fever, they are probably underestimated. Inour study they were present in a third of IGAS and were associated with high levels of inflammatory markers, pleurisy and scarlet fever. The mechanism is unknown but is probably not limited to a molecular mimetism. New and prospective trials are needed to explore this phenomenon.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0819
18. S - HOST-PATHOGEN INTERACTIONS – INFECTIOUS DISEASES PATHOGENESIS

REPLICATION AND INFECTIVITY OF AN UNUSUAL G8P[14] BOVINE-LIKE HUMAN ROTAVIRUS STRAIN IN THE FECES OF AN ALPINE GOAT

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Background

Rotavirus group A (RVA) strains with G8P[14] specificities are usually detected in calves and goats. However, these strains have been reported globally in humans and have often been characterized as originating from zoonotic transmissions, particularly in area where ruminants and humans live side-by-side. Here we describe the receptiveness of an alpine goat to a human G8P[14] through an experimental infection.

Methods

The human MA31 RVA strain was identified in a four years old girl presenting an acute gastroenteritis hospitalized at the pediatric care unit in Rabat Hospital in 2011. The receptivity of MA31 strain by an eight month-old alpine goat was assayed by an orally and intraperitonally inoculation with a dose of 8.5 $TCID_{50}$ of virus stock at level 3 passage. The shedding of the virus was tested by a real time RT-PCR assay and the infectivity was assayed by virus isolation on MA104 cell lines and adapted further on Vero cells.

Results

The human MA31 RVA strain was able to induce bloody diarrhea at 2 days post infection (dpi) in the alpine goat kid. RVA virus shedding started by 2 dpi (Ct 28) and continued until 5 dpi (Ct 25) with a concomitant elevation in the body temperature. Virus was isolated from fecal samples at day 4 pi with a titer of 5.4 $TCID_{50}$/ml

Conclusions

Our study while limited to one animal, prove for the first time experimentally that a human P[14] genotype causes diarrhea and virus shedding in the goat. This result reinforce the potential role of inter- species transmission in generating novel and rare rotavirus strains such G8P[14] which infect humans. In addition, this strain is further adapted on vero cell lines aiming at the development of a new vaccine.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0801
18. S - HOST-PATHOGEN INTERACTIONS – INFECTIOUS DISEASES PATHOGENESIS

DEVELOPMENT OF A RECOMBINANT AUTOLUMINESCENT FLUORESCENT BCG STRAIN TO EVALUATE PAEDIATRIC IMMUNITY TO MYCOBACTERIA

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Background

Studying the host-pathogen interaction in paediatric tuberculosis is challenging: the bacteria are hazardous and grow slowly whilst obtaining sufficient blood samples from children can be difficult. The use of luminescent recombinant BCG LuxAB in a whole blood assay can generate a growth ratio over 96 hours, but measuring luminescence requires red cell lysis and substrate addition, thereby using up the sample. We aimed to develop a novel assay that would enable sequential non-destructive luminescence measurement, facilitate potential cellular studies through fluorescence, and require minimal blood volumes.

Methods

BCG Danish strain was transformed with plasmids encoding luciferase full operon (LuxFO - encoding both the luminescence enzyme and its substrate) and Green Fluorescent Protein (GFP) with kanamycin and hygromycin resistance markers respectively. Transformed bacteria (BCG-GFP-LuxFO) were grown on selective solid culture medium and colonies were picked and grown in selective liquid medium. Bacterial autoluminescence (Relative Light Units/ml/s=RLU/ml/s) and optical density in selective liquid medium were measured. 10µl was removed every 24 hours for dilution and plating on solid medium to enumerate viable bacteria after 3 weeks (Colony Forming Units=CFU).

GFP expression was tested using the BD Bioscences Fortessa.

225µl of paediatric whole blood samples from 9 children were diluted with equal volumes of RPMI 1640 and approximately 3 x 10^5 CFU of BCG-GFP-LuxFO were added to each tube. Samples were incubated at 37^{o}C for 96 hours. Every 24 hours autoluminescence was measured and 10µl was removed for CFU counting.

Results

Correlation of BCG-GFP-LuxFO growth characteristics in liquid media and whole blood:

Culture conditions	Comparison parameter for BCG-GFP-LuxFO luminescence (RLU/ml/s)	Number of pairs of observations	Spearman Rank Correlation coefficient	95% confidence interval (*p* value)
7H9 broth + ADC + Hygromycin 50μg/ml + Kanamycin 20μg/ml	Optical density	16	0.9853	0.9556 to 0.9952 ($p < 0.0001$)
	Colony Forming Units/ml	15	0.9714	0.9112 to 0.9910 ($p < 0.0001$)
Whole blood with equal volume RPMI (+ HEPES + L-glutamine)	Colony Forming Units/ml	45 (n=9 children, 5 timepoints)	0.7123	0.5230 to 0.8346 ($p < 0.0001$)

GFP expression was confirmed by flow cytometry.

Conclusions

BCG-GFP-LuxFO has strong correlations between luminescence and other growth parameters. Autoluminescence measurements enable greater characterization of the dynamics of paediatric host-pathogen interactions with minimal blood volumes.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0375
18. S - HOST-PATHOGEN INTERACTIONS – INFECTIOUS DISEASES PATHOGENESIS

NON INFECTIOUS INFLAMMATORY SYMPTOMS RELATED TO INVASIVE PNEUMOCOCCAL INFECTION

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Background

Serious invasive infections due to Streptococcus pneumoniae (Sp), as Meningitis or pleuresia, occurs mainly to children or elders. Sp is usually colonizing upper airways of healthy people. The ten most common serotypes are responsible for about 60% of invasive infections in the world. **The aim of this study is to seek links between epidemiological, clinical or biological details and non infectious inflammatory symptoms (NIIS) among children presenting invasive pneumococcal infection.**

Methods

In this retrospective study, we included patients aged less than 18 years old, recruited in Montpellier University Hospital, in between 01/01/2003 and 31/12/2012 with an invasive pneumococcal infection. We defined NIIS as a second episod of fever seen after 36 hours of clinical remission and with no evidence of infectious agent. We divided our cohort in 2 groups : with and without NIIS.

Results

Among 19 patients included, 6 (31%) had NIIS. The sex distribution and the average age was similar in the group with and in the group without NIIS. NIIS were significantly associated with meningitis (p=0.0095) and with a high score of C-reactive protein (261mg/l vs 162mg/l, p=0.044) but not with a high level of procalcitonin (32.4ng/ml vs 16.8ng/ml, p=0.099).

Conclusions

Children presenting invasive pneumococcal infection such as meningitis with a high level of C-reactive protein, have a higher risk to develop a NIIS even if they have appropriate antibiotics. More cases and further investigations are needed to characterise NIIS and their mecanism.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0110
18. S - HOST-PATHOGEN INTERACTIONS – INFECTIOUS DISEASES PATHOGENESIS

CHARACTERISTICS OF MORBIDITY IN SMALL CHILDREN WITH MATERNAL DEPRIVATION

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Background

The lack of maternal care is now known as an important stress factor for child's health state. Present study was designed to reveal the influence of maternal deprivation on immune status of children by characterizing clinical signs and outcomes of respiratory and urinary tracts infections among children living in orphanages.

Methods

The prospective cohort study during 1 year was performed in Tbilisi infant's orphanage and 2 mother & child shelters. The 3 cohort groups of 119 previously healthy children from orphanage (basic groups) and shelters (control) of age 1-26 months were investigated. Health status was measured according to following parameters: incidence of acute lower respiratory sistem and urinary tracts infections, the age of disease first episode, duration of illness, outcome of disease, cases with hospitalization. The immune status was studied in 50 children from orphanage and shelters. Following parameters were analyzed: total lymphocyte count, number of T- and B-cells, T-cell subpopulations: CD3, CD4 CD8 and CD4/CD8 ratio, plasma IgA concentration.

Results

Disease incidence, cases with hospitalization and duration of illness were higher in deprived children. There was no difference with the total lymphocyte and B-cells counts between deprived and non-deprived children. However the total T-cell count and concentration of mature T-cells (CD3) as the CD4 (T-helpers) were decreased in basic groups, there was elevated the number of CD8 (T-sup). Observed changes leaded to alteration in CD4/CD8 ratio. The level of secretory immunoglobulin A was significantly decreased in all investigated groups of deprived children in contrast to the control groups ($p<0,05$).

Conclusions

Thus in children with maternal deprivation under neuroendocrine mechanisms are disrupted the normal correlations between T-helper and T- suppressor cells resulting in high morbidity rate among them.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0569
18. S - HOST-PATHOGEN INTERACTIONS – INFECTIOUS DISEASES PATHOGENESIS

MENINGOCOCCAL INFECTIONS AND NON INFECTIOUS INFLAMMATORY SYMPTOMS

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Background

Meningococcal infections are responsible for severe infections in childhood and known to provoke post infectious inflammatory process as post meningococcal arthritis. **The aim of this study is to describe the non infectious inflammatory symptoms (NIIS) and to seek links between epidemiological, clinical or biological details and NIIS among children presenting MI.**

Methods

In this retrospective study, we included children aged 0-18 years hospitalized in Montpellier University Hospital between 01/01/2003 and 31/12/2012 for meningococcal infections. We defined NIIS as fever and/or inflammatory reactions (arthritis, orchitis) seen after 36 hours of remission and without evidence of infectious agent. We divided our cohort in 2 groups: with or without NIIS.

Results

41 children were included, from 3 month-old to 15 year-old. 14 children (34%) were in NIIS group, and 27 were in non NIIS group. The two groups were similar in terms of age and there was no difference in their clinical presentation (purpura, severe sepsis, maximal temperature, neurological symptoms). There was more boys in NIIS group (78,5% vs 40,5%, p = 0,04). In NIIS group there was more children with meningococcemia, (64% vs 18,5%, p = 0,005), and the average CRP was higher (262 mg/L vs 180 mg/L, p = 0,04). In the NIIS group, fever, arthritis or orchitis appeared between day 2 and day 11 of the infection, and lasted for 1 to 12 days, with a favourable evolution. Arthritis concerned mostly large joints.

Conclusions

Non infectious complications (arthritis of fever) are not rare in children who present a meningococcal invasive infection, especially in case of septicemia and high level of CRP. They are well-tolerated and their evolution is favourable. More cases and further investigations are needed to characterise NIIS and their mecanism.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0993
18. S - HOST-PATHOGEN INTERACTIONS – INFECTIOUS DISEASES PATHOGENESIS

GROWTH CONDITIONS AND CELL SIGNALLING AFFECT E. COLI COMMON PILUS PRODUCTION BY ATYPICAL ENTEROPATHOGENIC E. COLI

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Background

Atypical enteropathogenic *Escherichia coli* (aEPEC) are one of the most frequent pathotypes that causes diarrhea in infants. Unlike typical EPEC, aEPEC does not produce Bundle Forming Pilus (BFP). The absence of BFP strongly suggests that other fimbrial and non-fimbrial adhesins must be involved in aEPEC adhesion to the host cell, which could explain the different interaction patterns they present on adherence assays with HeLa cells. *E. coli* common pilus (ECP) is found in most pathogenic and non-pathogenic *E. coli* and probably has an important role in bacterial adhesion. This study purpose was to evaluate the production of ECP by aEPEC strains isolated from diarrhea cases with different genetic pili profiles.

Methods

For this study, the following strains were selected: BA2103, BA3378, BA4132 and BA4147. Bacterial growth conditions utilized were Luria Bertani broth (LB), DMEM and preconditioned DMEM (presence of cell signaling components from HeLa cell culture). ECP production was evaluated by immunofluorescence assay stained with rabbit serum against EcpA.

Results

A slight ECP production was observed only by BA2103, when strains were grown in LB medium. Using DMEM as growth condition, ECP production was detected in three at four tested strains. There was a significant increase of ECP production when strains were grown in DMEM with the presence of cellular signaling. With the increase of physiological condition simulation, there was a higher detection of ECP production by aEPEC strains.

Conclusions

These results suggest that for aEPEC, ECP has an important role at physiological conditions.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0508
18. S - HOST-PATHOGEN INTERACTIONS – INFECTIOUS DISEASES PATHOGENESIS

OUTBREAK CAUSED BY ESCHERICHIA COLI O18:K1:H7 SEQUENCE TYPE 95 IN A NEONATAL INTENSIVE CARE UNIT IN BARCELONA, SPAIN

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Background

Escherichia coli is one of the microorganisms most frequently found to cause early and late-onset neonatal sepsis, being sometimes the presence of K1 capsule antigen related to meningitis. The aim of this study was to characterize an outbreak of neonatal sepsis occurring in six patients of the neonatal intensive care unit (NICU) of the Hospital Clinic (Barcelona) from April to August 2013.

Methods

After the presentation of the index case, all *E. coli* isolates from previously hospitalized neonates, health care workers, and neonates admitted from April to October 2013 in the NICU were tested for K1 antigen positivity and epidemiologically compared by pulse-field gel electrophoresis. Furthermore, *E. coli* K1 strains collected from neonates during this period were analyzed by different methods (serotyping, phylotyping, antimicrobial and serum resistance, real-time PCR of virulence factors, and *in vitro* adhesion and invasion assays in HT29 cells).

Results

An *E. coli* O18:K1:H7 sequence type 95 and phylogenetical group B2 strain was the cause of the outbreak involving one term neonate with late septicaemia from urinary focus and five preterm neonates with late septicaemia and meningitis, three of them died (Table 1). All showed the same pulsotype, ampicillin, tetracycline and fosfomycin resistance, and were serum-resistant. Concerning virulence factors, only the expression of *papI*, related to the regulation of P-fimbriae, was higher and could explain the percentages of adhesion of HT29 cells showed by the outbreak strains compared with other K1

strains.

Table 1. Features of the neonates belonging to the outbreak

Date of sepsis	Sex	Gestational age (weeks)	Birth Weight (g)[a]	Age (days)	Diagnosis	Other pathologies
13/04/2013	Female	29.2	1,000	7[a]	Late sepsis & meningitis	IVH[c]-Grade II
03/05/2013	Female	28	750	12[a]	Late sepsis & meningitis	Hyaline membrane disease+ IVH-Grade II
31/05/2013	Male	28.2	3,240	105	Late sepsis &UTI[b]	Hyaline membrane disease + Inguinal hernia
09/07/2013	Female	25.2	776	96	Late sepsis & meningitis	Hyaline membrane disease+ IVH-Grade III + Necrotizing enterocolitis
08/08/2013	Male	26.3	900	11[a]	Late sepsis & meningitis	Hyaline membrane disease + central nervous system haemorrhage
15/08/2013	Female	27.3	870	23	Late sepsis & meningitis	Hyaline membrane disease

[a] Patient died

[b] UTI: Urinary Tract Infection

[c] IVH: Intraventricular haemorrhage

Conclusions

All the *E. coli* isolates responsible for this outbreak belonged to one single clone suggesting a common source of infection, and categorized as O18:K1:H7 which is related to neonatal meningitis. However, significant pathogenicity related to fatal outcomes was not detected indicating that host-associated factors were crucial.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0049
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

RAOUTELLA PLANTICOLA URINARY TRACT INFECTION IN A PAEDIATRIC RENAL TRANSPLANT PATIENT

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Title of Case(s)

RAOUTELLA PLANTICOLA URINARY TRACT INFECTION IN A PAEDIATRIC RENAL TRANSPLANT PATIENT

Background

Raoutella planticola is a recently recognized human pathogen known to be involved in low to moderately severe infections in susceptible hosts in nosocomial settings. Reports of death exist with bacteremia and polimicrobial infections. We aim to contribute to the available evidence by reporting a case of *Raoutella planticola* urinary tract infection (UTI) in a paediatric renal transplant patient and discussing clinical implications of this finding.

Case Presentation Summary

We present a case of two *Raoutella planticola* UTI episodes in a 12-year-old female within an eight month period. She first presented at six months post renal transplant following 11 years of peritoneal dialysis for end-stage renal disease (ESRD) secondary to complex malformations of the kydneys, urogenital tract and pelvic floor. Current immunosuppression therapy included prednisolone, tacrolimus and mycophenolate mofetil. Bacteria identification and antibiotic susceptibility were determined biochemically using the Vitek®2 automated identification system and Vitek®2 AST-192 kit (bioMérieux, Marcy l'Etoile, France; 99% probability). Both isolates were found to have similar antibiotic susceptibility patterns but in the absence molecular typing we could not ascertain reinfection by the same exact strain. In both episodes the patient responded quickly to the intravenous antibiotic therapy with no added morbidity and stable renal transplant function.

Learning Points/Discussion

This is one of the few published cases of UTI by *Raoutella planticola* in an immunosuppressed child following renal transplantation with a mild course of disease and immediate response to empirical treatment. In addition to standard clinical follow-up we view a broader strategy of correct strain identification, virulence factor detection and antibiotic resistance pattern surveillance as necessary to determine the clinical relevance of this germ.

ESP16-0396
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

VISCERAL LEISHMANIASIS AND CHRONIC GRANULOMATOUS DISEASE IN AN INFANT

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Title of Case(s)

Visceral leishmaniasis and chronic Granulomatous disease in an infant

Background

to report a case of an infant with disseminated leishmania Donovani (LD) and Chronic Granulomatous Disease (CGD).

Case Presentation Summary

The infant had indolent fever since the second week of life associated with skin lesions on the face, neck and the limbs. He came from an area where both visceral and cutaneous leishmaniasis is endemic. Skin biopsy and the bone marrow aspirate showed leishmania Donovani bodies and the culture revealed Staphylococcus aurous and serratia marssisinse on two different occasions. His immune work up confirmed CGD and living related bone marrow transplantation was successful but complicated with cerebro vascular accident.

Learning Points/Discussion

Although few case reports had been reported regarding this subject but up to my knowledge this is the first case to be reported in infant with CGD and disseminated VL. As the prognosis of CGD is poor, with high morbidity and mortality and infantile leishmaniasis also adds on high rate of morbidity and mortality if not treated early. Establishing an early diagnosis has important practical implications in the successful treatment of these patients. The description of this case and a brief review of the current literature are provided to familiarize physicians mainly in the endemic areas with the relatively rare presentations of these tow conditions together.

ESP16-1099
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

ACUTE LYMPHOBLASTIC LEUKEMIA DEBUTS AS RIGHT-SIDED INFECTIVE ENDOCARDITIS IN TWO CHILDREN OF COLOMBIAN CARIBBEAN COAST

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Title of Case(s)

Acute Lymphoblastic Leukemia Debuts As Right-Sided Infective Endocarditis in Two Children of Colombian Caribbean Coast.

Background

Right-sided infective endocarditis (RSIE) represents 5%-10% of all infective endocarditis (IE) in adults, it occurs less frequently in children than adults and very rarely encountered among patients with leukemia. (Yen-Ting, Kai-Shen et al 2013) (Keino, Tsuzuki et al 2015). We report two cases of RSIE without congenital heart disease in patients with *novo* acute leukemia.

Case Presentation Summary

In 6 months We had 2 patients with Acute Lymphoblastic Leukemia (ALL) who debuted with EI. **Case 1:** a 12-years-old girl with a depression, bulimia and suicide attempts without known disease, who presents with vomiting, diarrhea fever and history of trauma in the left trip by falling. Who developed respiratory distress, dizziness, hypotension and shock. Then She presented bilateral pneumonia complicated with pleural effusion and cellulitis in her left hip. *Methicillin-resistant Staphylococcus aureus* (MRSA) was isolated from blood cultures and the echocardiogram showed a vegetation on the tricuspid valve without regurgitation. For the continuing bicytopenia was performed bone marrow aspiration diagnosed with ALL. She received 6 weeks of treatment with vancomycin and then began chemotherapy cycle. **Case 2:** a 5-years-old girl presents fever, dizziness, respiratory distress, leukemoid reaction with bycitopenia. She develops shock with bilateral pneumonia and hepatosplenomegaly, positive blood cultures for MRSA and urine cultures for *Escherichia coli* producing extended-spectrum beta-lactamases. Echocardiography showed vegetation in the tricuspid valve without regurgitation until now she is treated with vancomycin and meropenem.

Learning Points/Discussion

Incidence of EI 0.5% among hematological malignancy complicated with sepsis by *S. aureus*. It is not clear why IE rarely devvelops in patientes with ALL, both has an extremely high risk of mortality, and requires early diagnosis and appropriate treatment.

ESP16-0211
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

PERSISTENT BACTEREMIA CAUSED BY VANCOMYCIN-RESISTANT ENTEROCOCCUS IN A CHILD WITH ACUTE MYELOID LEUKEMIA AND SUCCESSFUL TREATMENT WITH DAPTOMYCIN

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Title of Case(s)

PERSISTENT BACTEREMIA CAUSED BY VRE IN A CHILD WITH AML-M7 AND SUCCESSFUL TREATMENT WITH DAPTOMYCIN

Background

Multiple–drug-resistant enterococcal infections can be a serious problem in pediatric patients.VRE bacteremia is one of the major reasons of nosocomial infections with a significant morbidity and mortality especially in children with underlying severe chronic diseases

Case Presentation Summary

A 3-year-old patient with Down syndrome,congenital heart disease and AML-M7 was admitted to the emergency department due to fever.On physical examination;he was febrile(38,5°C),2/6 systolic murmur was audible and hepatosplenomegaly were detected.The diagnosis of AML relapse was confirmed with bone marrow biopsy examination.The patient was hospitalized and meropenem and was started due to neutropenic fever.Severe antibiotic treapies were empirically added on the following days as persistance of fever (Figure1)The patient was known to be colonized with vancomycin-resistant *Enterococcus faecium* in the surveillance cultures of stool.VRE was isolated from blood cultures which were taken from the central venous port and the peripheral vein on admission.(Table 1).Linezolid was added and immunoglobulin M-enriched immunoglobulin was administered.The central venous port was removed.Amikacin was switched with gentamycin and repeat blood cultures continued to grow VRE.Daptomycin(8 mg/kg/day,a single dose)was added to linezolid at the 12th day of therapy.Linezolid stopped two days after the beginning of daptomycin treatment.On the 10thday of daptomycin therapy,the blood culture of the patient was sterile.Daptomycin therapy was continued for 5-weeks during which the blood culture were negative.The patient died at the77th day of hospitalization due to pulmonary infection,bleeding and progression of AML.

Learning Points/Discussion

This report highlights the therapeutic approach of the persistent VRE bacteremia in a child with AML-M7 and Down Syndrome, in that,treated successfully with daptomycin.Daptomycin

may be an alternative therapy for VRE infections in children, more studies are needed for extended usage.

ESP16-0162
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

SUCCESSFUL TREATMENT OF INVASIVE PULMONARY ASPERGILLOSIS WITH VORICONAZOLE IN A PATIENT WITH CHRONIC GRANULOMATOUS DISEASE

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Title of Case(s)

Successful Treatment of Invasive Pulmonary Aspergillosis With Voriconazole In a Patient With Chronic Granulomatous Disease

Background

Chronic granulomatous disease (CGD) is a primary immunodeficiency with that results from absence or dysfunction of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase subunits of phagocytic cells. Patients with CGD are susceptible to life threatening infections caused by catalase-positive micro-organisms. Pneumonia is usually the most frequent type of infection and *Aspergillus* species are the most common cause of pneumonia. Most of CGD cases are X-linked and the mortality risk of them is higher compared with autosomal recessive forms. Herein, we report a patient with X-linked CGD successfully treated with voriconazole who had invasive pulmonary aspergillosis caused by *Aspergillus fumigatus.*

Case Presentation Summary

A 3 year old boy admitted with prolonged fever, fatigue and cough. He had the history of recurrent pulmonary infections and osteomyelitis due to *Serratia* infection at one year old. Physical examination revealed bilaterally coarse breathing sounds. He was evaluated for primary immunodeficiency. He was diagnosed as X-linked chronic granulomatous disease with mutation in *CYBB* gene. Bilateral diffuse infiltration was evident on chest x-ray. Computed tomography demonstrated bilateral, diffuse, nodules. These findings were suggestive of invasive aspergillosis. Septated hyaline hyphae were observed and *Aspergillus fumigatus* was isolated from the respiratory specimen culture. Galactomannan antigen was negative. The patient made a remarkable clinical and radiologic recovery without surgery with voriconazole treatment for 106 days. Two years after the diagnosis he had a successful allogenic hematopoietic stem cell transplantation.

Learning Points/Discussion

This case illustrates that both histopathologic demonstration of tissue invasion and culture are necessary for diagnosis of aspergillosis. Also, we suggest that monotherapy with voriconazole can be successful in treatment of invasive pulmonary aspergillosis.

ESP16-0862
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

AN OVERWHELMING POST-SPLENECTOMY INFECTION (OPSI): FATAL SEPSIS IN A CHILD, A CASE REPORT

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Title of Case(s)

An overwhelming post-splenectomy infection (OPSI) : fatal sepsis in a child, a case report.

Background

Splenectomized patients are prone to develop severe infection like sepsis, because of an immuno-suppressed state. They are especially susceptible to encapsulated bacteria such as *Streptococcus pneumoniae*, and also *Haemophilus influenza* and *Neisseria meningitidis.*

The life time risk to develop an OPSI is estimated at 5% and the mortality rate is 50-70%. Early diagnosis and empirical intravenous antibiotics can reduce the mortality.

Case Presentation Summary

We present a 14 year-old, who had a splenectomy for idiopathic thrombocytopenic purpura 8 years ago. He was admitted to the emergency department for fever at 39°C with chills, vomiting and headache. His current medications included daily Peni-oral and the vaccination status was in order.
The clinical examination was unremarkable. No signs of meningitis. He was haemodynamically stable.
Results from work-up proved reassuring (biology: CRP <10 mg/L, urine sediment and chest X-ray).
While return home was permitted, the patient died from septic shock 4 hours later. *Streptococcus pneumoniae* was identified in the blood culture.

Learning Points/Discussion

Clinical presentation for this patient was mild at the beginning and the examination was unremarkable, but rapidly deteriorated with septic shock resulting in a poor prognosis. Fever and chills in splenectomized patient must be interpreted as possible sepsis.

Administration of empirical intravenous antibiotics in a splenectomized patient with fever in the hospital should not be delayed and can reduce the mortality rate from 70% to 10-40%.

Patient education is primordial to recognize the first signs of infection, so as to initiate at the home oral antibiotics for fever or chills immediately.

Infection prevention strategies after splenectomy are important and include adequate immunization against encapsulated germs & Influenza and daily chemoprophylaxis.

ESP16-1042
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

PEDIATRIC NEUTROPENIC PATIENTS CARE IN TURKEY

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Background

Infection is a common complication in children with malignancies.There is no consistent guidance enviromental infection control for neutropenic patients(NP).There are differences between centers. The aim of this questionnaire study is to determine these differences in Turkey.

Methods

Multicenter-descriptive questionnaire study was conducted on 35 centers from different geografic-location of Turkey.Bone marrow transplantation units were excluded. Approximately 70%of centers that followed pediatric NP were included in this study.Each center has been contacted at least for three-times.Questionnaire was answered by two doctors from each center.The questionnaire including personal, general patient care and neutropenic patient care was formed as 64-questions.

Results

Thirty-five centers including 20(57,1 %) University Hospitals,12 (34,3%) Research Hospitals and 3 (8,6%) State Hospital participated in this survey.Total numbers of bed for pediatric patients were more than 51 in more than 95%of centers. Twenty-one centers(60 %) had pediatric infection ward that followed febrile NP.Pediatric infection units(PIU) most frequently (28,6%) had 11-15 beds in service.The median number of nurses in PIU was 7(minimum-maximum:1-15)nurses.

Nine centers(25,7%) always followed-up the neutropenic fever patients in a single room.All centers had infection control committee and provided training for infection preventation to patients and their hospital attendant.Eleven(31,4%) centers had isolation room with negative and/or positive pressure and nine (25,7 %) had hepa-filter system.One center always and four centers followed 50% and up of pediatric neutropenic fever patients in rooms with hepa-filter system. Sixteen(45,7%)centers determined policy about keeping toys in patient rooms.There was neutropenic diet specific for pediatric NP in twenty-seven centers(77,1%).

Conclusions

There are special approaches to avoiding infection at hospital for NP in Turkey.Neutropenic diet described in many centers.Further investigations are needed for determine potential benefits of neutropenic diet.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0236
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

SPECTRUM OF MICROBIOLOGICAL INFECTIONS AND RESISTANCE PATTERN IN PEDIATRIC ONCOLOGY PATIENTS: EXPERIENCE FROM A TERTIARY CARE CENTER IN NORTH INDIA

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Background

In developing countries, infections pose the major challenge in curing pediatric malignancies. Data on spectrum of infections in pediatric oncology from developing countries is sparse.

Methods

Pediatric oncology patients presenting with fever were enrolled (2007-2015). Results of microbiological investigations were recorded. The spectrum of infections and their sensitivity pattern were analyzed.

Results

There were 1023 episodes of fever evaluated. 590(57.6%) episodes were febrile neutropenia. 225(22%) had microbiologically documented infections. Since 2012, around 90% patients had central venous access devices. Gram positive, gram negative, fungal, viral, mycobacterial and parasitic infections accounted for 53(23.5%), 89(39.5%), 51(22.6%), 30(13.3%), 1(0.4%) and 1(0.4%) cases respectively. Spectrum of gram positive infections (n=53) included coagulase-negative Staphylococcus (65.7%), Staphylococcus aureus (11.3%), Enterococcus fecium (13.2%), Enterococcus fecalis (3.7%), Streptococcus pneumoniae (1.8%) and other Streptococcus species (4.3%). Gram negative infections (n=89) included Klebsiella pneumoniae (29.2%), Pseudomonas species (21.7%), Escherichia coli (16.8%), Acinetobacter species (8.9%), Stenotrophomonas maltophilia (5.6%), Proteus mirabilis (2%), Salmonella species (2%), Nocardia (1%), Chryseobacterium (1%), Elizabethkingia meningoseptica(1%) and unidentified (11%). Invasive aspergillosis was diagnosed in 34 cases (using galactomannan assay). Fungus isolated from body fluids (n=17) included Candida albicans(5), Candida tropicalis(3), Candida parapsilosis(3), Candida glabrata(1), Candida haemulonii(1), Candida pelliculosa(1), Aspergilllus(1) and Trichosporon asahii(2). Documented viral infections included Cytomegalovirus(19), Dengue(6), Epstein-Barr virus(4) and Herpes simplex virus(1). One child had Cryptosporidiosis. With advancing years, incidence of gram positive infections decreased. Vancomycin resistance has not been observed among gram positives. Among Klebsiella and E.coli, extended spectrum beta lactamases were produced by 96% and 81% respectively, whereas carbapenemases were produced by 44% and 31% respectively.

Conclusions

Gram negative bacteria are the major isolates at our center. Gram positive isolates have shown reduction with time. Multidrug resistant gram negative bacteria and aspergillus infections are emerging concerns.

ESP16-0851
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

SELECTIVE DIGESTIVE TRACT DECONTAMINATION IN A CHILD WITH ACUTE MYELOID LEUKEMIA COLONIZED BY MULTIDRUG RESISTANT ESCHERICHIA COLI – CASE REPORT AND REVIEW OF LITERATURE.

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Title of Case(s)

Selective digestive tract decontamination in acute myeloid leukemia

Background

Multi-drug resistant (MDR) gram negative infections cause significant morbidity and morbidity in oncology patients. The role of selective digestive tract decontamination (SDD) has been extensively been evaluated in surgical and intensive care patients. SDD has become obsolete in pediatric oncology.

Case Presentation Summary

A 14 years old girl presented to us with menorrhagia for 2 months, fever for 1 week and rashes for 5 days. On examination, she had pallor, multiple petechiae and ecchymoses all over the body. Bone marrow aspiration and flowcytometry revealed a diagnosis of Acute Myelogenous Leukemia (AML-M1). She was started on chemotherapy as per COG protocol (which contains 5 courses of intensive chemotherapy). Initial 4 cycles of chemotherapy were complicated by significant and prolonged episodes of febrile neutropenia. Three of these episodes were associated with perianal induration and tenderness. Multi-drug resistant (MDR) Escherichia coli was isolated from blood in all these episodes. Colonization of gastrointestinal tract with MDR Escherichia coli was suspected and was evaluated accordingly. Stool culture isolated MDR Escherichia coli on two different occasions. SDD was performed using oral colistin (5 mg/kg/day in two divided doses). Stool culture repeated after one week was negative for MDR Escherichia coli. Child was started on fifth course of chemotherapy once blood counts recovered and was continued on oral colistin. Neutropenic phase after chemotherapy was managed smoothly without Escherichia coli sepsis. Oral colistin was stopped once blood counts recovered. Child is currently well and free of disease till date (9 months after completion of treatment).

Learning Points/Discussion

SDD should be considered in selected high-risk patients on chemotherapy under proper microbiological surveillance.

ESP16-0779
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

IS THERE A RELATIONSHIP BETWEEN IMMUNOLOGICAL ABNORMALITY IN 22Q11 DELETION SYNDROME AND THE RISK INFECTIOUS EVENT? RETROSPECTIVE STUDY IN A FRENCH COHORT OF 86

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Background

Introduction :Di George syndrome that have to be called 22q11.2 Deletion syndrome, the most common congenital chromosome deletion syndrome, is associated with developmental defects including cardiac abnormalities, hypocalcemia, and hypoplasia or abnormal migration of the thymus. These patients have variable defects in T-cell immunity with an increased incidence of infection. The purpose of this study was to investigate immune function to determine infectious risk factors in a cohort of 86 childrens.

Methods

This study characterized the laboratory and clinical features of the immunodeficiency in a cohort of 86 patients with chromosome 22q11.2 deletion syndrome. We analysed lymphocyte phenotypes, immunoglobulins, clinical features and the course of severe and recurrent infections.

Results

Our patients had a low lymphocyte T cells count and immunoglobulins levels. 29 patients (34%) had a severe infections and 72% recurrent infections.At multivariate analysis, the only risk factor for severe infections was the level of CD4 lymphocytes : patients with low level of CD4 T cells had 3,3 times more severe infections (IC [1,263-8,991], p=0,04).There was no risk factor for recurrent infections. Although, patients with recurrent infections have more abnormal IgA levels than those without recurrent infections (p=0,03).

Conclusions

We found that patients with 22q11 deletion syndrome have a high rate of severe and recurrent infections. CD4 lymphocytes and IgA levelscan help physicians to determine a population with high risk of severe infections.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0088
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

RESPIRATORY VIRAL AND ATYPICAL BACTERIAL INFECTIONS IN FEBRILE CANCER CHILDREN ATTENDING A LARGE PAEDIATRIC ONCOLOGY CENTRE IN HONG KONG

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Background

Children with malignancies are known to be susceptible to bacterial and fungal infections, but relevance of respiratory viruses in paediatric oncology remains unclear. This study determined the epidemiology of respiratory viral and atypical bacterial infections and their possible co-infections with bacteraemia among febrile children with cancers.

Methods

77 cancer children with fever ≥38ºC provided 140 nasopharyngeal aspirates or flocked nasopharyngeal swabs. Nineteen controls without any infective symptom within two weeks and matched for age and timing as cases provided data for comparison. Their nasopharyngeal samples were subjected to both rapid immunofluorescence (IF) antigen detection for seven common viruses and multiplex molecular assays for 20 known and emerging respiratory viruses and atypical bacteria.

Results

Seventy and three viruses were detected in cases and controls respectively. The leading viruses were influenza A (26%), respiratory syncytial virus (20%), rhinovirus (17%) and metapneumovirus (14%), but none of these viruses differed between cases and controls. All case and control samples were negative for *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*. Nine cases and two controls had positive blood culture, and 2 cases were positive for respiratory viruses at the same time. There was no significant difference in these outcomes between cases and controls. Two febrile cancer children required intensive care admission, but all patients survived the infective episodes. Of 44 positive samples, 10 viruses were identified only by molecular assays and three only by IF test.

Conclusions

Influenza, respiratory syncytial virus, rhinovirus and metapneumovirus are the commonest viruses identified in cancer children with infective symptoms. Co-infections between two viruses and between virus and bacteraemia are rare. Our findings do not support empirical coverage of atypical bacteria in febrile cancer children. (Grant sponsor: Hong Kong Children's Cancer Foundation Research Grant)

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0474
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

INVASIVE FUNGAL DISEASE IN PEDIATRIC ACUTE MYELOID LEUKEMIA: A RETROSPECTIVE STUDY IN A MEDICAL CENTER

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Background

Patients with acute myeloid leukemia (AML) are at high risk of invasive fungal disease (IFD). The aim of the retrospective study was to evaluate the incidence, risk factors, and outcome of IFD in pediatric AML patients in a medical center in Taiwan.

Methods

Retrospective chart reviews were conducted, and pediatric patients with AML were enrolled in the study between 2005 and 2014. IFD was defined and classified according to the European Organization for Research and Treatment of Cancer/Mycosis Study Group (EORTC/MSG) 2008 consensus criteria.

Results

In all, 80 patients were enrolled over the 10-year period. The overall incidence of proven, probable, and possible IFD was 20% (n = 16). If excluding possible IFD, the incidence of proven and probable IFD was 12.5% (n = 10). Four patients had 2 different episodes of IFD. Five patients were diagnosed with *Candida* infections, 4 with *Aspergillus* infections, and 1 with *Trichosporon* infection. The age of the patients with IFD was 11.6 ± 5.5 years, which is not significantly different from the age of the patients without IFD, 8.2 ± 5.5 years (p = 0.10). The median duration from the first date of neutropenia to the date of first identification of IFD was 29.4 days (-5-120). The median neutrophil counts on the date of first identification of IFD were 137.5/μL (range 0-9090). Of these 16 patients with IFD, 9 died, and 3 deaths might be attributed to IFD.

Conclusions

In our study, *Candida* spp. are the most common pathogens in IFD in AML patients. Prolonged neutropenia and induction phase of chemotherapy may be the risk factors of IFD.

ESP16-0509
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

DIAGNOSTIC CHALLENGES IN CLEAR CSF MENINGITIS. CASE PRESENTATION.
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Title of Case(s)

Diagnostic challenges in clear CSF meningitis. Case presentation.

Background

Thepediatric cases of acute lymphoblastic leukemia (ALL), often curable, are traditionally diagnosed secondary to the clinical manifestations associated with inaugural pancytopenia induced by malignant medullar infiltration. The neurological onset of ALL without detectable peripheral hematological involvement is quite rare.

Case Presentation Summary

This paper summarizes the diagnostic process of a 7 year old female patient, without significant medical history, who was admitted for the diagnosis of a chronic and progressive meningoradiculopathy, associated with clear CSF and hypoglycorrhachia and pleocytosis

Onset was 9 months prior to admission in our clinic, with convergent strabismus, later associated with fever and meningeal syndrome. The illness was classified as acute meningitis and specific antibiotic treatment was instituted with partial clinical improvement. After cessation of treatment, there is a reoccurrence of the strabismus alongside other motor deficits, therefore the patient is further investigated in multiple other pediatric departments and other related specialties, but without any diagnosis. Because of the progression of symptoms, monthly cortisone treatments are instituted, with temporary clinical improvement. Tuberculous meningitis is infirmed through extensive CSF investigations. Due to a lack of etiology of the illness despite several pediatric, rheumatologic and neurologic consults, a morphopathologic assessment of the CSF sediment and immunofenotyping of the small and medium lymphocytes present in the CSF were performed, which showed massive infiltration with B precursor cells, finally yielding the diagnosis of pre B-cell acute lymphoblastic leukemia with meningeal involvement.

Learning Points/Discussion

Although multiple etiologies were taken into consideration, especially tuberculous, autoimmune or parasitic, the oncologic diagnosis was masked by repeated administration of cortisone. Systemic cortisone treatment initiated before diagnosis can modify laboratory investigations of CSF, thus delaying the establishment of etiology.

ESP16-0518
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

SUPPURATIVE CERVICAL ADENITIS DUE TO STREPTOCOCCUS PNEUMONIA IN A GIRL WITH HYPER IGM SYNDROME AND PI3KR1 MUTATION

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Title of Case(s)

Suppurative cervical adenitis due to *Streptococcus pneumoniae* in a girl with hyper IgM syndrome and PIK3R1 mutation

Background

Hyperactive phosphatidylinositol 3' -kinase (PI3K) signaling caused by PIK3R1 splice site mutations is associated with recurrent infections (sinopulmonary and viral), lymphoproliferation, hypogammaglobulinemia, elevated IgM levels (Hyper IgM syndrome (HIGM) phenotype) and increased lymphoma risk. *S. pneumoniae* is an infrequent cause of adenitis in previously healthy children and may indicate underlying immune defects/dysregulations.

Case Presentation Summary

A 2-year-old girl, born to non-consanguineous healthy parents, presented with unilateral suppurative cervical lymphadenopathy requiring intravenous antibiotics and repetitive surgical drainage. The identification of *S. pneumoniae* lead to a immunology work-up showing low IgG (7mg/dl) and IgA (2mg/dl) and markedly raised IgM (769 mg/dl), normal lymphocyte subsets, reduced class-switched memory B cells and, elevated transitional B cells. The patient showed a complete resolution of the infection signs after a 2-week course of amoxicillin clavulanic acid (7 days IV), but generalized lypmphadenopathy persisted despite intravenous Immunoglobulin substitution (0.6g/kg/4 weeks). An autosomal recessive HIGM syndrome was suspected and PIK3CD and PIK3R1 sequencing revealed a previously reported mutation in PI3KR1 (G>A chr5:67589663). Sirolimus (2mg/m2/24h/vo) treatment was subsequently initiated. Despite a good initial response with lymphadenopathy reduction (number and size), recurrent aphthous stomatitis appeared and caused sirolimus discontinuation.

Learning Points/Discussion

PI3K mutations should be part of the differential diagnosis of HIGM. Whilst an increased infection risk for these patients has been described, this is the first reported case of a suppurative *S. pneumoniae* adenitis. Current management approaches include immunomodulation (mostly mTOR-inhibitors), immunoglobulin substitution and antimicrobial prophylaxis in order to prevent invasive or current infections. Selective p110d inhibitors (e.g. GS-1101) are attractive agents as they promise to have a lower side-effect profile due to their increased specificity.

ESP16-0297
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

OUTCOME OF VARICELLA INFECTION IN IMMUNOCOMPROMISED CHILDREN: 5 YEARS ANALYSIS OF NATIONAL REFERRAL HOSPITAL DATABASE IN INDONESIA

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Background

Varicella frequently caused serious problems among immunocompromised patient and can even lead to death. In the developing countries where varicella vaccine is not established as part of national immunization program, the risk of transmission is very high. Similar condition can be found in areas where there is low coverage of immunization program, such as in certain parts of developing countries.

Methods

Retrospective analysis was performed for patients from 2011-2015 in national referral hospital of Indonesia. Analysis performed to describe the course and outcome of patients with varicella in immunocompromised patients.

Results

There were 20 cases of varicella in immunocompromised children, 11 of which are having underlying hematologic malignancy, while the others are non hematologic malignancy (2), HIV infection (2), chronic kidney disease (1) or patient on high dose steroid treatment (4). Treatment wise, 11 patients were treated by intravenous Acyclovir only, 5 oral Acyclovir only, while the rest were treated with combination of oral and iv Acyclovir. Median duration of Acyclovir treatment was 7 (Range 1-11) days. Clinical resolution achieved at day 5 (range 0-11). Among the 20 patients presented, 6 of them developed complications such as pneumonia, encephalitis, visceral varicella, or septicemia. All of the patients with complication eventually lead to death. It is valuable to note that all patients have never received varicella immunization.

Conclusions

We concluded that varicella in immunocompromised patient may result in complications that can lead to death. Prevention of complications through proper treatment is important in increasing the survival of varicella in immunocompromised patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0888
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

COMPARISON OF DIFFERENT SPECIMENS FOR CYTOMEGALOVIRUS SCREENING IN PAEDIATRIC HAEMATO-/ONCOLOGIC PATIENTS

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Background

Cytomegalovirus (CMV) infection or reactivation may lead to relevant complications in immunocompromised patients including haemato-/oncologic patients and stem cell transplant recipients. Detection of DNA by quantitative polymerase chain reaction (qPCR) is used for diagnosis and screening with consecutive pre-emptive treatment. However, optimal screening techniques and interpretation of PCR results (breakpoints for DNA levels, different specimens) are under discussion.

Methods

We retrospectively analysed CMV PCR results performed for CMV screening in paediatric haemato-/oncologic patients of the Medical University of Graz between 2001 and 2010, in order to describe in-/congruence between results from serum (S), urine (U) and mouthwash (MW) obtained in the same patient on the same day. Fisher´s exact test was used for statistical analyses.

Results

We analysed 6726 qPCR results from serum (n=2662), urine (n=2050) and mouthwash (n=2014) obtained from 439 patients. In 852, 291 and 1764 screening tests 1, 2 and 3 specimen(s), respectively, were analysed concurrently. Screening tests with at least 1 positive specimen were observed in 39 (8.88%) of 439 patients. While urine was significantly more often positive than serum (6.29% vs. 3.83%, p=0.0001), difference between mouthwash and serum missed statistical significance (5.01% vs. 3.83%, p=0.0507). For details on in-/congruence between different concurrently collected specimens see table 1.

Analysed specimen	No. of specimens		positive	negative
Serum (S)	2662		102 *(3.83%)*	2560 *(96.17%)*
Urine (U)	2050		129 *(6.29%)*	1921 *(93.71%)*
Mouthwash (MW)	2014		101 *(5.01%)*	1913 *(94.99%)*
Serum and Urine	1837	**any +**	127 *(6.91%)*	1710 *(93.09%)*
within 1 screening test		**S+ / U+**	16 *(0.87%)*	
		S+ / U-	38 *(2.07%)*	
		S- / U+	73 *(3.97%)*	
Serum and Mouthwash	1850	**any +**	119 *(6.43%)*	1731 *(93.57%)*
within 1 screening test		**S+ / MW+**	14 *(0.76%)*	
		S+ / MW-	45 *(2.43%)*	
		S- / MW+	60 *(3.24%)*	
Urine and Mouthwash	1895	**any +**	156 *(8.23%)*	1739 *(91.77%)*
within 1 screening test		**U+ / MW+**	44 *(2.32%)*	
		U+ / MW-	62 *(3.27%)*	
		U- / MW+	50 *(2.64%)*	
Serum and Urine and Mouthwash	1764	**any +**	154 *(8.73%)*	1610 *(91.27%)*
within 1 screening test		**S+ / U+ / MW+**	7 *(0.40%)*	
		S+ / U+ / MW-	7 *(0.40%)*	
		S+ / U- / MW+	5 *(0.28%)*	
		S+ / U- / MW-	31 *(1.76%)*	
		S- / U+ / MW+	22 *(1.25%)*	
		S- / U+ / MW-	46 *(2.61%)*	
		S- / U- / MW+	36 *(2.04%)*	

Conclusions

CMV DNA was detected in 8.88% of patients. However, there was a considerable incongruence between results from concurrently obtained specimens (serum, urine and mouthwash). Neither urine nor mouthwash proved to be reliable surrogate markers for viremia. On the contrary, CMV DNA was frequently detected in urine and/or mouthwash without concurrent detection of CMV DNA in serum. Possible causes and clinical impact of this incongruence has to be determined in further studies.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0539
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

IMMUNE RESPONSE TO INFLUENZA IMMUNIZATION IN CHILDREN WITH CANCER

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Background

In this study, our aim was to evaluate the ability of influenza immunization to evoke a protective immune response among children with cancer receiving chemotherapy

Methods

The study was undertaken over the 2012-13 influenza season. We evaluated children with cancer who received influenza vaccination. Hemagglutination Inhibition antibody titers were determined before and after vaccination.

Results

We evaluated 77 children with cancer (39 boys, 38 girls; median 5 7/12 years). The protective response rates (proportion of patients with fourfold or more antibody rise) were: 51% (39/77) for H1N1, 36% (28/77) for H3N2 and 39% (30/77) for influenza B virus. Especially for children in whom the sample was obtained within 45 days after vaccination (n=37), the protective response rates were 59.5% for H1N1, 43% for H3N2 and 49% for influenza B virus. Among children with hematological malignancies (n=54) the response rates were 44% for H1N1, 33% for H3N2 and 28% for influenza B virus. The corresponding rates for children with solid tumors (n=23) were 65%, 44%, 65%. Among children who were vaccinated during intensive chemotherapy (n=30) the protective response rates were 50% for H1N1, 43% for H3N2 and 47% for influenza B virus. The corresponding rates for children receiving less intensive chemotherapy (n=47) were 51%, 32%, 34%. In the previously mentioned analyses, no statistically significant differences were detected.

Conclusions

1. Influenza vaccination provides protection in a remarkable proportion of cancer patients 2. Protection provided against H1N1 was higher compared to H3N2 or influenza B 3. The protective rates seem to be higher within the first 45 days after the vaccination 4. The protective response rates for patients with hematological malignancy are obviously lower than those for patients with solid tumors.

ESP16-1049
19. INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

COMPLICATED ACUTE PYELONEPHRITIS IN DIABETIC TEEN

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Title of Case(s)

COMPLICATED ACUTE PYELONEPHRITIS IN DIABETIC TEEN

Background

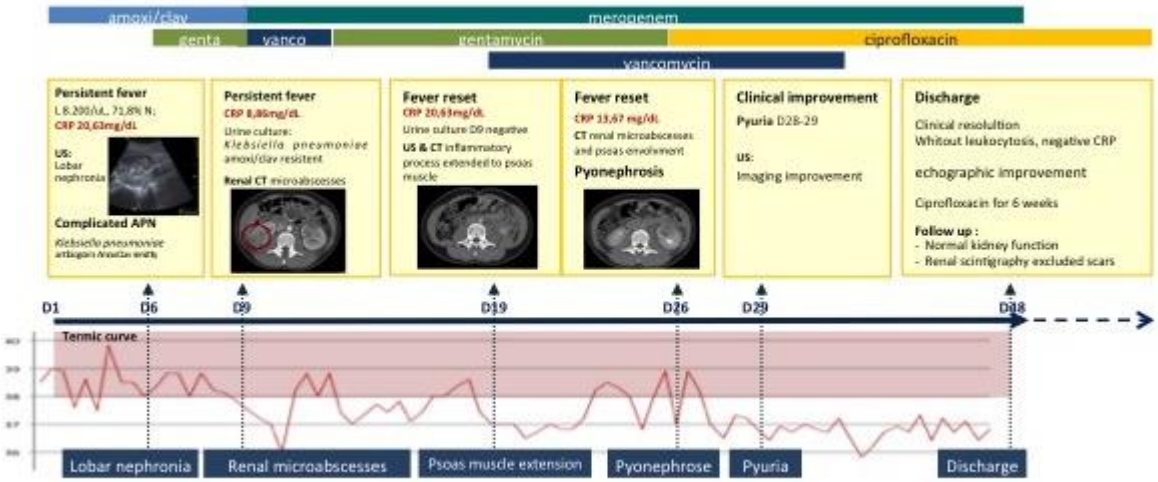
Acute pyelonephritis (APN) is a common infection in Paediatrics, usually with good prognosis. Renal abscess is a possible complication, mainly when genitourinary disease or diabetes mellitus (DM) are present.

Case Presentation Summary

We report the case of a 14-year-old boy, with DM type I, that presented with high fever, abdominal pain and vomits. At admission, he had moderate dehydration and left flank pain. Blood analysis revealed leucocytosis and CRP elevation, as well as, leucocyturia and microscopic haematuria. Renal ultrasonography revealed no abnormalities. APN diagnosis was considered and he was started endovenous amoxicillin and clavulanic acid. Urine culture revelled multisensitive *Klebsiella pneumoniae*.During hospitalization, the fever persisted and we saw a progressive imagiologic worsening (lobar nephronia, bilateral renal microabscesses, extension of the inflammatory process to psoas major muscle and ureter hydronephrosis), despite different antibiotic regimens, all adjusted to antibiotic sensitivity test.

He had no indication to percutaneous or surgical drainage, so he completed 30 days of antibiotherapy with clinical and imagiologic improvement and normalization of inflamatory markers.

Nowadays, diabetes is controlled, kidney function is normal with negative microalbuminuria and the renal scintigraphy excluded renal cortical scars.



Learning Points/Discussion

The clinical presentation of APN in diabetic patient can be more severe and may have major complications, in particular renal abscesses. Therefore we must have a high degree of suspicion to make an early diagnosis.

DM is a poor prognosis factor in systemic infections. In these situations a more extensive empirical antibiotherapy should be used, until a consistently favourable clinical evolution is observed.

Serial imaging of abscesses is crucial to monitor clinical evolution and support therapeutic decisions (medical or surgical).

These patients require careful long-term follow-up to prevent renal failure and to rule out renal scarring.

ESP16-0270
20. INFECTION CONTROL

IMIPENEM-RESISTANT PSEUDOMONAS AERUGINOSA OUTBREAK IN A NEONATAL INTENSIVE CARE UNIT - AN EFFECTIVE AND RAPID INTERVENTION

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Background

Pseudomonas aeruginosa (PSAR) is an opportunistic pathogen, found widely in water, and an important cause of severe healthcare-associated infections, particularly among infants in neonatal intensive care units (NICUs). Since perinatal infections are rare, infections in neonates are usually considered of environmental origin. We describe an outbreak of imipenem-resistant PSAR in NICU at Galilee medical center in northern Israel and the successful intervention. The outbreak was suspected when similar imipenem-resistant PSAR isolates were first cultured in 12/2013 from 5/25 neonates in rectal swab cultures, taken weekly as routine surveillance measures.

Methods

After PSAR isolation, colonized infants were placed in cohort and isolated, infection control principles were discussed and reinforced, and environmental cultures from potential reservoirs were taken.

Results

Five Of 18 environmental cultures were positive for imipenem-resistant PSAR with similar antibiogram to colonizing strain. These isolates were cultured from 3 taps, liquid medication, and diapering table. Additional interventions included use of alternative taps, treatment of disassembled infected taps with mechanical cleaning and chemical disinfection by soaking in hypochloric solution (2000 ppm) for 20 minutes; policies of handling liquid medications and disinfection of contact surfaces were reinforced . Routine weekly thermal disinfection of taps is performed since 12/2013, by using hot water at 60^{o}C for 30 minutes. Since the intervention, repeated environmental cultures and weekly rectal surveillance cultures revealed no growth of imipenem-resistant PSAR. No infections were documented among the colonized neonates.

Conclusions

In PSAR outbreak in NICU, environmental cultures, especially of water systems and liquid containing equipment, can provide the outbreak source and the main target for successful and

rapid intervention. Weekly rectal surveillance cultures in NICU detect early colonization by multi-drug resistant pathogens allowing for rapid interventions and appropriate isolation.

ESP16-0471
20. INFECTION CONTROL

ANTIMICROBIAL USE IN A PEDIATRIC DEPARTMENT OF A REFERRAL HOSPITAL: POINT-PREVALENCE SURVEYS IN 2015

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Background

Antimicrobial resistance is a global concern. Reliable ongoing data on prescribing practices are essential to guide antibiotic stewardship programs

Methods

Nine point-prevalence surveys (PPS) were performed from March, 2015 to January, 2016 at a 127 bed tertiary pediatric hospital in São Paulo, Brazil. All children in the pediatric wards at 8:00 am on the day of the survey and receiving any antimicrobial treatment were included. The number of hospitalized children and total available beds were used for denominator data

Results

Average bed occupancy rate during the studied period was 74,6%. Antibiotic prescription ranged from 39% to 63%, with higher use during respiratory infections season (from March to June). The majority of children on antimicrobials were under 2 years of age. The proportion of prescriptions for hospital acquired infection (HAI) was 52%. Empirical treatment constituted the majority of prescriptions and increased over surveys, accounting for 85% of all cases. Parenteral administration was the preferred route in 86% of cases. Ceftriaxone remained the most frequently prescribed antibiotic for community acquired infections whilst the carbapenems associated with vancomycin were most frequently prescribed for HAI

Conclusions

Minimal changes in practice suggests a need for increased antibiotic stewardship interventions focused on parenteral to oral switch and increased use of targeted therapy. Point-prevalence surveys remain a cheap, simple and reproducible method to identify targets for stewardship interventions

ESP16-0468
20. INFECTION CONTROL

THAT SINKING FEELING: HOSPITAL OUTBREAKS OF KLEBSIELLA PNEUMONIAE LINKED TO SINKS IN A PAEDIATRIC CENTRE.

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Title of Case(s)

Hospital outbreaks of *Klebsiella pneumoniae* linked to colonised sinks within a paediatric hospital

Background

Background

Klebsiella species are known to spread rapidly from colonised to non-colonised patients, causing infection and leading to outbreaks. *Klebsiella pneumoniae* is the second most frequent cause of Gram-negative sepsis with isolates often being linked to antibiotic resistance. We describe three outbreaks of *K. pneumoniae* linked to sink contamination where environmental sampling and typing comparison was undertaken in order to identify the source of the outbreak and direct outbreak interventions.

Case Presentation Summary

Case Presentation Summary

Methods: Between 2011 and 2014 3 *K. pneumoniae* outbreaks occured over 4 wards (renal, haematology/oncology and cardiac intensive care). To aid in identification of the source of the outbreak 138 environmental samples were taken. Sites screened included near patient surfaces as well as sinks in patient rooms and bedspaces. In addition sinks in communal areas including drug rooms were also screened. Isolates were sent for typing and the following interventions were undertaken:
- All patients were screened to determine if they were colonised
- Routine prophylaxis was changed in the haematology/oncology wards
- Wards were closed to all routine admissions
- Enhanced cleaning (with chlorine) was undertaken of the colonised sinks and the ward environment

Results: 52 isolates were grown from 29 patients, 27 were linked to the outbreak strains. 11 of the 138 environmental samples were positive for the outbreak strains, with no surfaces outside of the sink environments found to be colonised. Ongoing transmission was not resolved until sinks were replaced/extensively decontaminated.

Learning Points/Discussion

Learning Points/Discussion

Sinks were demonstrated as the environmental reservoir in all outbreaks. How sinks were used in clinical environments played a significant role in transmission, as did sink location, cleaning methods and the suitability of the sink design. Therefore environmental sources should be considered/actively sought during *K. pneumoniae* outbreaks.

ESP16-1065
20. INFECTION CONTROL

ETHANOL LOCK THERAPY FOR CENTRAL LINE STERILIZATION IN A PAEDIATRIC HOSPITAL

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Background

Ethanol lock is being used to prevent and eradicate central venous catheter infections. This study describes the effectiveness of ethanol lock in clearing central lines. We also study the side effects and complications associated.

Methods

All paediatric patients who received ethanol lock therapy (ECVCA70%) between April 2012 and December 2015 were included. Therapy was considered effective if negative culture were obtained after ECVCA70% or clinical and laboratory improvement in cases without positive initial blood culture.

Results

ECVCA70% was used in 18 children (four times in one of them), with a median age of 10 yrs (IQR 2-13.5). Ten children were immunocompromised (cancer, transplant and immune deficiency) and 11 had long-term catheters. The alcohol dwell time ranged between 4 and 30 hrs with a median of 24 hrs. In 9/21 cases, catheter associated infection were considered. In 8 of them, ECVCA70% was effective. Blood culture remained positive in one case with catheter vegetation. In the other 12 cases, another focus for infection was identified: in 7 sterilization was obtained; in the others it was not possible to conclude about the effectiveness of ethanol by initial negative blood culture. There were no side effects. The only complication was catheter obstruction in 4 cases (transient in one of them), which forced its removal in two.

Conclusions

ECVCA70% seems to be effective in clearing central lines. The use of ECVCA70% appears to be well tolerated in paediatric patients and represents an inexpensive pharmacologic intervention that can help treat catheter-associated bloodstream infections and salvage central lines. Technical skills should be optimized to prevent catheter obstruction.

ESP16-1073
20. INFECTION CONTROL

CENTRAL VENOUS CATHETER CARE BUNDLE – IMPACT IN BLOODSTREAM INFECTION IN A NEONATAL INTENSIVE CARE

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Background

Central line-associated bloodstream infections (CLABIs) cause substantial neonate morbidity and mortality in Neonatal Intensive Care Units (NICU). A high incidence of CLABIs was found in Maternidade Bissaya Barreto (MBB) NICU and led to changes in daily clinical practice, with the implementation of a care bundle.
To assess the effectiveness of new strategies for prevention of infection implemented in the NICU of MBB.

Methods

We conducted a retrospective study that included all newborns admitted at the NICU of MBB: 12 months before (group 1) and 12 months after the protocol change (group 2), comparing the rates of infection in both groups. Central venous catheter (CVC) care bundle in the unit included: hand decontamination, full sterile barriers precautions, skin disinfectant (2% chlorhexidine if birth weight (BW) > 1000g; povidone-iodine if BW < 1000g), early removing unnecessary catheters.

Results

262 infants were included in group 1 and 274 in group 2; with no statistical evidence of different characteristics between them (weight, gestational age, CVC utilization rate and invasive ventilation). In group 1, there were 221 catheter days and 7 CLABSIs, for an incidence density of 22 per 1000 catheter days. After implementation of a care bundle, there were 252 catheter days and 4 CLABSIs for an incidence density of 12 per 1000 catheter days. In very low birth weight (VLBW) infants, we also observed the reduction of CLABSI for a incidence 30 vs 17 per 1000 catheter days.

Conclusions

This study demonstrated that implementation of central venous catheter care bundle were associated with a global CLABSI reduction of 45% and 43% in VLBW infants.

ESP16-0310
20. INFECTION CONTROL

HOSPITALIZATION COST OF THE NOSOCOMIAL ROTAVIRAL ENTERITIS

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[2]"Carol Davila" University of Medicine and Pharmacy- Bucharest- Romania, Chair of Infectious and Tropical Diseases, Bucharest, Romania

Background

Rotavirus is the most frequent cause of hospitalized enteritis in preschool children and nosocomial rotaviral enteritis increases the cost of hospitalization.

Methods

Cases of rotaviral enteritis (ICD 10 code: A08.0) in preschool children discharged between 2011 and 2014 from our 500 beds infectious diseases teaching clinic from Bucharest, Romania has been used as sampling population. From sampling population two groups of cases were drawn: (a) target group represented by nosocomial cases of rotaviral enteritis (NRE) and (b) reference group constructed by at random selection, for each NRE case, of a community acquired case of rotaviral enteritis (CARE) with similar age, gender, and onset year as the correspondent NRE case.

For each case included in study the hospitalization cost was iterated in an MS Excel table; Epi Info 2000 soft was used for generating means, prevalence, confidence intervals and for statistical comparing.

Results

Prevalence of NRE cases in the sampling population was 7.6% (5.5% - 10.6%).

Means of hospitalization cost (equivalent Euro) in NRE group was 156.1 (± 274.5) Euros and for CARE group was 45.2 (± 20.6) Euros, difference between means being statistically significant: (Kruskal-Walis test= 100.82; Degree of freedom= 1; p value= 0.0000).

The difference between the two above means was 111 Euros; the means cost of NRE hospitalization was roughly 300% higher than that of CARE's hospitalization.

Conclusions

Cases of NRE are associated with important wasting of health resources; preventing of these cases is an important objective; however halting transmission at population level through universal rotavirus mass immunization is for sure the best preventing strategy.

ESP16-0700
20. INFECTION CONTROL

RISK OF NEONATAL INFECTIONS AND BREASTFEEDING PATTERN IN MALAYSIA: A PROSPECTIVE INSIGHT

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Background

To assess the newborn feeding patterns and the risk of neonatal infections among neonates in a northern Malaysian state.

Methods

The study was done at private community clinics in a northern state of Malaysia. Neonates were enrolled within 72 hours-of-birth and followed-up after four weeks at the outpatients' clinics or/and homes to evaluate neonatal infections and their breastfeeding patterns.

Results

Breastfeeding patterns' association with neonatal infections was evaluated using multivariate logistic regression with adjustment of possible confounders. Total 340 neonates were enrolled from March 2014 to October 2015. Around 38% of them were presented with any/some infections, illness, whereas 15.8% reported with at least one Integrated Management of Neonatal and Childhood Infections (IMNCI) risk i.e. signs of severe infections. Semi-breastfed neonates showed more likelihood to develop signs of severe infections like fever, stomach pain in contrast to solely breastfed neonates (Adj. OR=7.9, CI=95%, $p< 0.05$) as well as IMNCI infections (Adj. OR=7.1, CI=95%, $p< 0.05$). Likewise, semi-breastfed neonates were considerably more likely to develop other illnesses like diarrhea, vomiting (Adj. OR=4.6, CI=95%, $p< 0.05$) as well as IMNCI illnesses (Adj. OR=3.5, CI=95%, $p< 0.05$) as compared to solely breastfed neonates.

Conclusions

Solely breastfeeding during neonatal period was considerably protective against severe infections, illnesses as well as IMNCI illnesses as compared to semi-breastfeeding neonates.

ESP16-0460
20. INFECTION CONTROL

COMPARISON OF THE QUIKREAD GO WRCRP POINT-OF-CARE TEST TO AFINION AND SIEMENS ADVIA CRP TESTS

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[3]Orion Diagnostica, Supply Chain, Espoo, Finland

Background

A new, easy-to-use point-of-care (POC) test, QuikRead go wrCRP, has been introduced on the QuikRead go® instrument. The test gives the C-reactive protein (CRP) result from whole blood, plasma and serum samples.
For evaluating the performance of the QuikRead go wrCRP test comparisons were performed against one commercially available POC CRP test and one clinical chemistry CRP analyzer.

Methods

Whole blood samples were used with the QuikRead go wrCRP and Afinion CRP POC tests. Corresponding plasma samples were determined with Siemens CRP Wide range assay on Advia 1800 Clinical Chemistry System.
The QuikRead go wrCRP is an immunoturbidimetric CRP assay. The sample is added into a cuvette and closed with a reagent cap. The cuvette is placed into the QuikRead go instrument, which automatically measures CRP in two minutes. The sample volume is 10 µl and measurement range is 0.5-300 mg/l with whole blood and 0.5-180 mg/l with serum/plasma samples. The system automatically detects the sample type and the whole blood CRP value is corrected based on the hematocrit level of the sample.

Results

The correlation results (using Passing & Bablok analysis) of the QuikRead go wrCRP whole blood samples to the Afinion CRP test was y=1.11x+1.3, r=0.99 (n=64). The correlation results of the QuikRead go wrCRP whole blood samples to the plasma samples determined with the Siemens Advia 1800 CRP Wide range assay was y=1.00x-1.3, r=0.99 (n=73).

Conclusions

The QuikRead go wrCRP test correlated very well with both the Afinion CRP and the Siemens Advia 1800 CRP Wide range CRP assay. The study shows that the QuikRead go wrCRP test gives reliable results.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0222
20. INFECTION CONTROL

KNOWLEDGE REGARDING DANGER SIGNS OF NEONATAL ILLNESS AMONG MOTHERS IN POSTA NATAL WARD, B.P. KOIRALA INSTITUTE OF HEALTH SCIENCE

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Background

It has been estimated that out of 8 million infant deaths, about 5 million die in the neonatal period each year. Virtually, all of them die in the developing countries. Majority of deaths occurred during the newborn period from infections, asphyxia and birth injuries, and complications of premature birth. Objective: to find out the knowledge regarding danger sign of neonatal illness among mother having babies up to 1 month. And find out the association of knowledge of danger sign of neonatal illness with selected variable.

Methods

The study was carried out in post-Natal ward of BPKIHS, Dharan, Nepal, using quantitative research designs. Study participants were mothers admitted in ward and having their babies up to 1 month of age. A pre-tested semistructured questionnaire was used as research tool. A total of 108 samples were taken by Non Probability purposive Sampling Technique. Data were collected by using pretested, semi-structured interview scheduled. Independent sample t-test and one- way Anova test

Results

The research findings showed that mean and standard deviation of knowledge level of mothers were 69.75 and 12.94 respectively. The result showed that mother's knowledge is highly significant with educational level of mother. All mothers know at least one danger signs of neonatal illnesses. More than 90% of mothers know fast breathing and difficulty, pus mixed discharge from cord, fever and decreased body temperature, poor sucking, excessive crying as the danger signs of neonatal illnesses.

Conclusions

The finding indicates that education and socio-economic condition of mothers plays an important role in increasing and improving the knowledge. In spite of various maternal child health program there is still need for further need of health awareness program about danger sign of neonatal illnesses.

ESP16-0878
20. INFECTION CONTROL

PREPARATION OF PREBIOTIC FROM KONJAC GLUCOMANNAN BY USING RECOMBINANT MANNANASE OF BACILLUS SP. SWU60

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Background

Glucomannan consist of glucose and mannose that can be used to prepare glucomanno-oligosaccharides by degrading enzymes such as endo-1,4-β-mannanase, and α-glucosidase. The aim of this study was to assess the prebiotic properties of glucomanno-oligosaccharides prepared from konjac powder.

Methods

A mannanase gene from *Bacillus* sp. SWU60 was cloned and expressed in *E.coli*. The recombinant enzyme was used to digest konjac powder. The enzymatic products were purified by activated carbon and analyzed by thin layer chromatography (TLC). Prebiotic properties were examined by using *Lactobacillus acidophilus.*

Results

The molecular mass of recombinant mannanase was 54 kDa. Optimal pH and temperature for enzyme activities were pH 6.0 and 60°C, respectively. The enzyme was stable up to 60°C for 1 h and at pH 5–9 at 4°C for 16 h. Konjac glucomannan was a favorable substrate. The products of natural konjac powder hydrolyzed by the recombinant enzyme were glucomanno-oligosacharide and a little amount of mannose. The glucomanno-oligosacharide display a prebiotic properties.

Conclusions

The glucomanno-oligosacharide from konjac powder can be used as prebiotic for prevent infection.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0068
20. INFECTION CONTROL

AN OUTBREAK OF ESBL PRODUCING KLEBSIELLA PNEUMONIAE IN A RESOURCE POOR NEONATAL UNIT: A CHALLENGE OVERCOME

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Title of Case(s)

A nosocomial outbreak of ESBL producing *Klebsiella pneumoniae* causing neonatal sepsis.

Background

Extended spectrum beta lactamase (ESBL) producing *Klebsiella pneumoniae* is an emerging threat as a nosocomial infection with significant mortality. Many outbreaks were reported in neonatal intensive care units recently worldwide. Prematurity and prior treatment with antibiotics are identified risk factors.

Case Presentation Summary

From 27/02/2013 to 12/04/2013, blood cultures of 06 babies grew ESBL producing *K. pneumoniae* in the Special Care Baby Unit of Base Hospital Avissawella, Sri Lanka. All had identical antibiograms with multidrug resistance, but sensitivity to carbapenems and amikacin. Blood cultures became positive after a mean of 1.8 days since admission. Five babies were premature (mean 32 weeks). All had umbilical venous catheters and two underwent exchange transfusion for hyperbilirubinaemia. All developed thrombocytopaenia and high CRP levels. All were started on prophylactic intravenous antibiotics on admission and changed to meropenem when clinically deteriorating.

During the outbreak investigation none of the environmental samples became positive. Admissions were restricted. Cleaning techniques were optimized. Each patient's documents and equipment including stethoscopes were never taken into other patient cubicles. Separate sinks and single use hand towel boxes were installed for each cubicle. Hand washing technique of staff members was corrected. Minimum handling of babies was encouraged. Staff number was increased to provide one on one barrier nursing. Duties were delegated and the responsible staff members name was written for each aseptic procedure. Infection control meetings were held weekly.**Learning Points/Discussion**

With these interventions, outbreak was limited to 06 cases out of 45 admissions during 06 weeks. Three deaths occurred. In a resource limited tropical setting, simple and cost effective infection control methods proved to be effective in containing this ESBL producing *K. pneumoniae* outbreak.

ESP16-0066
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

FIVE ASPECTS OF CRP MONITORING FOR PNEUMONIA IN CHILDREN

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Background

To determine the correlation of CRP as initial and control after 72 to 96 hours of antibiotic therapy and its possible percentage falls determining the success of antibiotic therapy.

Methods

In the first stage of statistical analysis, presentation of the characteristics of the sample, first used calculation of the mean at all, and for each group in terms of age (4 groups), gender (two groups), season-month (7 group) , type of antibiotics (10 groups), the size of initial value of CRP (4 groups), size of fall in relation to ordinal ratings (8 groups). Then we examined the correlation between volume elements of CRP values, and all other variables eg. age group, sex, category values increase CRP where it belongs, percentage decrease of CRP after 3 or 4 days, types of antibiotics and by groups of months of events disease.

Results

We can say that the null hypothesis has have no significant decline in CRP after treatment with antibiotics and calculating the mean of 54.06%, we must reject that there is a high difference. Therefore, immediately accept the hypothesis that there is a significant drop after extensive computing and testing the first hypothesis, since p is usually larger than 0.05, mean of 0.06 to 0.13 p≥ in three of five aspects except for the sex and the starting value CRP. Other values for the type of antibiotic, the age and the month in which pneumonia occurred indicate acceptance of the main working hypothesis, a rejection of the null hypothesis.

Conclusions

Use monitoring CRP for pneumonia in children in outpatient and clinical conditions, should be suspended the gold standard of diagnosis with physical pediatric examination for monitoring pneumonia and successful treatment.

Clinical Trial Registration (Please input N/A if not registered)

CRP, Monitoring, Pneumonia, Children.

ESP16-0147
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

EVALUATION OF THE SENSORY QUALITIES OF READY TO SERVE BLENDS OF ALOE VERA (Aloe barbadensis Mill.)

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Background

Aloe vera has been used for its medicinal worth for several thousand years. Its use is also mention in the Bible where it was taken as the plant of immortality

Methods

The research was conducted Karachi, Pakistan in year 2013-14. The main objectives of this study are to develop the economical Aloe drink using available resources and to evaluate the sensory properties of different blends of Aloe vera drink.

Results

The sensory qualities that were evaluated include color, taste, smell, appearance and feelings. The panelists were asked to record their observations and give marks to each parameter of different blends out of 10 on the sensory sheet. The most least liked Aloe blend was T4 that include Aloe gel, water, sugar and mint leaves. It was due to the strong smell and taste of mint leaves as mint leaves contain menthol. The overall acceptability of T8 was at the top as it contained complete blend of Aloe gel, mint leaves, fresh lemon juice and ginger.

Conclusions

The potential of Aloe vera to be used in Food Industry and Pharmaceutical Industry has been increased. Aloe vera has many antibacterial, antifungal and antiviral active biological compounds which make it best for many disorders. An effort was made to make Aloe drink using the available resources and to develop awareness about its importance among the people.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0182
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

COLISTIN EXPERIENCE IN NEWBORN INTENSIVE CARE UNIT

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Background

The prevelance of severe infections with resistant microorganisms especially the *Acinetobacter spp*. is increasing among critically ill newborns. Colistin may be a good therapeutic option for the treatment of severe infections. The aim of this study was to evaluate efficacy and safety of colistin use in neonatal intensive care unit (NICU).

Methods

We retrospectively reviewed medical records of newborns who received colistin for at least 7 days duration, during their hospitalization at the NICU of Eskisehir Osmangazi University Faculty of Medicine between 2011 and 2014. We recorded the indication of colistin use, risk factors, yielded microorganisms, and laboratory features before and 7 days after colistin use.

Results

During the study period 25 newborns (14 boys, 11 girls) with a mean gestational age of 31.4 ± 4.7 weeks and a mean birth weight of 1725 + 910 g received colistin (5 mg/kg twice daily) due to nosocomial infections (30% due to *Klebsiella pneumoniae*, 24% due to *Acinetobacter baumanii*). Study population have the presence of umbilical catheter (72%), presence of central access (92%), presence of hypoxia at birth (100%), required mechanical ventilation requirement (96%), and received total parenteral nutrition (100%). All newborns had received broad spectrum antibiotic therapy prior to colistin use. Colistin has been used together with other group antibiotics. Before and 7 days after colistin use, serum electrolytes, blood urea nitrogene, creatinine, AST and ALT levels were similar ($p>0.05$).

Conclusions

The use of colistin for nosocomial infections seems safe and well-tolerated in critically ill newborns.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0853
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

USE OF INTRAVENOUS FLUCLOXACILLIN INFUSOR FOR PAEDIATRIC PATIENTS WITH SEVERE STAPHYLOCOCCUS AUREUS INFECTIONS

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Title of Case(s)

Invasive *S. aureus* infection treatment at home environment

Background

Severe *S. aureus* infections often require a prolonged course of antimicrobial therapy. Flucloxacillin is the drug of choice but requires administration four times daily. Continuous infusion of flucloxacillin via an elastomeric infusor device allows flucloxacillin to be administered over 20 hours and facilitates the administration of intravenous (IV) home therapy.

Case Presentation Summary

We present two cases of invasive *S. aureus* infection treated with a prolonged course of IV flucloxacillin administered via a continuous elastromeric infusor device.

12 year old female who presented 2 weeks post corrective scoliosis surgery with sepsis and surgical site infection. Antibiotics were started and wound washout and exploration was performed. Blood, bone cultures and wound swabs grew sensitive *S. aureus*.She was treated for spinal osteomyelitis/rod infection with IV flucloxacillin via elastomeric infusor. A total of 6 weeks of IV flucloxacillin was completed plus 6 weeks of oral therapy.

12 year old female with known mitral valve prolapse presented to her local hospital with sepsis following a fall at school. She was diagnosed with *S. aureus* sepsis with endocarditis, cerebral emboli, left sacroiliac collection and ostemyelitis. She was managed conservatively and discharged on IV flucloxacillin via elastomeric infusor for 7 weeks plus 3 weeks of oral therapy

Learning Points/Discussion

Continuous flucloxacillin infusion allows the gold standard of care for the home treatment of *S. aureus* infection. Alternative once daily administration options may include ceftriaxone, a broad-spectrum agent, which does not support the principles of antimicrobial stewardship. In selected patients, this technique will allow administration of multiple daily dose antibiotic therapy to a child in their home environment, via a convenient, easy to use device, leading to improved patient and carer satisfaction.

ESP16-0288
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

ANTERIOR NECK MASSES IN CHILDREN: ANTIBIOTIC MANAGEMENT

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Title of Case(s)

ANTERIOR NECK MASSES IN CHILDREN: ANTIBIOTIC MANAGEMENT.

Background

Cervical swellings are frequently encountered in pediatrics and commonly they are found to be a lymphadenitis (with an inflammatory or infectious etiology). Differently, neck masses, notably those having an anterior location, in children of any age, are relatively uncommon. Neck tumors and congenital developmental abnormalities are the principal differential diagnosis. Thyroid tissue has a high resistance to infections, so diagnosis as acute suppurative thyroiditis or thyroid abscess are quite rare. Early management is based on clinical and radiological findings and is usually conservative, preparing for subsequent surgery.

Case Presentation Summary

We illustrate 3 cases of congenital neck mass (fourth branchial arch fistula with left thyroid phlegmon, fourth branchial arch remnant abscess with left thyroid lobe infiltration, left thymic remnant phlegmon, without abscess) with relatively similar clinical scenario, but with different radiological findings and diagnosis. The diagnosis of these left-sided neck swelling was made after the first clinical presentation (no history of recurrent neck infection) and all cases improved under amoxicilline-clavulanate treatment. They currently await surgical intervention.

Learning Points/Discussion

In pediatric population, the diagnosis of branchial and thymic anomalies should be suspected before any mass infected or not, localized in the anterior neck, on the left side. Their main clinical presentation is either a rapidly appearing mass with local and systemic infectious characteristics, or, repetitive cervical infections with intermittent swelling. Definitive diagnosis should be ascertained by radiologic and otolaryngologic studies. Early management, based on clinical and radiological findings, usually includes specific antibiotics targeting the oral flora, allowing an appropriate control of infectious process to prepare for surgery.

ESP16-0928
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

CURRENT CHEMOSENSITIVITY OF SHIGELLA SPP. CORRELATED WITH BIOTHERAPY OF BACTERIAL DYSENTERY IN CHILDREN

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Background

Bacterial dysentery is a major public health problem both in whole world and in our country because of the large number of cases, especially in infants. The dysentery is an endemic disease in Romania, but it may occur in small epidemic outbreaks, especially in hot season.

Methods

We made a retrospective study on bacterial dysentery cases in infants who were hospitalized in Paediatric Department Clinic IX in National Institute for Infectious Diseases "Prof. Dr. Matei Bals" between 2010 and 2015. On those children we watched their age and sex. All bacterial strains were isolated by inoculating the faeces on differential selective media and the identification was made by standard laboratory methodology. To determinate the spectrum of sensitivity for the antibiotics that we used in dysentery therapy we used API ATB G-5 tests which evaluate the sensitivity at Ampicillin, Chloramphenicol, Co-trimoxazole, Nalidixic Acid, Ciprofloxacin, Ceftriaxone.

Results

During the study we have recorded a 246 number of cases of dysentery bacterial on children. Of these cases only 68 had bacteriological confirmation, most of them being caused by *Shigella Flexneri* and the others by *Shigella Sonnei*. Bacterial dysentery on children predominates at boys, with ages between 1 and 4 years. The sensitivity of *Shigella* strains at Ciprofloxacin, Colistin, Nalidixic Acid and Ceftriaxone is high. The resistance of dysenteric bacillus is high for Ampicillin and Co-trimoxazole.

Conclusions

The increasing use of antibiotics, sometimes without justification led to the selection of strains of dysenteric bacillus more and more resistant on classic treatment. In conclusion when we choose an antibiotic for the treatment of bacterial dysentery we must take into account both the sensitivity criteria of isolated germs, the tolerability, side effects and even the cost of the treatment.

ESP16-0650
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

COMPARISON OF VANCOMYCIN VERSUS TEICOPLANIN FOR GRAM-POSITIVE BACTEREMIA DURING FEBRILE NEUTROPENIA IN CHILDREN

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Background

There are few studies comparing the efficacy and adverse events of Vancomycin (VCM) versus Teicoplanin (TEIC) for the treatment of Gram-positive bacteremia during febrile neutropenia in children.

Methods

We conducted a retrospective analysis of children who developed bacteremia during febrile neutropenia, between January 2012 and January 2016 at our institution. Data was collected from medical records. We compared patient demographics, development of nephrotoxicity (elevation of serum creatinine levels above twice the baseline) and duration of positive blood culture, between those who received VCM or TEIC using standard statistical methods.

Results

Overall, 36 episodes from 30 patients were recorded. Fifteen patients received VCM and 21 received TEIC. Patient background was similar for both groups. Median age was 94 vs. 80 months for groups receiving VCM and TEIC. Underlying disease consisted of: leukemia (VCM/TEIC = 9/12), primary immunodeficiency (1/1), and solid tumor (5/8). The distribution of neutrophil count at onset was also similar [≦100/μL (9/15), 101-500/μL (6/6)]. Causative agents consisted of gram-positive cocci (11/19) and gram-positive rods (5/3). Median duration of antibiotics was 10 days for VCM vs. 12 days for TEIC. Clearance of bacteremia was achieved within 2 days in 86.7% (13/15) of VCM recipients and 81.0% (17/21) of TEIC recipients and not statistically significantly different [Odds ratio (OR) =1.53, 95%CI: 0.24-9.67]. One patient who received VCM developed nephrotoxicity and none who received TEIC but there was no statistical difference [OR= 0.22, 95%CI: 0.01-5.91].

Conclusions

There was no significant differences in the time to clearance of bacteremia or rate of nephrotoxicity between those who received VCM and TEIC in children who developed gram-positive bacteremia during febrile neutropenia. Greater number of patients need to be evaluated prospectively.

ESP16-0266
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

EVALUATION OF NITAZOXANIDE FOR EMPIRIC TREATMENT OF INFECTIOUS DIARRHEA IN INDIAN CHILDREN

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Background

Childhood Infectious Diarrhoea (CID) is a major challenge and priority in global healthcare.

Current standard of CID treatment is lifesaving Oral Rehydration Therapy, Zinc and selective empiric antimicrobials.

Nitazoxanide(NTZ) is an anti-parasitic thiazolide effective in treatment of giardiasis and cryptosporidiosis, having promising broad spectrum activity against range of parasites, viruses and anaerobic bacteria.

Nitazoxanide is projected and promoted as a viable, specific, primary option in the empiric therapy of CID with very limited clinical evidence.

Evaluation of Nitazoxanide for empiric therapy of CID is attempted to guide it's rational use in Indian children.

Methods

A two arm clinical study combining
1)A critical narrative review of published studies,
and
2)A prospective exploratory observational efficacy cohort study on 154 children over 5months at a small hospital in rural India.

Primary outcome-Comparative efficacy of Nitazoxanide,probiotics and antibiotics in empiric treatment of CID in Indian Children measured as time to "resolution of diarrhoea" in days.

Secondary Outcome– Place of Nitazoxanide as primary candidate for empiric treatment of pediatric infectious diarrhoea

Results

The critical narrative review shows a very low grade evidence for use of NTZ in empiric treatment of CID.

The prospective observational study shows

1)comparable efficacy of Nitazoxanide, probiotics and antibiotics in the treatment of CID.

2)Diarrhoea in 85% of patients resolved on day 4 of treatment in Nitazoxanide group and on day 3 in other treatment groups

3)Treatment Failure was higher in Nitazoxanide group

Conclusions

1)There is insufficient current clinical evidence for efficacy of Nitazoxanide in empiric treatment of infectious diarrhoea in Indian children

2)Nitazoxanide can not be currently recommendend as a primary candidate for empiric treatment of childhood infectious diarrhoea .

Premature promotion and irrational empiric use of this potentially valuable molecule needs to be discouraged.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1062
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

COMPARISON OF ANTIBIOTIC COMPLETION RATES BETWEEN CHILDREN DISCHARGED FROM HOSPITAL AND PATIENTS TREATED IN PRIMARY CARE.

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Background

Good antibiotic stewardship may require paediatric patients with tonsillitis to take bitter tasting Phenoxymethylpenicillin four times a day for up to ten days. Our hypothesis was that few of our hospital patients completed their courses of antibiotics and fewer primary care patients. We found a paucity of current literature on antibiotic completion rates in children in the UK. The audit aimed to find what percentage of paediatric patients completed their prescribed course of antibiotics.

Methods

Approval was granted by the trust audit department and a local GP surgery to conduct phone interviews. Parents of inpatients admitted during the preceding three months were phoned by a consultant paediatrician or medical student. If parents consented they were asked about difficulties giving their child antibiotics. Details of doses missed and the reason were recorded alongside diagnosis, laboratory or radiological confirmation of infection, antibiotic prescribed and the length of the course. Contact was made with 30 parents of former inpatients and anonymised details recorded in Excel. 40 paediatric patients, recently prescribed antibiotics were identified in a local GP practice. 11 of these parents were contacted.

Results

5 of 30 patients from the inpatient cohort did not complete their course. These patients each took 3 days treatment. 4 of the parents stopped giving the antibiotic as the child was spitting out the antibiotic. One stopped because of a rash. 2 of the 11 community patients failed to complete the course, completing 3 and 5 days and both stopped early as the child was spitting out the antibiotic.

Conclusions

Antibiotic course completion rates by parental report of 83% were surprisingly high. There was no difference between completion rates in discharged hospital patients and community patients.

ESP16-0747
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

USE OF FLUOROQUINOLONES IN HOSPITALIZED CHILDEN, PRELIMINARY REPORT OF A CHART REVIEW IN A BELGIAN UNIVERSITY CHILDREN'S HOSPITAL

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Background

Fluoroquinolones (FQ) should be prescribed with concern to children due to the limited amount of paediatric drug studies and the emerging resistance patterns. This study aims to quantify the number of off-label FQ prescriptions for children hospitalized in a Belgian university children's hospital and to assess whether dose recommendations were respected fir these prescriptions.

Methods

We reviewed all prescriptions of FQ for children up to 17 years of age who were hospitalized at Universitair Ziekenhuis Brussel, a Belgian university children's hospital, in the period 2010–2013. Patient characteristics, indication for the FQ prescription and microbial cultures were obtained from the medical file. The study was approved by the institutional review board.

Results

A total of 203 FQ prescriptions for 86 children were analyzed. The majority of children had major comorbidities such as childhood cancer, cystic fibrosis or inflammatory bowel disease. FQ prescription was based on a microbial culture in 15.4% of cases. Frequent indications for FQ prescription were Pseudomonas eradication in cystic fibrosis patients, selective bowel decontamination in neutropenic patients and wound infections. Prescribed daily doses per kilogram varied widely, even for chidren the same indication, with a tendency for underdosing.

Conclusions

Fluoroquinolones are frequently prescribed off-label for hospitalized children. Prescribed daily doses per kilogram were highly variable with a tendency for underdosing.

ESP16-0251
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

ACUTE OTITIS MEDIA AMONGST CHILDREN ATTENDING OUT-PATIENT CLINIC IN TERTIARY HOSPITAL IN SOUTH-EAST NIGERIA

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Background

Acute Otitis Media (AOM) is the most common pediatric condition for which antibiotics is prescribed. Due to the advent of newer antimicrobials, the microbiological flora is changing constantly. The Study determined the prevalence, microbial etiology and antibiogram of pathogens implicated in acute otitis media in Chukwuemeka Odimegwu Ojukwu University Teaching Hospital, Awka

Methods

Forty nasopharyngeal swab samples were collected aseptically, by a medical personnel, from patients attending the Pediatric Out-patient Clinic in the hospital from January to April 2015 and cultured for bacterial and fungal pathogens. Antimicrobial susceptibility testing was done by Kirby – Bauer's disc diffusion method.

Results

Out of the 2,025 child- patients who visited the hospital during the study period, 40 were clinically diagnosed of acute otitis media giving an incidence of 1.98%. Out of the 40 samples studied for bacterial and fungal isolates, 30 samples yielded growth of potential pathogens, 10 samples did not yield any growth at all. More male (62.5%) than female (37.5% were affected ($P<0.05$). The most predominant organisms was *Staphylococcus aureus* (34.9%) followed by *Pseudomonas aeruginosa* (30.2%) *Escherichia coli* (9.3%), *Streptococcus sp* 92.3%), *Candida krusei* (14%), *Candida glabrata* (4.7%) and other *candida* species (4.7%) All bacteria were resistant to Ampicillin and Amoxicillin – clavulanate. *Staphylococcus aureus* isolates were sensitive to Gentamicin (60%) and sparfloxacin (73.3%). *Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus* were resistant to ceftriaxone, ciprofloxacin, streptomycin cefuroxime, Erythromycin and Azithromycin. Nystatin and Voriconazole had comparable efficacy against the fungal isolates and fluconazole was ineffective

Conclusions

There is high level of multiple antibiotic resistant bacteria associated with AOM. Gentamicin and sparfloxacin may be used for empiric treatment of AOM of bacteria origin, while Nystatin or Voriconazole will be for AOM of *Candida* origin.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0673
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

CASE REPORT OF GASTROENTERITIS CAUSED BY PSEUDOMONAS AERUGINOSA, DIAGNOSIS USING A NEW DIRECT SENSITIVITY TECHNIQUE. THE PATIENT LOST 22 POUNDS.

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Title of Case(s)

Case report of gastroenteritis caused by *Pseudomonas aeruginosa,* diagnosis using a new direct sensitivity technique. The patient lost 22 pounds.

Background

This case report presents a patient with gastroenteritis by *Pseudomonas aeruginosa,* a bacteria not generally considered a cause of infectious diarrhea, with an incidence very low (3.2%-8.6%). A novel direct sensitivity technique (DST) show that bacteria can be isolated from mixed stool cultures, when compared to the gold standard technique (CLSI-Clinical and Laboratory Standards Institute) which did not recovered it.

Case Presentation Summary

The case was a man 80 years old, White-Hispanic patient with diarrhea for six months, losing 22 pounds. No organism was isolated in stool analysis with CLSI technique. Following diagnostic work-up included endoscopy, colonoscopy, chemical labs and tumoral markers, which were negative or showed no apparent cause. *Pseudomonas aeruginosa* was only identified with the new DST, sensitivity test followed. The patient had a rapid resolution of symptoms after antibiotic treatment. *Ps aeruginosa* was confirmed via stool cultures.

The stool sample was inoculated at the same time by: 1. CLSI technique 2. DST (can give a preliminary sensitivity result in 6 hours or in 18 hours). The latter was smeared directly onto Mueller Hinton agar, with 8 sensidiscs and incubated for 18 hours at 37^0C.

Learning Points/Discussion

This case shows the importance to modify CLSI method to isolate *Pseudomonas*. DST might be crucial in stools with negative CLSI technique. Therefore, it is recommended and suggested that clinical laboratories to use DST for stool cultures in order to recover various bacteria. Plus it is very easy, cheap, simple, and it can give faster, convenient, accurate results; also it can help patients in time of reduction of hospitalization, costs of diagnostic tests and deteriorating health.

ESP16-0562
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

USING AN ELASTOMERIC PUMP TO ADMINISTER CONTINUOUS INFUSIONS OF ANTIBIOTICS AS PART OF AN OUTPATIENT PARENTERAL ANTIMICROBIAL THERAPY (OPAT) PROGRAMME

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Background

Continuous intravenous infusion using elastomeric pumps is an alternative delivery method in paediatric patients who need intravenous antibiotics (IVAB) which normally need three times daily administration, such as piperacillin/tazobactam or ceftazidime. We describe the experience at Alder Hey Children's Hospital using elastomeric pumps in the OPAT setting.

Methods

A retrospective case series of 6 children (aged 5 – 17 years) discharged home on IVAB continuous infusion administered via an elastomeric pump. One child received this mode of delivery twice. Outcomes were assessed using the BSAC p-OPAT (British Society of Antimicrobial Chemotherapy Paediatric Out-patient Parenteral Antimicrobial Therapy) criteria.

Results

In 6 of the episodes the indication was lower respiratory tract infection treated with continuous IV piperacillin/tazobactam. All patients had a background of neurodisability, recurrent respiratory tract infections and *Pseudomonas aeruginosa* carriage. The remaining patient was treated for an infective exacerbation of cystic fibrosis with a regimen that included continuous IV ceftazidime. All episodes had an OPAT outcome defined as "Success" according to the BSAC p-OPAT criteria with no side effects reported.

Conclusions

Elastomeric pumps are a safe and effective option for administering continuous infusion of selected antibiotics in children. They should be considered for admission avoidance or to facilitate early discharge of inpatients under the guidance of an OPAT service.

ESP16-0547
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

JUDICIOUS USE OF ANTIMICROBIALS: EVIDENCE FROM REAL-TIME SETTING

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Background

Children present to the clinic with an array of problems ranging from GIT upsets to cough, cold, and infections. The practitioner is often compelled to prescribe an antimicrobial agent. The objective of this year-long study was to evaluate the prescribing pattern with a special focus on the use of antimicrobials at a pediatric clinic setting.

Methods

The data on the prescribing was collected in a pre-designed format and analyzed for the WHO recommended prescribing indicators.

Results

The average age of patients was found to be 4.77±0.12 years (411 girls and 589 boys). Upper respiratory tract infections were noted in 26% of the patients, followed by Fever in 18%, reactive airway disease in 14%, acute gastroenteritis and cough in 11% each. The average number of drugs prescribed was found to be 3.10±0.04. Mostly 3 drugs per prescription were prescribed. The percentage of drugs prescribed from NLEM-2011 was 29%. Of all the drugs prescribed, only 177 drugs were prescribed by generic name accounting for only 6%. Injections were prescribed in only 3 patients.The drug categories most often prescribed were cough & cold preparations (17%), antihistamines (13%), NSAIDs (11%), and gastrointestinal drugs other than antiemetics (11%). Antibiotics constituted 23% of the total number of drugs prescribed. The most common class of AMDs prescribed was macrolides followed by penicillins and cephalosporins.

Conclusions

The most common diagnosis was URTI which could also have a viral origin. Antimicrobial in most cases may not be required.The small number of antimicrobial prescribed in this study confirms that the practitioner has been judicious to limit the use of antimicrobial agents in children.

ESP16-0824
21. S - CLINICAL USE OF ANTIMICROBIALS FOR TREATMENT

PILOT PROJECT OF ANTIBIOTIC STEWARDSHIP (ABS) AT A PAEDIATRIC TERTIARY CARE CENTRE IN GERMANY

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Background

Previous data suggest that up to 50 % of hospitalised patients receive antibiotics and 20-50 % of antibiotics prescribed are unnecessary or inappropriate. This causes side effects, avoidable healthcare expenditures and increasing rates of antibiotic resistance. Due to the lack of empirical data from German paediatric hospitals, we conducted a pilot survey to evaluate individual antibiotic regimens and to develop ABS-strategies for our paediatric care center.

Methods

During a prospective four-month period, therapeutic and laboratory parameters of all patients receiving any antibiotic were collected at bedside in four paediatric wards of the Dr. von Hauner Children's Hospital. Accuracy of choice and dosing of antibiotics was evaluated based on (inter-)national recommendations. Particular focus was laid on the extent of therapeutic drug monitoring (TDM) for antibiotics with narrow therapeutic ranges.

Results

Out of 422 prescribed antibiotics, the dose of only 77.5 % was within a range of ±30 % of (inter-)national dosing recommendations. According to this standard, 17.1 % of administered antibiotics were underdosed, 5.4 % overdosed. We observed that TDM was performed in only 8 out of 21 (38 %) patients treated with Vancomycin, an antibiotic where TDM is widely recommended. In these monitored patients, target range trough levels were only achieved in 17.5 % of treatment days.

Conclusions

Our data demonstrate that there is still a great need for improvement of antibiotic therapies in our tertiary care centre. Our main objectives are currently to avoid incorrect antibiotic dosing and to attain correct monitoring of vancomycin and aminoglycosides. Implementation of precise dosage recommendations, guidelines on empiric antibiotic choices as well as correct TDM and regular interdisciplinary paediatric ID ward rounds are our main ABS-strategies and will most certainly be effective to improve patient care.

ESP16-0152
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

A PROSPECTIVE OBSERVATIONAL STUDY OF THE PREVALENCE AND RISK FACTORS FOR EXTENDED-SPECTRUM ß-LACTAMASE-PRODUCING BACTERIA CAUSING URINARY TRACT INFECTIONS IN A FRENCH PEDIATRIC EMERGENCY CENTER

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Background

Urinary Tract Infections (UTIs) are frequently observed in pediatric emergency department. Over the last decade, there has been a significant increase in extended-spectrum ß-lactamase (ESBL)-secreting organisms responsible for UTI in children. The objectives of this prospective study were to determine the prevalence of febrile ESBL-UTIs and to analyze the risk factors associated with ESBL-UTIs in a French pediatric emergency department of a University Hospital.

Methods

In this prospective observational study, all children with febrile UTIs were included from May 2012 until April 2013. Children 0-16 years old with a history of symptoms suggestive of febrile UTI and with a positive urine culture were included.

Results

Of 488 diagnosed febrile UTIs, 23 (4.7% [95% CI 3.2%-7.0%]) were due to an ESBL-producing organism. Significant independent risk factors of ESBL-UTIs were a prior hospitalization (odds ratio=3.4, [95% CI 1.3-9]) and an urinary tract abnormalities (odds ratio=3.4, [95% CI 1.3-8.9]) (Table 1). In 6/23 cases, the oral treatment was an association of cefixime and amoxicillin-clavulanate.

Table 1: Characteristics of the 460 patients

	All patients with febrile UTI N = 460 (%)	Patients with febrile UTI caused by ESBL-producing bacteria N=22 (%)
Sex ratio (M/F)	1.25	1.75
Median age in months [range]	11.4 [0.3-201.9]	18.6 [0.6-72.3]
Urinary tract abnormalities	92 (20.0%)	10 (45.4%)
Chronic diseases	65 (14.1 %)	6 (27 .2%)
Travel abroad (family or children)	170 (36.9%)	9 (40.9%)
Previous UTI	106 (23.0%)	13 (59.0%)
Antibiotic therapy within the last 3 months	181 (39.3%)	15 (68.1%)
Hospitalization within the last 6 months	105 (22.8%)	11 (50.0%)

UTI: Urinary Tract Infections.

Conclusions

The prevalence of febrile ESBL-associated UTIs was 4.7% in a French pediatric emergency department of a University Hospital. This survey confirmed the alarming rate of ESBL-UTIs. However, this rate do not seem sufficiently high enough to change our guidelines.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0800
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

MULTIDRUG-RESISTANT BACTERIAL RESPIRATORY ISOLATES IN HOSPITALISED PATIENTS WITH CYSTIC FIBROSIS PULMONARY EXACERBATION

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Background

Cystic Fibrosis (CF) is an autosomal recessive genetic disease which includes frequent respiratory tract infections and recurrent hospitalised. Emergence of resistance to multiple antimicrobial agents in pathogenic bacteria has become a significant problem in this patients. Due to this problem we aimed to analyze the multidrug-resistant (MDR) bacterial isolates characteristics in hospitalised cystic fibrosis patients with pulmonary exacerbation.

Methods

MDR was defined as resistant to three or more antimicrobial classes. A total of 45 acute exacerbation attacks with MDR bacterial growth were detected in 32 hospitalised CF patients in Marmara University Pendik Training and Research Hospital.

Results

Of 32 CF patients with 45 exacerbation attacks, 22 (68.8%) were female and 10 (31.2%) were male. The mean age was 114.7 + 62.1 months. The three most common complaints were increased sputum (73.3%), cough (%60) and fever (31%). Previously known colonization rate of *Pseudomonas aeruginosa* was 55.6%. All the patients had a MDR bacteria growth in the respiratuar samples and three most common isolates were *Pseudomonas aeruginosa* (53.4%), *Staphylococcus aureus* (17.8%) and *Acinetobacter baumannii* (4.4%). Only 8 (18%) exacerbation attacks were treated with monotherapy and 37 (82%) attacks were treated with combination antibiotherapy. The most common used combination antibiotherapy was ceftazidime and amikacin (22.2%). Empirical antifungal therapy was used in 8 (17.8%) patients. Mean hospitalization duration was 17.3 + 8.4 days. The mortality rate was 6.2% (n=2).

Conclusions

Presence of MDR growth is significant impacts about mortality and morbidity in CF patients. Effective infection control measures and the choice of appropriate antibiotic treatment are fundamental components for prevention of increased MDR isolates.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0148
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

DRUG RESISTANCE PROFILE AND BIOFILM FORMING POTENTIAL OF PSEUDOMONAS AERUGINOSA ISOLATED FROM CONTACT LENSES IN KARACHI-PAKISTAN

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Background

The contaminated contact lens provides *Pseudomonas aeruginosa* an ideal site for attachment and biofilm production. Continuous contact of the eye to the biofilm-infested lens can lead to serious ocular diseases, such as keratitis (corneal ulcers). The biofilms also prevent effective penetration of the antibiotics, which increase the chances of antibiotic resistance.

Methods

For this study, 22 *Pseudomonas aeruginosa* isolates were obtained from 36 contact lenses and 14 contact lens protective fluid samples. These isolates were tested against eight commonly used antibiotics using Kirby-Bauer disk diffusion method. The biofilm forming potential of these isolates was also evaluated using various qualitative and quantitative techniques. Finally, a relationship between biofilm formation and antibiotic resistance was also examined.

Results

The isolates of *Pseudomonas aeruginosa* tested were found resistant to most of the antibiotics tested. Qualitative and quantitative biofilm analysis revealed that most of the isolates exhibited strong biofilm production. The biofilm production was significantly higher in isolates that were multi-drug resistant ($p < 0.0001$).

Conclusions

Our study indicates that multi-drug resistant, biofilm forming *Pseudomonas aeruginosa* isolates are mainly involved in contact lens associated infections. This appears to be the first report from Pakistan, which analyzes both antibiotic resistance profile and biofilm forming potential of *Pseudomonas aeruginosa* isolates from contact lens of the patients with contact lens associated infections.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1059
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

ANTIMICROBIAL SUSCEPTIBILITY OF ESCHERICHIA COLI IN A PEDIATRIC POPULATION IN NORTHERN SPAIN OVER AN 11-YEAR PERIOD

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Background

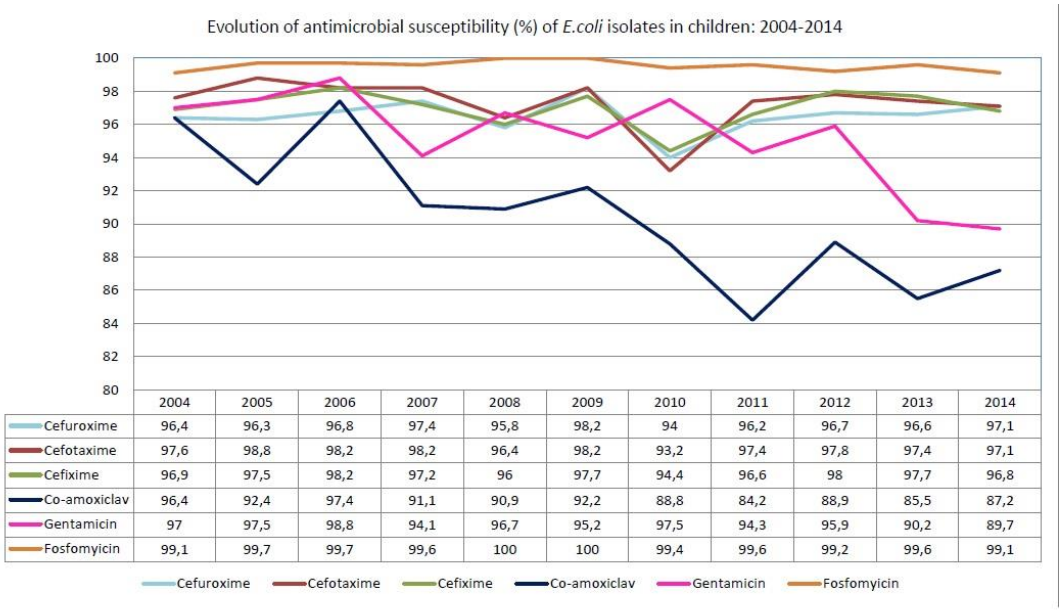
Escherichia coli is the main etiologic agent (70-90%) in urinary tract infections (UTI) and its antimicrobial susceptibility guides the empirical antibiotic therapy. The aim of this study is to analyse *E. coli* isolates and their susceptibility to several antibiotics in the pediatric population in a region in Northern Spain, in order to choose the most suitable empirical treatment when suspecting an UTI.

Methods

Descriptive retrospective study of antimicrobial susceptibility of *E. coli* isolates in pediatric patients (<14 years old) between 1st January 2004 and 31st December 2014 in Gijón (Spain), with a population around 303,000.
We analysed epidemiological data, antimicrobial susceptibility to several antibiotics (ampicillin, co-amoxiclav, cefuroxime, cefixime, cefotaxime, trimethoprim-sulfamethoxazole, gentamicin, fosfomycin, nitrofurantoin and ciprofloxacin) and rate of extended-spectrum β-lactamase (ESBL) producing *E. coli*.

Results

A total of 3.343 *E. coli* isolates were analysed (93.5% from urine cultures). Patients' median age was 2.7 years; 71% were female. Susceptibility rates to ampicillin (40.3%) and trimethoprim-sulfamethoxazole (78.2%) were low with little variations along the study. Susceptibility to co-amoxiclav (94.6% to 87.2%) and to gentamicin (97% to 89.7%) progressively decreased from 2004 to 2014. Susceptibility rates to cefuroxime (96.4%) cefixime (97%), cefotaxime (97.2%), fosfomycin (99.6%), nitrofurantoin (99.2%) and ciprofloxacin (95%) remained stable. There has been a low and stable rate of ESBL producing *E. coli* (2,2%).



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Cefuroxime	96,4	96,3	96,8	97,4	95,8	98,2	94	96,2	96,7	96,6	97,1
Cefotaxime	97,6	98,8	98,2	98,2	96,4	98,2	93,2	97,4	97,8	97,4	97,1
Cefixime	96,9	97,5	98,2	97,2	96	97,7	94,4	96,6	98	97,7	96,8
Co-amoxiclav	96,4	92,4	97,4	91,1	90,9	92,2	88,8	84,2	88,9	85,5	87,2
Gentamicin	97	97,5	98,8	94,1	96,7	95,2	97,5	94,3	95,9	90,2	89,7
Fosfomyicin	99,1	99,7	99,7	99,6	100	100	99,4	99,6	99,2	99,6	99,1

Conclusions

Most *E. coli* strains remain susceptible to 2nd and 3rd generations cephalosporins, fosfomycin, nitrofurantoin and quinolones, while susceptibility rates to co-amoxiclav and gentamicin have progressively decreased in the last eleven years. The rate of extended-spectrum β-lactamase producing *E. coli* is low (mean of 2,2%) in our pediatric population.

ESP16-0822
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

MONITORING PAEDIATRIC CARBAPENEM USE WITH AN ELECTRONIC-PRESCRIBING DATABASE

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Background

Carbapenem use is increasing, as are reports of carbapenemase resistant organisms (CROs), especially in hospitals. CROs represent a considerable challenge that calls for improved processes for monitoring carbapenem use. Electronic (e)-prescribing allows for regular, systematic analysis of antibiotic use at a patient level. In this survey we collected data on carbapenem prescribing through our new e-prescribing system to assess the feasibility of regular data collection to monitor carbapenem and other antibiotic use.

Methods

E-prescriptions of carbapenems at a tertiary Children's Hospital in the UK from April to October 2015 were extracted to a database. Accuracy of data extraction was validated by comparison with the electronic patient record. We included 2 general paediatric, 2 surgical and 1 oncology ward. Paediatric and neonatal intensive care units were excluded. Data were analysed with respect to total carbapenem use by department, indication and whether the carbapenem was rationalised appropriately.

Results

There were 946 carbapenem doses administered to 44 patients. The specialties administering the most carbapenem doses were general paediatrics (242/946), respiratory (211/946) and haematology/oncology (164/946). The most common indications were cystic fibrosis (9/44), sepsis (9/44) and meningitis (6/44). The carbapenem was changed to an alternative antibiotic within 24 hours of positive cultures in 7/28 of cases and stopped within 24 hours of negative cultures in 5/16 of cases.

Conclusions

Carbapenem use was relatively common, with the majority of prescriptions occurring within 3 paediatric specialties. The survey highlighted the need to improve rationalising carbapenem use in response to culture results. Analysis of e-prescribing data provides an easy and rapid way to assess antibiotic use, which could be utilised to provide real-time audit and feedback as part of a stewardship programme.

ESP16-0596
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

SKIN AND SOFT TISSUE INFECTIONS CAUSED BY STAPHYLOCOCCUS AUREUS STRAINS RESISTANT TO MUPIROCIN AND FUSIDIC ACID ARE EMERGING IN ATHENS, GREECE

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Background

Mupirocin (MUP) and fusidic acid (FA) resistant *Staphylococcus aureus* strains have been emerging since summer 2013. The aim of this study was to evaluate the epidemiologic and microbiological characteristics of these cases (Jul 2013-Dec 2015).**Methods**

Cases with culture-proven mupirocin resistant *S. aureus* infection were reviewed retrospectively and epidemiologic data were obtained through telephone survey. Antimicrobial susceptibility testing, low (LLR) and high-level (HLR) resistance to MUP, inducible (MLSBi) and constitutive (MLSBc) lincosamides resistance were performed according to CLSI.

Results

In total, 210 cases ofinfections were recorded among previously healthy children (57.1% boys, ranging in age 18d-15y, median 3y). Types of infection included impetigo (non-bullous or bullous) (81.5%), epidermolysis bullosa (5.7%), atopic dermatitis [MT1] (4.7%), otorrhoea, ophthalmia, pustulosis each below 3%) and bacteremia (1 case). The most affected area was the face (38%), followed by multiple site spread (33%) and the trunk or extremities (29%). Past use of MUP or/and FA ointment had 34.2% of patients, 21.7% reported the infection as recurrent and 37% had another case in the family occurring within the past year. Hospitalization was required for 15.7% of patients of which one in PICU. All but 3 strains (1,4%) were MSSA. High level resistance to MUP and MLSBc resistance to clindamycin were prevalent (97.6% and 92.4% respectively). The most common resistance phenotypes were PEN/MUP/FA (57.6%) and PEN/MUP/FA/ERY/CL (22.3%). There was an increasing rate of infections yearly, during summer and early autumn (figure).

Conclusions

Resistance to both MUP and FA confers adaptability for persistent staphylococcal carriage. Widespread usage of topical antimicrobials for skin infections may be the reason for the emergence of these isolates. So far, this regards MSSA strains. Molecular study of these newly spread isolates is warranted.

ESP16-0664
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

CLINICAL USE OF BLOOD CULTURES AND ANTIBIOTIC STEWARDSHIP IN A LARGE TEACHING HOSPITAL IN MALAWI

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Background

Infection is a major cause of paediatric death in Malawi.Antimicrobial resistance is increasing, as it is worldwide.The information gained from microbiologic culture and antibiotic sensitivities is crucial to guide selection of appropriate antimicrobial therapy, and in turn improve clinical outcomes. In a large government teaching hospital in Malawi we audited whether paediatric Blood Cultures (BC) were being processed in a timely manner, and whether the results were being used to guide antibiotic prescribing

Methods

We prospectively reviewed electronic BC reports and patient notes for 66 paediatric patients admitted to Queen Elizabeth Central Hospital, Blantyre in January 2015. We looked at whether there was daily documentation regarding BC results, antibiotics prescribed and processing times of BC samples by the microbiology laboratory.

Results

Once received in the laboratory, positive growth was identified within satisfactory timeframes. Only 8/66 patients had daily documentation of BC results. 42/66 had no reference to the BC result documented at any stage of admission. 27/47 patients who did not have a result known at time of discharge had no documented review planned. Of 5 patients who had a significant positive growth, 3 were prescribed an appropriate antibiotic; 1 was prescribed without reference to the BC result. The outcome of 2 other patients discharged home on inappropriate treatment is unknown.

Conclusions

In this audit BC processing by the laboratory was satisfactory. However clinicians were poor at following up and acting on results. BC was used to guide antibiotic prescribing in only 2 of 5 patients with significant bacteraemia. Blood culture surveillance is crucial for appropriate antimicrobial stewardship but better clinician training and supervision are recommended to improve the translation of microbiology results into patient care.

ESP16-0689
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

GRAM NEGATIVE BACTERIA - A CHILDRENS HOSPITAL PATTERN OF ANTIBIOTIC RESISTANCE

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Background

Gram negative bacteria are becoming increasingly resistant to most available antibiotics limiting treatment options.

Aim: determine most prevalent Gram negative bacteria from different site cultures and their antibiotic susceptibility pattern.

Methods

Retrospective study from 01.01.2009 through 31.12.2014. A total number of 11119 strains were collected: 3969 Gram negative bacteria were isolated in children <1 year of age that were admitted at the Clinical Childrens Hospital, Brasov, Romania for infections at different sites. For all strains, E-tests were performed in order to determine MICs values.

Results

The number of Gram negative bacteria decreased according to the total number of positive isolated cultures from 21.3% in 2009 to 13.9% 2014 respectively. The most common Gram negative bacteria were: E.coli 47.5% followed by Pseudomonas aeruginosa 21.8%, Klebsiella pneumoniae 12.7%. There was a slight predominance of girls 57% in our study.

E.coli antibiotic resistance was 77% to ampicillin and 44% to piperacillin, IInd generation of cephalosporin 31%, ESBL E.coli strains were resistant 100% to piperacillin and 90% to ceftazidime, ceftriaxone, cefuroxime, 65.7% to Gentamicin, 58.4 levofloxacin, 50.9% norfloxacin, 50% tobramycin.

Klebsiella pneumoniae 100% resistant to beta-lactams, 73% to Cefaclor, 69% Cefuroxim, 62% to ceftriaxone. ESBL strains were resistant 100% ceftriaxon and cefuroxim, 95% amoxicillin and clavulanat, 61.3% levofloxacin., 33% gentamicin, 100 % chloramfenicol.

Klebsiella oxytoca was ,69% resistant to cefaclor, 40% to ceftriaxon.

ESBL Klebsiella oxytoca strains were 100% resistant, piperacillin, ceftriaxon, 84.6% to amoxicillin and clavulanat, 71.7% gentamicin and 61.2 % levofloxacin.

Conclusions

Gram negative bacteria have an alarming growing resistance rate to amino-penicillin. Due to the MDR of these strains empirical treatment is prone to fail.

ESP16-0703
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

NEW HORIZON IN THERAPEUTICS: ANTIMICROBIAL ACTION OF DENDROBIUM NOBILE AND PHALAENOPSIS AGAINST PYOGENIC SKIN INFECTION ISOLATES

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Background

Orchids are well-known around the globe as plants of decoration and called as gems in the area of horticulture. The basic idea of research was the assessment of the flower extracts of Dendrobium nobile and phalaenopsis plants

Methods

***in vitro* for their antibacterial activity against pyogenic skin infection isolates, that is, *Staphylococuus aureus* and *Staphylococcus epidermidis* by means of agar disc diffusion method. For this intention, strains were isolated from skin acne patients and were identified by conventional methods.**

Results

The flower extracts of Dendrobium nobile and phalaenopsis showed antibacterial activity against pyogenic skin isolates. In comparable, several antibiotics also tested alongside the isolated organisms.

Conclusions

The information demonstrated potential outcome for Dendrobium nobile and phalaenopsis in contrast of five different antibiotics. Moreover, analysis also confirmed that the pyogenic organisms were challenging besides several antibiotics.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1083
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

POSITIVE BLOOD CULTURES IN A PAEDIATRIC MEDICAL WARD OF A PORTUGUESE CHILDREN'S HOSPITAL: ANTIMICROBIAL RESISTANCE PATTERNS OVER A FIVE-YEAR PERIOD

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Background

The surveillance of paediatric blood cultures (BC) is central to monitoring changing epidemiology, which guides the choice of empirical therapy. **Aims:** To determine trends of bacteraemia in children over a 5-year period and assess resistance patterns.

Methods

Retrospective study including all positive BC from children aged<18 years admitted to a medical paediatric ward in Coimbra Paediatric Hospital from 2011 to 2015. Medical records were analyzed to assess risk factors, underlying illness and contamination rates. Duplicate isolates were excluded. Definitions: community associated infection (CAI)-positive BC within 48 hours of hospital admission; hospital acquired infection (HAI)-positive BC>48 hours of admission; contaminated BC-patient's clinic or laboratory results did not suggest infection or follow-up negative BC.

Results

A total of 69 positive BC were reported, with 67% HAI and 12% CAI; 21% were considered contaminated BC. Regarding blood stream infections (HAI/CAI), 59% of cases occurred in children aged <5 years old and 35% <12M. The main associated diagnosis were septicemia (81%) and urinary tract infection (7%). The majority of isolates (81%) were Gram positive species. Most commonly isolated organisms were coagulase-negative *Staphylococcus* (52%), *S.aureus* (17%), *K.pneumoniae* (9%) and *E.coli* (6%). MRSA corresponded to 1/3 of *S.aureus* isolates with a decrease in incidence along the study period. No *E.coli* isolateswere resistant to co-amoxiclav and only 1 was resistant to 2nd generation cephalosporins. Three isolates were ESBL-producers (1 *E.coli* and 2 *K.pneumoniae*) with no resistances to meropenem. 89% of patients had risk factor for HAI (mainly central/peripheral lines (89%), imunossupression (26%) and gastrostomy (26%)).

Conclusions

This study identifies the commonest agents isolated from BC in our medical ward and highlights shifts and trends observed over time. Medical devices remain an important source of infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1089
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

EPIDEMIOLOGY OF URINARY TRACT INFECTIONS NEEDING PROLONGED MEDICAL WARD ADMISSION OVER A 6-YEAR PERIOD

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Background

Urinary tract infections (UTI) remain a common cause of acute illness in children. Although most cases can be managed effectively on an outpatient basis, some still account for a substantial number of paediatric hospitalizations, mainly in infants. **Aims:** To identify the main reasons for prolonged admissions of children/adolescents with UTI, trends in the etiology, risk factors and to assess antimicrobial resistance patterns over a 6-year period.

Methods

We performed a retrospective analysis of clinical processes of all children admitted for UTI to a paediatric medical ward for > 72h, from 2010 to 2015. We excluded cases of patients with urine culture collected by non-aseptic techniques or those under antibiotherapy in the 72 hours prior to urine sample.

Results

A total of 23 admissions fulfilled the requested criteria; 57% were female and 65% were <12M (median 2,5M). The main reason for admission was age<3M (48%), followed by congenital urinary tract abnormalities (UTA) (22%). Risk factors were identified in 52% patients (UTA 52%, vesicoureteral reflux 39% and chronic/daily vesical catheterization 9%). Urinalysis showed abnormalities in 78%. Median length-of-stay (LOS) was 5 days (2-24 days). *E.coli* accounted for 70% of cases; there was no resistance to amoxiclav and only 1 case was resistant to 2nd and 3rd generation cephalosporins. *Enteroccus faecalis* was the agent in 17%, with 50% resistance to ampicillin/penicillin G. One third of pathogens were multiresistant (35%), but only one (*E. coli*) was ESBL producer, which was sensitive to meropenem and piperacillin/tazobactam.

Conclusions

There was a small number of UTI needing prolonged admissions. A large portion has identified risk factor and identification of multiresistant pathogens.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0185
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

BACTERIA WITHOUT BORDERS: A HIGH CARRIAGE RATE OF ANTIBIOTIC-RESISTANT BACTERIA AND INFECTIONS AMONG SYRIAN CHILDREN HOSPITALIZED IN GALILEE MEDICAL CENTER, ISRAEL

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Background

For three years, severely-wounded children from Syria's civil war and ill Syrian children have been secreted across the border for treatment in Israeli hospitals, mainly in Galilee Medical Center (GMC). Due to incomplete medical history and compromised Syrian healthcare, screening cultures for multi-drug resistant (MDR) bacteria and contact isolation are conducted upon admission. This survey characterizes MDR carriage and infections among hospitalized Syrian children, information valuable to international centers treating Syrian refugees.

Methods

Prospective collection of MDR culture data of all Syrian children (0-18y) admitted to GMC from 6/2013-10/2015. MDR's included: Extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBL), Carbapenem-resistant *Enterobacteriaceae* (CRE), methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), MDR *Acinetobacter baumannii* (MDR-AB).

Results

Of 100 children, 72 had multi-trauma and 25 were ill. Screening cultures for all MDR's were collected in 78 children; 65/78 (83%) were MDR-positive: 76%, 5%, 3%, 1%, and 1% for ESBL's, MDR-AB, CRE, VRE, and MRSA, respectively. Twenty four percent carried > one MDR. MDR carriage was higher in 2015 than 2013-2014 (p=0.02). Most MDR's were ESBL-producing *Escherichia coli,* variably resistant (27%-71%) to non-beta-lactams but not to amikacin. Although MDR carriage rate was similar between wounded and ill children, 15 wounded children vs. 1 ill child had infections caused by MDR's (p=0.035); in 60%, the infection was caused by MDR similar to isolate on screening. Empiric therapy with meropenem+amikacin was appropriate in all MDR infections.

Conclusions

An alarmingly high rate of MDR carriage is evident among Syrian children treated in Israel. Higher MDR carriage prevalence nowadays implies further deterioration of healthcare in Syria. Early MDR screening provides valuable information in sepsis and isolation decision-making. In infected Syrian children, meropenem+amikacin had an appropriate antibacterial spectrum, but may be inadequate for ~10% of children.

ESP16-0868
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING ENTEROBACTERIACEAE IN CHILDREN AT MUSTAPHA BACHA UNIVERSITY HOSPITAL, ALGIERS, ALGERIA

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Title of Case(s)

Extended-spectrum beta-lactamase-producing Enterobacteriaceae in children at Mustapha Bacha University Hospital, Algiers, Algeria.

Background

Extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBLPE) is a major concen worldwide. The aim of the study was to review children cases infected with extended-spectrum beta-lactamase-producing Enterobacteriaceae at Mustapha Bacha University Hospital (MBUH), Algiers, Algeria.

Case Presentation Summary

All children (0-16 years) who had an ESBLPE isolated at the MBUH Microbiology Laboratory from January 2012 to December 2014 were included in this review.

Learning Points/Discussion

During the review period, 306 ESBLPE were isolated from children. There were 93 isolates in 2012, 115 in 2013, and 98 in 2014. The three prevalent isolates were *Klebsiella pneumonia, Escherichia coli,* and *Enterobacter clocae*. ESBLPE were isolated from a wide range of specimens including blood, urine, respiratory and cerebrospinal fluid. From the 306 ESBLPE isolates, 61.4% (n=188), 21.2% (n=65), and 17.3% (n=53) were recovered from medical, surgical and newborn departments respectively. Most of the ESBLPE were no susceptible to gentamicin, and one isolate was no susceptible to ertapenem.

Infections due to ESBLPE in children are prevalent at Mustapha Bacha hospital. Therefore, regular monitoring is needed. However, infection control practices and careful antibiotic prescribing will be necessary to reduce the rate of ESBLPE infection, and prevent the emergence and diffusion of carbapenemase producing Enterobactericeae in our Hospital.

ESP16-0691
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

IMPLEMENTATION OF ANTIMICROBIAL STEWARDSHIP IN CRITICALLY ILL CHILDREN

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Background

Outside USA, the literature regarding antimicrobial stewardship programs (ASP) in hospitalized critically ill children is limited. The aim of this study was to assess the pattern and time trends of antibiotic consumption (AC) in a Pediatric Intensive Care Unit (PICU) after implementation of an ASP.

Methods

Since 2010, an ASP has been implemented in a polyvalent 8-bed PICU. The core structure of this ASP included daily audits by dedicated PID physicians with intervention. Data of AC (antibiotics for systematic use, J01) were obtained from the hospital pharmacy and expressed as defined daily doses per 100 bed-days (DDD/100BD) from 2001 to 2015.

Results

A significant increase ($p<0.001$) of AC was found between 2001 and 2009 from 77.3 to 268.4 DDD/100BD (Figure). However, since 2010, AC discontinued to increase and annual average was 215 DDD/100BD. Beta-lactams, the most frequently used antimicrobial agents, showed a significant increase through 2001 to 2009 ($p=0.002$). ASP resulted in a significant reduction of beta-lactam consumption ($p=0.02$) including significant reduction of carbapenems ($p=0.018$). Consumption of glycopeptides and aminoglycosides (2nd and 3rd most commonly used antimicrobial class, respectively) had a significant increase between 2001 and 2009 ($p=0.03$). During ASP a tendency of decrease was found for both glycopeptides and aminoglycosides. Consumption of fluoroquinolone and lincozamides constituted 3 and 4% of total AC, respectively. Both of them showed a significant increase throughout study period. Colistin use was significantly increased between 2003 and 2009 but since 2010 annual rates were constant.

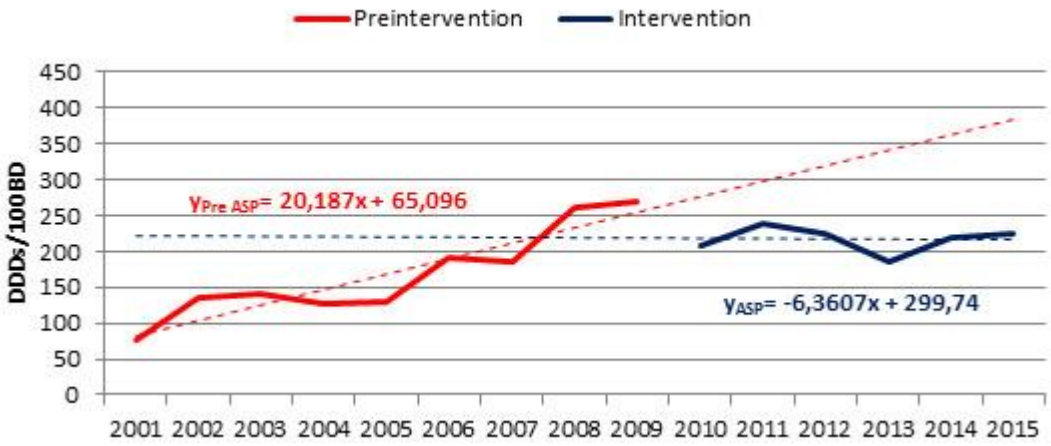

Figure: Annual antimicrobial consumption

Conclusions

Significant increase of total AC in a PICU setting was stopped after implementation of an ASP. ASP resulted in a significant reduction of beta-lactams, and a trend of decrease of the other commonly used antimicrobial agents.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0338
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

HIGHER RATES OF ANTIBIOTIC RESISTANCE IN PEDIATRIC VERSUS NEONATAL GRAM-NEGATIVE NOSOCOMIAL SEPSIS: A TWO-YEAR HUNGARIAN SURVEY

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Background

Sepsis due to antibiotic-resistant Gram-negative pathogens remains a frequent cause of morbidity and mortality of hospitalized children. Identification of patient groups with higher risk of antibiotic resistance may increase the success rate of empiric antimicrobial treatment.

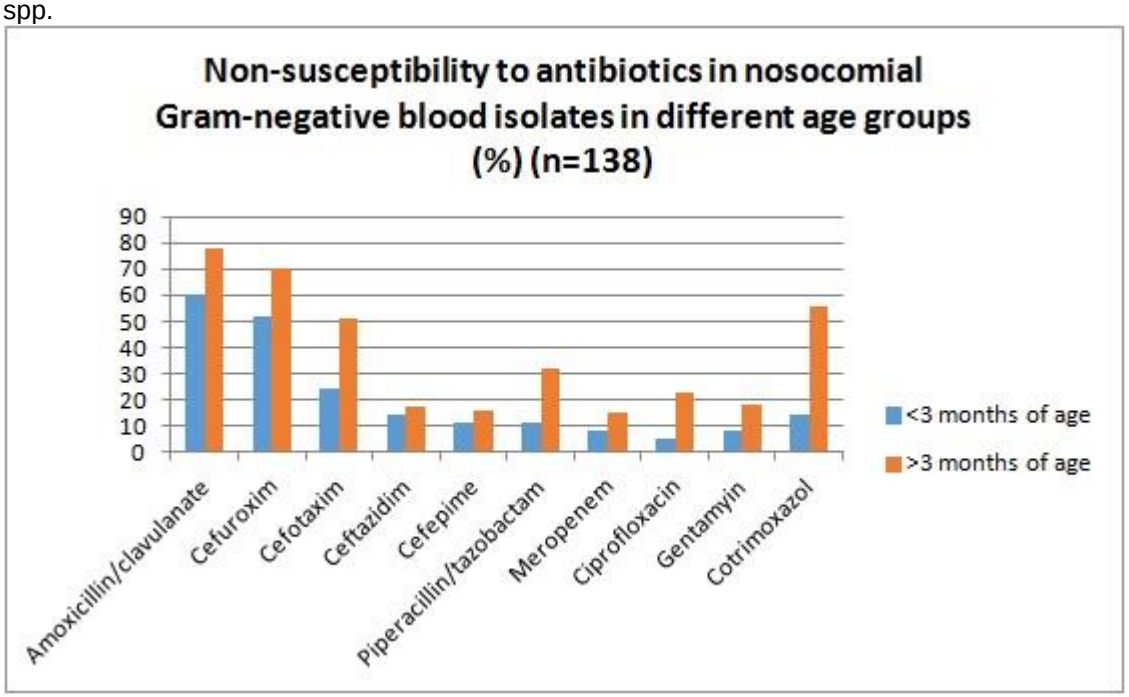
Methods

Between January 2010 and December 2011 we prospectively collected cases of Gram-negative sepsis of neonates and older children in six different pediatric hospitals in Budapest, Hungary. We analyzed data regarding distribution of nosocomial pathogens and antibiotic resistance patterns comparing the neonatal and pediatric patient groups.

Results

We collected 138 strains from 127 nosocomial bloodstream infections. In the neonatal group (age <90 days) (n=61) Enterobacteriaceae represented 72% of all isolates (49/61), *Klebsiella* spp. being the most prevalent pathogen (20/61). In older children (n=77), *Esherichia coli* was isolated most frequently (45/77), followed by *Pseudomonas aeruginosa* (21/77). Rates of cefotaxime, meropenem, ciprofloxacin and gentamycin non-susceptibility were 51.9%, 15.58%, 23.2% and 19.5% in pediatric, and 24.6%, 6.6%, 4.8% and 11.5% in neonatal patients, respectively. Multidrug resistance reached 46.8% in children >3 months of age vs. 14.8% in younger infants. Most prevalent multiresistant pathogen was *Esherichia coli* in both neonatal (4/61), and pediatric age group (16/77), followed by *Pseudomonas aeruginosa* and *Enterobacter*

spp.



Conclusions

In our population children with nosocomial Gram-negative sepsis beyond the neonatal period are more prone to be infected with antibiotic-resistant strains. Consequently early empiric therapy with combination of broad-spectrum antibiotics could be recommended especially in the older patient group.

Acknowledgments
We thank to the patients, parents and colleagues (physicians, nurses and laboratory assistants) of every institution involved in the study for their contribution in our work.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0609
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

ANTIMICROBIAL RESISTANCE OF URINARY TRACT PATHOGENS IN CYPRIOT CHILDREN HOSPITALIZED FOR A FIRST EPISODE OF URINARY TRACT INFECTION

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Background

Urinary tract infection(UTI) is one of the most common bacterial infections diagnosed in children. Empirical treatment should be based on local data of resistance of uropathogens. There are scarce data on antibiotic resistance of uropathogens in Cypriot children. This study aims at examining the resistance patterns of bacteria causing a first episode of UTI in children.

Methods

We retrospectively analysed the resistance patterns of bacteria isolated from the urine cultures of children admitted for a first episode of UTI to the central referral hospital in Nicosia the capital of Cyprus between 2005 and 2015

Results

During the study period a total of 182 children were admitted for a first episode of UTI. Of these children 107 were males (58.8%) and 75 females (41.2%). The age range was 0.33 to 96 months. The median age of males was 2 months and of females 6 months. The most frequent uropathogen was *Escherichia coli* (76.7%) which was more commonly resistant to Ampicillin (45.9%), followed by trimethoprim-sulfamethoxazole (22.0%) and amoxicillin-clavulanate(21.5%), cefuroxime (9.2%), cefotaxime (5.1%), gentamicin (3.9%). No resistant strains were detected to imipenem-cilastatin or meropenem. Resistance of total uropathogens to ampicillin, amoxicillin-clavulanate, trimethoprim-sulfamethoxazole and cefuroxime was 53.4%, 28.0%, 25.0% and 15.3% respectively.

Conclusions

Community acquired uropathogens appear to have become resistant to some oral antimicrobials frequently used for empirical treatment of UTIs such as ampicillin, trimethoprim-sulfamethoxazole and amoxicillin-clavulanate. Cefuroxime appears to remain effective for oral treatment. For hospitalized cases parenterally used antimicrobials such as third generation cefalosporins, aminoglycosides and the carbapenems appear to remain quite effective.

ESP16-0584
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

DETERMINANTS OF NON-COMPLIANCE TO HOSPITAL ANTIBIOTIC GUIDELINES FOR THE EMPIRIC TREATMENT OF LOWER RESPIRATORY TRACT INFECTIONS (LRTIS) IN CHILDREN IN EUROPE: AN ARPEC PROJECT ANALYSIS

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Background

(on behalf of the ARPEC project group members)

Antibiotic prescribing guidelines are key in efforts to control antibiotic use in children. The aim of this study was to assess the compliance of hospitals in Europe to existing guidelines for the empiric treatment of Lower Respiratory Tract Infections(LRTIs) in children and to establish the determinants in cases of non-compliance.

Methods

This study represents the combined analysis of two sub-work packages of the Antibiotic Resistance and Prescribing in European Children (ARPEC) study: a) a cross-sectional web-based survey on hospital antimicrobial prescribing guidelines and b) a Point Prevalence Survey (PPS) on antibiotic use in matched hospitals.We extracted and analyzed cases of LRTIs, without comorbidities that received empiric antibiotic treatment.

Results

We analyzed 218 LRTI cases from 17 European countries. 134(61.5%) cases derived from hospitals that had access to guidelines and 54/134(59.7%) were compliant. Of the 80 non-compliant cases, 63 (78.8%) were cases of non recommended antibiotic administration and in 17(21.2%) there was redundant cover with 2 antibiotics.

Univariate analysis revealed lower compliance to guidelines in a) Children >5 years old vs <5 years (12.5% v 44.07%,p=0.016), b) those treated in teaching vs non-teaching hospitals (28.57% v 51.13%,p=0.004), and c) those treated in Southern vs Western European countries (28.8% v 67.7%,p=0.003).

Following multivariate logistic regression, children treated in teaching hospitals have 64% lower probability to receive antibiotics as recommended by the local guideline compared to

non-teaching hospitals (p=0.018) after adjustment for potential confounders such as age and region(Table 1)

Table 1: Multivariate logistic regression to assess compliance (LRTI)

Covariate	Odds Ratio	95% CI	p-value
Age			
3m – 5year	Ref.Cat.		
5 year+	0.24	(0.05, 1.19)	0.081
Hospital			
Non-Teaching	Ref.Cat.		
Teaching	0.36	(0.16, 0.84)	**0.018**
Region			
North	Ref.Cat.		
South	1.38	(0.51, 3.73)	0.529
Central	5.48	(0.96, 31.33)	0.065
West	3.73	(1.35, 10.27)	**0.011**

Conclusions

We documented low compliance to existing antibiotic guidelines for LRTI in hospitals that participated in the ARPEC study and identified determinants in non compliant cases. Similar analysis for other common infections can guide interventions at a national and international level.

ESP16-0254
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

NEONATAL BLOOD STREAM INFECTION AT LEVEL III NEONATAL INTENSIVE CARE UNIT NEW DELHI: ROLE of GRAM POSTIVE ORGANISMS AND THEIR ANTIMICROBIAL SUSCEPTIBILITY

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Background

The organism responsible for neonatal sepsis vary across geographical boundarie. Gram positive organisms are implicated as the most common cause of neonatal sepsis in developed countries. In most developing countries gram negative bacteria remain the major source of infection. Microorganism implicated have developed increased resistance to commonly used antibiotics making treatment extremely difficult.
Objective: was to Investigate Gram Positive Microrganisms causing Blood Stream Infection (BSI) and to find their antimicrobial susceptibility

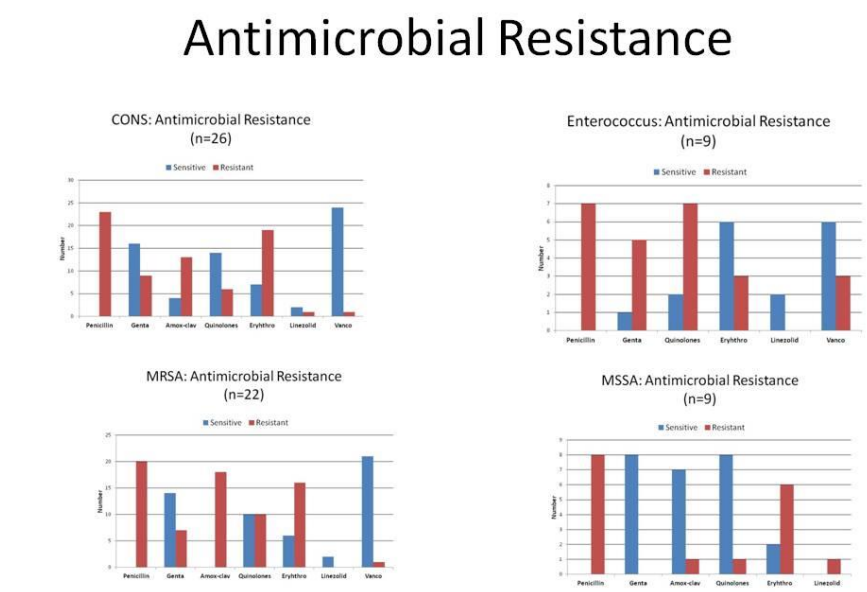
Methods

A Retrospective Cohort Study between January 2013 and December 2014 in a Level III Neonatal Unit New Delhi. Study population included babies who grew gram positive organism on blood culture. Charts were reviewed and data on microorganism grown and their antimicrobial susceptibility were retrieved. Analysis was performed using SPSS Version 20.0 and frequency distribution tabulated

Results

Sixty six out of 4038 admitted newborns grew gram positive organisms. Forty one had early onset sepsis (EOS) and 25 late onset sepsis (LOS). Common organisms responsible for EOS were Coagulase negative *Staphylococcus aureus* (CONS), Methicillin resistant *Staphylococcus aureus* (*MRSA*), *Enterococcus* sp. and Methicillin Sensitive *Staphylococcus aureus* (*MSSA*). Organisms responsible for LOS were *MRSA*, *MSSA*, CONS and *Enterococcus* sp. CONS were mostly resistant to penicillin, amoxyclav and erythro but moderately to highly sensitive to genta, quinolones, linezoid and vanco. Most of the *MRSA* were sensitive to genta, linezolid and vanco but resistant to penicillin, amoxyclav, quinolone and erythro. *MSSA* were sensitive to genta, amoxyclav and erythro. *Enterococci* sp. were

resistant to most of the antibiotics including vanco (30% resistance).



Conclusions

Our study demonstrated high level of resistance among Gram positive organisms to commonly used antibiotics. Local bacterial surveillance and microbial susceptibility pattern is essential to promote prudent use of antibiotics.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0710
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

MANAGEMENT OF HELICOBACTER PYLORI INFECTION IN ADOLESCENTS WITH LONG HISTORY OF FUNCTIONAL DYSPEPSIA

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Background

The eradication rates of H. pylori remain insufficient due to growing antibiotic resistance of the bacterium. The aim of the present study was to investigate how prevalence of H. pylori is affected by the duration of the disease and previous eradication treatments in adolescents with functional dyspepsia.

Methods

The study group included 132 consecutive adolescents with functional dyspepsia aged from 9 to 18 years, and was compared with 33 aged-matched controls. *H pylori* infection was determined by ELISA technique for serum IgG against H. pylori and HELIC urea breath test.

Results

Prevalence of H. pylori was 62.6% in patients and 33.3% in controls. Never treated patients with a history of the disease less than a year (n=21, 15.9 ±3.2 %) had the highest rates of the infection (71.4%); dyspepsia lasting from one to three years (n=49, 37.1 ±4.2 %) was associated with lower prevalence of H. pylori (58.8%). 29.6% of adolescents with the history of dyspepsia > 3 years and eradication treatments, (n=62, 46.9 ± 4.3%) were H. pylori positive ($p<0.01$ for the differences between groups 1 and 3).

Conclusions

Despite previous eradication treatments almost one third of patients with a long history of dyspepsia remained H. pylori positive and therefore should undergo the examination of culture and determination of its resistance and antibiotic susceptibility.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0919
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

WHOSE RESPONSIBILITY IS ANTIMICROBIAL RESISTANCE? A PILOT QUALITATIVE SURVEY INTO PUBLIC VALUES ON PUBLIC SPENDING AND DOCTORS' RESPONSIBILITIES

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Background

The NHS Antibiotic Quality Premium was introduced in April 2015, providing commissioners with financial rewards linked to reduction of antibiotic prescribing. This policy raises important value-based judgements yet there has been no formal evaluation of public opinion on these judgements. These include (i) whether patients think restrictive prescribing impinges upon autonomy (ii) whether the government is felt to bear responsibility for tackling AMR (iii) whether individuals should make a personal sacrifice (through taxation) to publicly fund research or policy initiatives and (iii) ways to encourage for behavioural change. UK-based surveys so far have focused on knowledge about *use* of antibiotics.

Methods

We reviewed the literature for public opinion surveys on AMR and qualitative surveys used to elicit responses on the topic of climate change, an issue which often draws comparison with AMR. We piloted a novel ten-item online survey distributed by e-mail to explore the questions above and provide data for further development of the questionnaire. 98 responses were received over 2 weeks from individuals affiliated with St Georges' University, London.

Results

Question	% respondents agreeing/average response
On a scale of 1-10, how responsible do you think doctors should be for helping to control antimicrobial resistance by reducing their prescribing rates? (1 not responsible at all, 10 completely responsible)	8.56
I trust my doctor's decision whether or not to prescribe me antibiotics	75
I think the government should intervene to try and control antibiotic resistance	86
I would be willing to pay higher taxes to try to improve antibiotic resistance	70
Research has shown that, in a group patients treated with oral antibiotics for suspected urinary tract infection, they then had an increased risk of getting a resistant infection in the next 6-12 months. Would this information change your behaviour a) as a patient b) as a clinician?	a – 78 b – 89

Equity of access to antibiotics regardless of socioeconomic status ranked as a higher priority than personal access to antibiotics; both of these ranked above patient autonomy, as measured by the ability to challenge a clinician's decision to withhold antibiotics. Free text responses indicated that some individuals had changed their behaviour due to AMR within the last 12 months.

Conclusions

AMR is recognised as a public health issue requiring government intervention, together with prioritisation of socioeconomic equity in the healthcare system. Individuals largely trust the current system to distribute antibiotics appropriately and equitably. If replicated in larger, representative samples, these findings have important implications for future health policies designed to change behaviour.

ESP16-0519
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

DECREASING PREVALENCE OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS IN PEDIATRIC PATIENTS OVER THE LAST TWO YEARS IN ALEXANDROUPOLIS, THRACE, GREECE

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Background

Staphylococcus aureus is a major pathogen implicated in skin, soft tissue, and osteoarticular infections, pneumonia and bacteremia. We report our findings regarding the antibiotic susceptibility patterns (ASP) of *S. aureus* strains isolated from pediatric patients cared for in our department.

Methods

We retrospectively reviewed the ASP to various antibiotic agents of all pediatric *S. aureus* isolates recorded in the electronic charts of the hospital's microbiological laboratory over the period January 1, 2011 to December 31, 2015. Bacterial identification and antibiotic susceptibility testing were performed by the automated VITEK® 2 system GP and AST 613 cards (bioMerieux, Marcy-L' Etoile, France).

Results

Overall, 108 clinical isolates [males: 70 (64.8%), females 38 (35.2%)] of *S. aureus* were recovered over the study period from an equal number of children (1 isolate per patient). These isolates were recovered from the following sites: Skin wounds and abscesses (n=53), nasal cavity (n=23), middle ear (n=11), conjunctivae (n=10), blood (n=3) and various other sites (n=8). Among the 108 clinical isolates, 25 (23.1%) were MRSA, and 23 expressed the mecA phenotype. Among all isolates, resistance to clindamycin and erythromycin was 31.48% and 33.33%, respectively, followed by resistance to fusidic acid (6.48%), tetracycline (3.7%) and cotrimoxazole (0.92%). All isolates were susceptible to tobramycin, and only one was resistant to gentamicin (0.92%). All isolates were susceptible to rifampicin, glycopeptides and quinolones. Comparing the first 2 (2011-2012) with the last two study years (2014-2015) a highly significant drop in the number of MRSA isolates was noted in recent years [16/32 versus 5/57, $p<0.0001$).

Conclusions

The prevalence of infections due to MRSA has significantly declined in our area in recent years. The reasons for this finding require further study.

ESP16-0937
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

EPIDEMIOLOGY OF BLOOD STREAM INFECTIONS IN A TERTIARY PEDIATRIC HOSPITAL DURING A 2 YEAR-PERIOD

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Background

Blood stream infections (BSIs) are serious problems in pediatric hospitals. Although fungemias affect mainly immunocompromised children and neonates, bacteremias create problems to both immunocompetent and immunocompromised children.

Methods

In order to analyze the epidemiology of BSIs in the major Greek tertiary pediatric hospital we retrospectively reviewed the medical records of children with BSIs during the period from 4/2012 to 3/2014. Data regarding the pathogen's identity and antibiotic resistance profile were retrieved and analyzed.

Results

During the study period a total of 424 BSIs were identified, accounting for 17.37 BSIs/1000 admissions. More specifically 402 bacteremias (16.47/1000 admissions) and 22 fungemias (0.9/1000 admissions) were found. Gram positive pathogens were detected in 254 (59.8%) episodes, Gram negative in 148 (34.7%) and fungi in 22 (5.2%). Most prevalent pathogens were coagulase negative *Staphylococci* (CNS) (42.9%), *S.aureus* (5.4%), *Streptococcus* spp (6.1%), *E.coli* (8.7%), *Pseudomonas* spp (8.0%), *Klebsiella* spp *(*6.1%), *Enterobacter* spp 5.9% and *Candida* spp (5.2%). Most BSIs were detected at Oncology departments (40%-86.1/1000 admissions), Neonatology units (33%-7.5/1000 admissions) and in the Intensive care unit (26%-6.4/1000 admissions).

Conclusions

A considerable incidence of BSIs among hospitalized children was identified although a significant number were CNS that could be skin contamination. Implementation of better infection control practices are required in order to avoid central or peripheral line infections in our setting.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0996
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

UROPATHOGENS FREQUENCY AND ANTIMICROBIAL RESISTANCE PATTERNS REPORTED IN NON-HOSPITALIZED CHILDREN WITH URINARY TRACT INFECTION

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Background

Urinary tract infections (UTI) are common in paediatric age. *Escherichia coli* and *Proteus* are the most common found pathogens. Antimicrobial resistance patterns vary regionally.

The aim of this survey was to study the frequency of uropathogens in our community, their resistance pattern to antibiotics and the need for antibiotic (AB) adjustment after knowing the result of the urine culture (UC).

Methods

Culture and sensitivity data of the uropathogens from UTI suspected cases were prospectively collected from the records of Microbiology Department for study period (2014-2015). Urethral catheterization or midstream clean-catch specimen were used. Samples were processed for microscopy, culture, and antimicrobial susceptibility testing. Descriptive statistics were used to analyze the data.

Telephone contact with parents was made, except if UC was negative and no empiric AB had been initiated.

Results

Cases with incorrect patient identification, hospitalization, UC not obtained or inadequate collection method were excluded.

Empiric AB was initiated in 52,2%. The main choice was amoxicillin-clavulanate (56,8%) followed by cefuroxime (36,0%).

Of 2890 urine samples, 32,6% were positive. *Escherichia coli* (61,3%) was the most common microorganism followed by *Proteus* (24,8%).

The overall resistance to amoxicillin-clavulanate was 12,1% and to cefuroxime was 2,5% (*p value*<0,05).

We contacted 51,5% of the patients. From these: 68,1% maintained the initial AB, 3,3% started AB, 3,0% changed it and 25,6% stopped AB.

Conclusions

E. coli is still the most common uropathogen in children. Resistance to amoxicillin-clavulanate was higher than to cefuroxime. Therefore, cefuroxime should be the first line antibiotic for UTI in our community.

Contacting the parents after knowing the UC result is very important for AB adjustment.

Routine monitoring of the drug resistance pattern will help to identify the resistance trends regionally. This will help in the empirical treatment of UTI.

ESP16-0910
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

MICROORGANISMS CAUSING URINARY TRACT INFECTIONS AND THEIR ANTIMICROBIAL SUSCEPTIBILITY IN A PEDIATRIC POPULATION IN A REGION IN NOTHERN SPAIN

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Background

The aim of this study is to analyze the main microorganisms causing urinary tract infections and their antimicrobial susceptibility in a pediatric population in a region in Northern Spain

Methods

Descriptive retrospective study of urine cultures collected in pediatric patients (0-13 years old) between 2006 and 2015 in Emergency Department and Admission Ward in Hospital de Cabueñes (Gijón). Epidemiologic data, pathogenic agents and their antimicrobial susceptibility along the study period are analyzed.

Results

There was a total of positive 1980 urine cultures from 1448 children (59% females; median age 14 months old). Escherichia coli was the most common pathogen found (75.3%) followed by Proteus spp (12.4%), Enterococcus spp (8.6%) and Klebsiella spp (4%). In patients <6 months-old, E. coli (66%) and Enterococcus (16%) were the microorganisms most frequently isolated.E. coli susceptibility rates to co-amoxiclav and gentamicin decreased (from 95% to 87% and from 99% to 87%, respectively) during the study period; susceptibility patterns for other antibiotics and pathogens remained stable.

Conclusions

Escherichia coli is the most common causative organism for UTI in children in our region. There have been no significant changes in the etiology of UTI throughout these last 10 years. The decrease of E Coli susceptibility to co-amoxiclav and gentamicine should be taken in consideration in the selection of empiric antibiotic treatment of UTI.

ESP16-0057
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

IDENTIFYING STARTING POINTS FOR A PAEDIATRIC ANTIMICROBIAL STEWARDSHIP INTERVENTION IN A UK DISTRICT GENERAL HOSPITAL

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Background

Paediatric antimicrobial stewardship (AMS) is now commonly practiced in settings of high usage of broad spectrum antibiotics (Intensive Care Units, Oncology). Less data is available on the bulk of antimicrobial prescribing that occurs in secondary care. This study investigates prescribing patterns and attitudes of paediatricians in a large District General Hospital in order to identify starting points for an effective AMS intervention.

Methods

A covert point prevalence survey of antibiotic prescribing was conducted on sixteen time points over a two month period in a general paediatric inpatient ward. Concurrently, attitudes towards antimicrobial resistance and prescribing were evaluated through an anonymous survey of the same prescribers.

Results

88 prescribing episodes were captured, representing a proportion of 35% of patients. 46 prescriptions were captured within the first 72 hours; with 76% guideline compliance. At 72 hours antibiotics were continued in 16 (76%) patients with negative cultures. In 21 patients with positive cultures, antibiotics were adjusted in 8 patients (38%). Intravenous to oral switch at 72 hours would have been appropriate for 32 (76%) prescriptions, but was done in only 17 (40%). Prescribers demonstrated a good understanding of antimicrobial resistance and knowledge of stewardship.

Conclusions

Adherence to guidelines on empirical antibiotic prescribing was high in this unit, but clinicians were reluctant to adjust their prescribing (stop/change/switch to oral) when culture results became available. This stands in contrast to an existing awareness of antimicrobial resistance and potential interventions to improve prescribing. Revising guidelines, establishing a review point at 48-72 hours, and specific education were identified as intervention points for this unit. This study shows there is a scope in secondary care to reduce antibiotic misuse and antimicrobial resistance.

ESP16-0111
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

A FRAMEWORK TO ASSESS THE RISK OF ANTIMICROBIAL RESISTANCE DEVELOPMENT FROM USE OF PERSONAL CARE PRODUCTS INCLUDING HAND SOAPS

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Background

Every year, 2 million children under the age of five die from infections linked to diarrhoeal and respiratory diseases. Many of these deaths could be prevented by effective handwashing. Consumer studies have shown that many people spend <30 seconds washing their hands and clinical trials have shown that combinations of antimicrobial actives in soap can have greater efficacy over this short time period than washing with plain soap. There is a need to develop frameworks to assess potential risks regarding development of bacterial resistance to antimicrobial actives and the potential for cross-resistance to antibiotics.

Methods

A tiered risk assessment framework has been developed to assess the risk of antimicrobial resistance (AMR) development (at point-of-use) to formulations or actives of interest in personal/home care products and the potential for cross-resistance to clinically relevant treatment options, such as antibiotics. Tier 0 of the framework utilises existing data from the literature or internal studies, whilst Tier 1 is an experimental protocol, created to assess any changes in susceptibility (including cross-resistance) following realistic exposures to formulations or actives of interest. If Tier 1 shows potential for resistance development, the mechanisms of resistance could be investigated further (Tier 2).

Results

Validation of the framework has been conducted with several commercial products, but results presented here will focus on two hand hygiene products. One was deemed to be a low/acceptable risk using Tier 0, whilst the other was taken onto Tier 1 where no significant changes in susceptibility (or cross-resistance) were observed following realistic exposures, including repeat exposures.

Conclusions

The AMR risk assessment framework gives an approach/methodology which ensures that personal/home care products containing antimicrobial actives are safe by design with regard to resistance and cross resistance risks.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0552
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

IMPACT OF AN ANTIMICROBIAL STEWARDSHIP SERVICE IN A LARGE UK PAEDIATRIC HOSPITAL

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Background

Increasing antimicrobial resistance is linked with intense use of antimicrobials. This has led to the development of antimicrobial stewardship (AMS) services aimed at the rational use of these antimicrobials. In February 2015, Alder Hey Children's Hospital initiated AMS rounds where all inpatients receiving intravenous antimicrobials (IVAB) are reviewed and assessed using the "antibiotic question": can the patient be changed to a narrow spectrum antibiotic, oral antibiotics, stopped, discharged via outpatient parenteral antimicrobial service (OPAT) or continued on the current regime with daily review?

Methods

Prospective audit of the AMS rounds which are conducted three times a week on general and specialist medicine and surgery wards. Evaluations of patients on IVAB are followed by written recommendation in the medical notes. Follow-up of recommendations was undertaken at 48 hours. The audit was conducted for a period of one month from 16/09/2015 to 14/10/2015.

Results

A total of 723 inpatients were screened and 161 (22.2%) were on IVAB. Most frequently used IVAB were piperacillin/tazobactam (32, 22%), co-amoxiclav (22, 15%) and cefotaxime (19, 13%). Forty-one patients were already under the care of the infectious disease/microbiology team and were excluded from this audit. In 54 (45%) of the remaining 120 patients on IVAB, the AMS team made a recommendation to alter therapy. This advice was followed in 56% of cases. In patients where the recommendation was not followed, the leading indications were surgical prophylaxis and community acquired pneumonia.

Conclusions

This audit in a large UK paediatric hospital shows the positive impact of regular AMS rounds. It however underscores the ongoing challenges of successful collaborations with medical and surgical teams in improving antimicrobial stewardship decisions for individual patients.

ESP16-0101
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

PREVALENCE OF BACTERIA AND ANTIBIOTIC RESISTANCE FROM CLINICAL SPECIMENS OF HOSPITALIZED CHILDREN IN MOFID HOSPITAL

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Background

Bacterial infections can be an important cause of morbidity and mortality in hospitalized children. The most common etiologic agent that can cause bacterial infection and antibiotic susceptibility patterns may vary in different area of the world. The aim of this study was to assess prevalence of bacteria that cause infection and also antibiotic susceptibility from clinical specimens of hospitalized children by BACTEC system.

Methods

BACTEC 9120 was used for aerobic and anaerobic culture and recovery of bacteria from clinical samples (blood, CSF, shunt, etc.) of hospitalized children in Mofid hospital during September 2014 to December 2015. Samples sub-cultured on Blood and MacConkay agar. Gram staining and bacteriological conventional methods were used for identification. Antibiotic susceptibility testing was done by disk diffusion according to CLSI guideline.

Results

A total of 600 clinical specimens were tested. 225 (37.5%) Out of 600 cultured specimens were positive. 106 (47%) of bacteria were gram positive and 119 (52.8%) gram negative. The most common gram positive bacteria were *Coagulase-negative staphylococci* (50%) and followed by *Staphylococcus aureus* (28.3%). The most common gram negative bacteria were *Pseudomonas spp* (49.5%) and *E. coli* (16.8%). 94.3% of *Coagulase-negative staphylococci* and 80% of *Staphylococcus aureus* were multi-drug resistance (MDR). 93.2% of *Pseudomonas spp* and 100% of *E. coli* were MDR.

Conclusions

Bacterial infections can have important role in mortality and morbidity in hospitalized patients especially in children. Appearance of MDR *S. aereus* and *P. Spp.* strains are the very considerable alarming in our research center. The results of this study can use for preparation of antibiotic stewardship in our teaching hospital. So, we can inhibit spread of MDR bacteria in hospital settings.

ESP16-0483
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

PAEDIATRIC ANTIMICROBIAL STEWARDSHIP IN INTENSIVE CARE UNIT: EXPERIENCE IN A TERTIARY CHILDREN'S HOSPITAL

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Background

Paediatric patients are often treated with an antimicrobial therapy during the course of hospitalization, especially patients admitted in intensive care unit. Unfortunately, a substantial proportion of antimicrobial prescribing is inappropriate, including errors in antimicrobial selection, dose, and duration. Antimicrobial stewardship programs (ASPs) are one of the core strategies used to address the problems of antibiotic overuse, resistance and cost management.

Methods

In march 2015 we started an ASP in our Hospital involving three intensive care areas: 2 Intensive Care Unit (PICU), 1 Neonatal Intensive Care Unit (NICU), 1 Cardiological Intensive Care Unit (CICU). We chose an open ASP with weekly meeting on clinical cases selected by the intensive care physicians. Focus was on appropriate diagnostic tools, empirical treatment, de-escalation therapy, duration, toxicity and outcome.

Results

The AS team confirmed the empiric treatment in 37% of consultations, it opted for de-escalation therapy in 39% of cases and modify treatment in 24% of consultations due to inadequate dose/molecule or toxicity. We compared the number of extended spectrum beta lactamase (ESBL) isolates in March-November 2014, with the same period in 2015 in the three ICUs. Results in Fig 1 show the reduction in ESBL in CICU, the ICU with the highest number of consultations, compared with the increase in the other ICUs.

Conclusions

An interactive discussion on infectious clinical cases chosen by the intensive care physicians could be a correct strategy to start ASP. However a daily consult is needed to obtain best results. Despite the limited duration of the study, our paediatric ASP seems to be a promising tool to reduce antimicrobial utilization, costs and circulation of resistant germs with no evidence of adverse effects.

ESP16-0204
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

AN AUDIT OF ANTIBIOTIC RESISTANCE IN ESCHERICHIA COLI PAEDIATRIC SPECIMENS

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Background

Antibiotic resistance is an increasing problem in *Escherichia coli* infections worldwide. Extended spectrum beta-lactamase (ESBL) *E. coli* are resistant to most penicillins and cephalosporins, and often many other classes of antibiotic, and are increasingly prevalent in Western Europe. Understanding patterns of resistance is important for development of local antimicrobial guidelines and can be used to help inform antimicrobial stewardship initiatives.

Methods

We undertook a retrospective audit of all *E. coli* cultures processed at the John Radcliffe Hospital microbiology laboratory, Oxford, between September 2013 and May 2014. A total of 14,093 samples were positive for *E. coli*, of which 1,218 were from children aged <16 years. Of these, 300 (25%) were from hospital settings and 918 (75%) were from the community. The majority of specimens were urine cultures (1,129; 93%).

Results

Amoxicillin resistance was reported in 52% and co-amoxiclav resistance in 31%. In urine samples, co-amoxiclav resistance was more common in hospital compared with community settings (39% vs 29%, p=0.003), and in children <2 years compared with children ≥2 years (39% vs 30%; p=0.032). The prevalence of ESBL was 5% of all paediatric isolates. ESBL were more common in hospital compared with the community (7% vs 4%, p=0.0170). ESBL prevalence in hospital urine cultures was 6% in paediatric specimens and 9% in adults.

Conclusions

We have demonstrated high rates of amoxicillin and co-amoxiclav resistance in *E. coli*, in line with national rates. Our data suggest that broader spectrum antibiotics may be more appropriate empirical treatment for serious infections suspected to be due to *E. coli*, particularly in hospital settings and for children aged <2 years. Of concern, ESBL prevalence has increased markedly from previously published adult data from the same laboratory in 2010 (1.5%).

ESP16-0863
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

PARADOXICAL POTENTIATION OF ANTIMICROBIAL PHOTOINACTIVATION BY SODIUM AZIDE USING SEVEN PHENOTHIAZINIUM PHOTOSENSITIZERS

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Background

Phenothiazinium-based photosensitizers have been employed in photoantimicrobial research for nearly 80 years, both as established and novel compounds. We carried out a comparative study of 7 phenothiazinium dyes: Methylene blue (MB; 3,7-bis(dimethylamino)-phenothiazinium chloride), Azure A, Azure B, Azure C, 1,9-Dimethyl-Methylene Blue, New Methylene Blue N- zinc free form, Toluidine Blue O. The relative photobactericidal activity against Gram-positive *Staphylococcus aureus* 8325-4 and Gram-negative *Escherichia coli* K-12 (both wild type) was investigated.

Methods

All 7 dyes possessed significant photoantimicrobial activity and structure-activity relationships were established for both bacterial killing and binding to Gram-positive and Gram-negative bacterial cells.

Results

Sodium azide is routinely employed as a physical quencher of singlet oxygen, but we found that azide anion did not inhibit the photoantimicrobial killing and protect the bacteria as expected, but rather potentiated the bacterial killing. The explanation for this surprising observation appears to be a direct oxidation of azide anion to azide radical by photoexcited phenothiazinium salts. Azide radicals presumably have an additional bactericidal effect. We showed that MB was able to mediate photodynamic inactivation in the absence of oxygen, but only if azide was present,

Conclusions

The role of azide radicals in the bacterial killing was confirmed by electron spin resonance spectroscopy using 5,5'-dimethyl-1-pyrroline-N-oxide (DMPO) spin trap in both the presence and the absence of oxygen.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0280
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

RISK FACTORS ASSOCIATED WITH ISOLATION OF GENTAMICIN RESISTANT E. COLI IN URINARY TRACT INFECTIONS IN CHILDREN

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Background

Gentamicin is frequently used as empiric IV antibiotic for urinary tract infections (UTIs). We describe clinical characteristics of children presenting with UTIs caused by gentamicin-resistant *E. Coli*.

Methods

Descriptive, retrospective study including children presenting with UTIs caused by gentamicin-resistant *E. coli* in a tertiary care hospital in Spain, during 2014. Urine cultures collected by *catheterization,* clean-catch, or ≥two collection bags and leukocyturia were included.

Results

Out of 258 episodes, 201 (78%) were caused by *E.coli*; 15% gentamicin-resistant. Twenty-five UTIs in 21 patients were included. Median age was 12.4mo [IQR 3.6-23.4]. Fifteen samples (60%) were obtained by clean-catch, 9 by *catheterization,* and one by isolation in two collection bags. 52% of patients required hospitalization.

A 61% of children (13/21) had at least one risk factor for resistance: 8 (38%) had *nephropathy* (5 were on *antibiotic prophylaxis* and 3 had been hospitalized during the previous 6 months), 3 suffered from chronic conditions (2 of them had been recently hospitalized), 1 had previous UTIs. A 57% (12/21) and 28% (6/21) of children showed ≥2 and 3 risk factors simultaneously.

A 44% of isolates were resistant to amoxicillin-clavulanate, 43% cefuroxime, 36% cefotaxime, 32% quinolones. 8% (2/25) and 28% (7/25) were carbapenemase and ESBL-producing bacteria. 90% were sensitive to amikacin.

Empiric treatment consisted of cefixime in 6 cases (27%), 5 (22%) cefotaxime, 4 (18%) gentamicin and 7 (31%) other. Antibiogrami adjusted treatment was required in 6 patients (27%). Median treatment duration was 10 days [IQR 7-10], with two cases of recurrency (9,5%).**Conclusions**

In our study, isolation of gentamicin-resistant *E. coli* was generally associated to history of hospitalization, antibiotic prophylaxis, nephropathy or other chronic conditions. Simultaneous resistance to cephalosporins and ESBL was frequent.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0939
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

PAEDIATRIC ANTIMICROBIAL STEWARDSHIP (PASP), METHODOLOGY AND CHALLENGES: EXPERIENCE FROM A TERTIARY UNIVERSITY HOSPITAL IN LONDON, UK

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Background

We describe the outcome of PASP in a Tertiary Hospital and draw comparisons with point prevalence surveys (PPS) conducted in 2011 and 2012. Our aim is to describe results and highlight methodological challenges.

Methods

A weekly PASP conducted between 7/10/2015 – 8/01/2016 in a tertiary unit (including 10 PICU) at St George's University Hospital. A standardized questionnaire was used to collect anonymous data including antibiotics, dose and frequency, reason for treatment and advise given. We compared results with a point prevalence survey (PPS) conducted in 2011/12.

Results

517 antimicrobial prescriptions (7% antifungal, 3% antiviral, 90% antibiotics) were recorded in 306 children with a median age of 4 years (IQR 1.1, 9) and with underlying conditions in 54%. Commonest indications were medical/surgical prophylaxis (20%), febrile neutropenia (16%) and surgical treatment (9%). The commonest antibiotics prescribed were Co-amoxiclav (14%), Ceftriaxone (9%) and Piptazobactam (8%). Advice to stop was given in 21% of prescriptions. Co-amoxiclav and Ceftriaxone use was similar to the 2011/12 PPS results, (16% and 6% respectively) and meropenem use was 3% compared to 1% in 2011/12.

Conclusions

No significant differences were observed in antimicrobial prescribing overtime in our Unit. Second and third line antibiotics were mainly prescribed in children with underlying conditions, of which the proportions admitted remained stable. One fifth of antimicrobial prescriptions were avoidable. PASP data collection should include the number of children with underlying conditions in view of the implications on antimicrobial prescribing and interpretation of local data.

ESP16-0896
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

ANTIMICROBIAL STEWARDSHIP PROGRAM (ASP) IN A NEONATAL INTENSIVE CARE UNIT (NICU)

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Background

Antimicrobial stewardship program (ASP) efforts are aimed to achieve clinical cure, limit toxicity and adverse events, decrease health-care –associated infections and cost, and reduce the development of resistant organisms. We aim to describe results of ASP on NICU of a UK teaching hospital.

Methods

Twice weekly ASP for one month from 15th of December in NICU (20 Incubators) from St George's Hospital, London. Data collection through a standardized questionnaire included: type, dose, route of the antimicrobials, and the advice given. The antibiotic stewardship includes a paediatric ID middle grade and consultant.

Results

Overall 144 prescriptions were recorded for 77 patients with 62% receiving ventilation support. Of the 144 prescriptions 106 (73.6%) were antibacterial, 37(26%) antifungal, all for medical prophylaxis, and 1(0.4%) antiviral. The median age was 12 days (IQR 2.27) with 25% <=27 weeks of gestation at birth. The commonest antibiotics used were Gentamicin (22.2%), Benzylpenicillin (17%) and Flucloxacilin (9%). Meropenem use was 2%, for late onset sepsis and Catheter related infection. The commonest reasons for prescribing the antibiotic were early onset sepsis (32%), prophylaxis for medical or maternal reasons (30.5%), and late onset sepsis (21%). Advise to stop the antimicrobial prescription was recorded in 8%**.** All but 2 children received Benzylpenicillin and Gentamicin as per NICE guidance for EOS.

Conclusions

Overall good antimicrobial prescribing observed in neonates in intensive care at St. George's University Hospital. Three antimicrobial agents account for the majority of treatment prescriptions. The neonatal ASP shows that Meropenem is still rarely used and prescribing for EOS is adhering to the NICE guidance. A third of all prescriptions were due to medical/surgical/ maternal prophylaxis, mainly antifungal prophylaxis due to either prematurity or surgical conditions.

ESP16-0345
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

NEONATAL SEPSIS: EPIDEMIOLOGY, CLINICAL SPECTRUM, RECENT ANTIMICROBIAL AGENTS AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERN

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Background

Neonatal sepsis is one of the major causes of morbidity and mortality in the newborns. This prospective study aimed to determine the incidence, the bacteriological profile of neonatal septicemia and their antibacterial susceptibility pattern in the tertiary care neonatal center.

Methods

Neonates admitted from January 2015 to December 2015 with clinical features of sepsis were thoroughly investigated for any evidence of bacterial sepsis. Blood culture specimens were collected; identification of organisms and their antibiotic susceptibility pattern detection was done. Data were analysed by student *t*-test and ANOVA test.

Results

Incidence of neonatal septicemia was 10.6%. Prematurity (58.15%), low birth weight (60.94%) and prolonged rupture of membranes (38.3%) were major predisposing factors for neonatal sepsis. Gram negative organisms were more common (71.4%) than gram positive ones (28.6%). *Klebseilla pneumoniae* was the commonest pathogens (54.2%) recovered; mostly presented with early onset sepsis. Amongst the gram positive organisms, *Enterococci* (17.6%) and coagulase negative *Staphylococcus* (CONS) (9.1%) were recovered commonly. Blood culture was positive in 49.2% of septicemic neonates. In cephalosporins, cefoperazone and cefotaxim both have activity against *Klebseilla* and CONS, while ceftazidime showed better results against *Klebseilla*, *E.coli*, *Pseudomonas* and unidentified gram negative bacilli. In aminoglycosides, amikacin has much better results than gentamicin ($p<0.01$). Piperacillin had better advantage over ampicillin ($p<0.01$). All organisms except *E.coli* showed sensitivity to cefotaxime, while only one organism (*S.faecalis*) is sensitive to ceftriaxone. Vancomycin had good activity against gram positive organisms (Enterococcus, CONS and MRSA). Neonatal mortality rate was 21.4%.

Conclusions

This study showed gram negative organisms as commonest cause of sepsis and their alarming antibacterial sensitivity pattern that routinely used antibiotics like ampicillin and ceftriaxone showed poor activity against most of the organisms.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-1066
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

NEONATAL SEPSIS – THE REAL BURDEN IN A PORTUGUESE CENTRE

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Background

In spite of improvements, neonatal sepsis in Neonatal Intensive Care Units (NICU) remains an important pathology, associated with significant morbi-mortality and costs. The main goals of our survey were to characterize the epidemiology of bacterial neonatal sepsis in Hospital de Braga NICU and to describe antibiotics used and its resistance. Hemocultures contamination's rate was also studied.

Methods

Retrospective survey of newborns admitted to NICU between January 2009 and December 2014 diagnosed with bacterial neonatal sepsis, meeting clinical diagnostic criteria (NEO-KISS) and positive hemoculture, through revision of medical records. Positive hemocultures in patients without clinical diagnostic criteria were considered contaminations and separately studied. Data were analyzed using Statistical Package for Social Sciences (SPSS®).

Results

Our survey included 209 positive hemocultures: 51,2%(107/209) were contaminations and 48,8%(102/209) corresponded to episodes of sepsis (87newborns). Of these, 9,8%(10/102) were early-onset sepsis and 90,2%(92/102) were late-onset sepsis. *Streptococcus agalactiae* was found in 30%(3/10) of early-onset sepsis, followed by *Escherichia coli* in 20%(2/10). Coagulase-negative *Staphylococcus* were identified in66,3%(61/92) of late-onset sepsis, being *Staphylococcus epidermidis* the most frequent (50%(46/92)). Ampicillin plus gentamicin were used in all cases of early-onset sepsis, being vancomycin plus cefotaxime the most common antibiotic regimen used in late-onset sepsis (32,6%(30/92)). In late-onset sepsis, microorganisms susceptibility was identified in 89/92(96,7%) and revealed susceptibility to gentamicin in 26,9%(24/89) while 9%(8/89) were susceptible to cefotaxime.

Conclusions

In our survey we had a high rate of late-onset sepsis. It's important to implement measures of infection prevention and control and their regular auditing, in an effort to decrease infection rates, once the occurrence of late-onset sepsis is related to NICU's care quality. Also, late-onset sepsis antibiotic schemes were revised and measures adopted in order to decrease hemoculture's contamination rates.

ESP16-1010
22. S - ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP

PERFORATED APPENDICITIS IN PEDIATRIC PATIENTS: ETIOLOGY AND SUSCEPTIBILITY OF PATHOGENS

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Background

Optimal selection of antimicrobial agents for complicated intrabdominal infections such as perforated appendicitis depends on local epidemiology. We aimed to evaluate pathogens identified and susceptibility patterns in children with appendicitis.

Methods

Microbiological results of tissue samples obtained at surgery from children with acute appendicitis during 18 months were evaluated retrospectively

Results

A total of 45 children operated for perforated appendicitis were included. 29 (64%) patients were male and mean age was 135 (18-218) months. The pathogens identified were *Escherichia coli* (73%), *Pseudomonas aeruginosa*. (20%), and *Candida* spp (2.2%). 60% of *E. coli* and 22% of *P. aeruginosa* were producing extended spectrum b-lactamase (ESBL).

Conclusions

High rate of ESBL-positive *E. coli* may indicate bowel colonization with resistant bacteria even in the community setting. Routine cultures from patients with intraabdominal infection may facilitate recognition of local changes in resistance as well as decisions on empiric therapy.

ESP16-0351
23. S - PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIMICROBIALS

THE CURRENT STATUS OF PAEDIATRIC ANTIMICROBIAL PHARMACOKINETIC RESEARCH

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Background and Objective

Improved pharmacokinetic data are urgently needed to optimize drug dosing in children, as off-label and unlicensed prescribing remains widespread. Antimicrobials are the most commonly used medicines in paediatrics and thus deserve prioritisation. Using registered records of clinical trials, this review aims to summarise the current paediatric antimicrobial pharmacokinetic research.

Methods

Registered clinical trials open to recruitment on 12th January 2016 were identified using a ClinicalTrials.gov advanced search. Search results were filtered to identify clinical trials of antimicrobials used in neonates and children up to 17 years-old. Each study record was then assessed for evidence of pharmacokinetic data collection.

Learning Points Discussion

Of 77 eligible studies, 40 were collecting pharmacokinetic data as a primary or secondary outcome (21% and 31%, respectively), and 37 (48%) were of pharmacokinetic design. 29% were recruiting in Europe, with the majority (48%) recruiting in North America. A higher proportion of studies recruited adolescents over neonates and infants (77% versus 30% and 60%, respectively). Just 2 studies specifically targeted preterm neonates. Antibiotics were the most common antimicrobial agent involved (53%). Antivirals and antifungals were less commonly studied (23% and 9%, respectively). Most studies focused on infectious diseases (62%), 2 of which exclusively recruited patients with sepsis. Cancer and metabolic diseases were the next most common underlying condition (both 8%). Table 1 shows the distribution of results in further detail.

This review highlights the power of the ClinicalTrials.gov registry to map the landscape of open paediatric antimicrobial research studies. There is a need for collection of pharmacokinetic (and pharmacodynamic) data in a larger proportion of paediatric studies to address the distinct gaps in knowledge about drug disposition in children, particularly in neonates and critically ill patients.

TABLE 1	Antimicrobial studied			
	Antibiotic	Antiviral/ Anti-retroviral	Antifungal	Anti-parasitic
Number of studies				
Age group(s) included				
Preterm neonates	1		1	
Term neonates	11	6	2	2
Infants and toddlers	25	12	3	6
Children	25	13	5	7
Adolescents	32	12	6	9
Underlying condition (ICD-10 classified)				
I Infectious and parasitic diseases	18	16	4	10
II Neoplasms	5			1
III Blood and immune disorders			2	
IV Endocrine, nutritional and metabolic disease	6			
V Mental/behavioural disorders				
VI Disease of nervous system	1	2		
VII Disease of eye and adnexa				
VIII Disease of ear and mastoid process	1			
IV Disease of circulatory system				
X Disease of respiratory system				
XI Disease of digestive system				
XII Disease of skin/ subcutaneous tissue				
XIII Disease of musculoskeletal system	1			
XIV Disease of genitourinary system	4			
XV Pregnancy, childbirth and puerperium				
XVI Conditions originating in perinatal period				
XVII Congenital or chromosomal abnormalities				
XVIII Symptoms, signs and abnormal clinical findings	4		1	
XIV Injury, poisoning and other external causes				
XX External causes of morbidity and mortality				
XXI Health status factors/ contact with health services	1			

ESP16-0760
23. S - PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIMICROBIALS

OPTIMISATION OF VANCOMYCIN DOSING REGIMEN IN NEWBORNS BY PERFORMING A POPULATION PHARMACOKINETIC ANALYSIS OF PROSPECTIVELY COLLECTED DATA

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Background

Vancomycin is a commonly used first line antimicrobial to treat hospital acquired infections in neonates. Although both intermittent and continuous dosing regimens are used, there is limited data on population pharmacokinetics (Pop PK) for continuous vancomycin usage to inform correct dosing.
AIM: To determine the PopPK parameters of vancomycin in neonatal patients with a wide range of gestational ages (GA) and birth weights receiving different dosing regimens.

Methods

Data were collected prospectively from 56 newborns who were receiving vancomycin for late onset sepsis (32 on continuous infusion and 24 on intermittent doses) after obtaining approval from Barts Health Clinical Effectiveness Unit. Peak and trough vancomycin concentrations were collected from infants on intermittent dosage, and random levels for continuous infusion. An enzymatic assay on the COBAS 702 platform was used to measure vancomycin (linear range of 1.7-80 µg/ml). PopPK analysis was performed using nonlinear mixed-effects modelling (NONMEM 7.3).

Results

183 vancomycin samples (n=81 from the intermittent, and n=102 from the continuous group) were analysed. The median (range) postnatal age at baseline was 26 (1-156) days; and GA 29 (23.7-41.9) weeks. The final model was a 1-compartment model. Allometric weight scaling and postmenstrual age (PMA) driven sigmoidal maturation function were included *a priori* and no further covariate provided a significant improvement in the model fit. For a typical infant from the studied population (weight=1.7kg, PMA=35.7 weeks), clearance was 0.10 L/h, and volume of distribution was 0.78 L.

Conclusions

A PopPK model was developed for both intermittent and continuous vancomycin dosage in newborns and was shown to have good descriptive and predictive properties. This model will be used to develop a new dosing scheme which will then be prospectively evaluated.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0193
23. S - PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIMICROBIALS

PHARMACOKINETICS AND SAFETY OF INTRAVENOUS SOLITHROMYCIN IN CHILDREN ≥6 YEARS OF AGE

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Background

Solithromycin is a new fluoroketolide antibiotic in clinical development for use in adults and children. We performed a phase 1 pharmacokinetics (PK) and safety study in children ≥6 years of age.

Methods

We enrolled children and adolescents with suspected or confirmed bacterial infections and administered intravenous solithromycin as add-on therapy: 6–11 years, 7 mg/kg daily; 12–17 years, 6 mg/kg daily (up to 400 mg) for up to 5 days. We collected PK samples at end of infusion, 2–4, 8–10, and 23–24 hours after the first and multi-dose administration. We performed a noncompartmental analysis and compared exposure to adult values.

Results

Eight children (median [range] 7 years [6–10]; weight 26 kg [11–36]) and 10 adolescents (age 14.5 years [12–17]; weight 53 kg [29–69]) completed the study. The median (range) daily dose was 183 mg (79–253) and 306 mg (172–400) in children and adolescents, respectively. Solithromycin exposure on Day 1 and Days 3–5 are shown in Table 1. The most common drug-related adverse events were infusion site pain/reaction (4), mild diarrhea (3), and headache (1). All children received concomitant medications.

Day	Parameter	6–<12 years (n=8)*	12–<17 years (n=10)*	Adult Value (n=10)*,†
1	C_{MAX} (µg/mL)	1.9 (0.8–4.7)	1.8 (1.2–8.4)	2.2 (1.6–3.0)
1	AUC_{0-24} (µg*h/mL)	8.3 (3.8–22.1)	7.8 (3.8–30.4)	5.3 (3.9–7.0)
3/4/5	C_{MAX} (µg/mL)	2.8 (1.0–8.1)	2.3 (1.2–7.7)	2.7 (2.2–3.5)
3/4/5	AUC_{0-24} (µg*h/mL)	10.6 (2.7–18.4)	12.3 (8.2–19.9)	12.1 (5.8–18.8)

*Not all participants contributed data because of samples observed below the quantification limit or partial data.

†Adult data taken from phase 1 studies (400 mg).

Conclusions

Solithromycin exposure and safety in a small cohort of children and adolescents was comparable to that reported in adults.

Clinical Trial Registration (Please input N/A if not registered)

NCT02268279

ESP16-0997
24. CHEMOPROPHYLAXIS

OUTBREAK OF ARTHRITIS CAUSED BY KINGELLA KINGAE IN A SPANISH CHILDCARE CENTER

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Background

Recently, *Kingella kingae* is increasingly recognized as an invasive pathogen of early childhood. It has currently been described as the most common agent of skeletal system infections in children 6 months-2 years of age. We describe the investigation of an outbreak of three cases of arthritis caused by *K. kingae*,one presumed case and the othertwo confirmed, detected within a 30-day period in a daycare center in Roses, Spain.

Methods

Surveillance throat swabs obtained from all attendees from the same class of the index daycare center assessed the prevalence of *K. kingae* colonization. The sample was composed of 9 toddlers (range: 16-23 months of age), which included the three index cases. Investigation was performed by culture and *K. kingae*-specific RT-PCR. Combined amoxicillin-rifampicin prophylaxis was offered to all attendees who were colonized by *K. kingae*. Following antimicrobial prophylaxis, a new throat swab was taken to confirm bacterial eradication.

Results

The two confirmed case patients were positive for *K. kingae*-specific RT-PCR in joint fluid and they had a complete recovery with antibiotic therapy. *K. kingae* was detected by RT-PCR throat swabs in the three index cases and five of the six daycare attendees. Cultures were negative in all cases. After administration of prophylactic antibiotics, three toddlers were still positive for *K. kingae*-specific RT-PCR.

Conclusions

A cluster of invasive *K. kingae* infections can occur in daycare facilities and closed communities. Increased awareness of this public health problem and use of sensitive detection methods are needed to identify and adequately investigate outbreaks of *K. kingae* disease. In our experience, the administration of prophylactic antibiotics could result in partial eradication of *K. kingae* colonization. No further cases of disease were detected after prophylaxis.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0086
25. S - INFECTION RELATED NUTRITION

LEAD OVERLOAD IN DRINKING WATER AND FEEDING INFANTS

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Background

Background; Lead enters drinking water by leaching from pipes and solder joints in household plumbing. Human activities can substantially increase lead release and dissemination into the environment. The presence of lead in water usually indicates contamination from metallurgical wastes or from lead–producing industries.

Methods

Material & Methods; This study was done on ninety drinking tap water samples (surface and groundwater) collected from different districts of Dakahlia governorate and ninety blood samples taken from infants who attended in some of Dakahlia governorate hospitals. All these samples were subjected for lead analysis by graphite furnace atomic absorption spectrophotometer.

Results

Results; **Mean lead level in drinking groundwater showed higher level than in drinking surface water. An elevation of blood lead level of bottle feeders using groundwater was noticed higher compared with that of their counterparts using surface water. Also, an elevation of blood lead level of breast feeders where mothers drink groundwater was noticed higher when compared with that of their counterparts born to mothers drinking surface water. There was a positive relationship between blood lead levels and drinking water (either surface or ground) lead levels**

Conclusions

Conclusions**; we concluded that bottle feeding was a strong predictor of elevated blood lead levels among infants**

Systematic Review Registration (Please input N/A if not registered)

N/A

ESP16-0107
25. S - INFECTION RELATED NUTRITION

DO ALL MALNOURISHED CHILDREN ARE AT RISK FOR SHIGELLOSIS? OBSERVATION FROM URBAN DIARRHOEAL DISEASE SURVEILLANCE IN BANGLADESH

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Background

Compromised immunity remains in the underlying causal pathway for shigellosis among under-5 malnourished children. To ascertain the factors that predict shigellosis among malnourished under-5 children in urban Bangladesh.

Methods

Design: Disease Surveillance.The study was conducted in the urban Dhaka Hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh, where every 50th patients were enrolled. A total of 12,389 under-5 children between 2004 and 2013 were studied. Of them, 5,580 were malnourished [either height-for-age z-scores (HAZ) or weight-for-height z-scores (WHZ) or weight-for-age z-scores (WAZ) <-2 SD]; and rest were well-nourished (HAZ and WHZ and WAZ ≥-2 SD).

Results

Four percent (n=215) and 3% (n=216) malnourished and well-nourished children respectively had shigellosis. In Poisson regression model, malnourished children aged 12-23 months [RR: 1.80 (95% CI: 1.31-2.47)] and 24-59 months [2.01 (1.43-2.82)], slum dwelling [1.63 (1.12-2.39)], maternal [1.39 (1.01-1.93)] and father's education [0.69 (0.49-0.96)] were significantly associated with shigellosis compared to those malnourished non-shigellosis children adjusted for time. The interaction between these predictors showed positive association between shigellosis and child's age, maternal and father's education among slum dwelling malnourished children. Positive association was also found between shigellosis and child's age in malnourished children of illiterate mothers, but negative association was observed between shigellosis and malnourished children of illiterate fathers.

Conclusions

Being malnourished all children are not at risk for shigellosis rather other factors such as child's age of 12 months and more, slum dwelling and lack of parental education were the other potential predictors of shigellosis among malnourished children.

ESP16-0611
25. S - INFECTION RELATED NUTRITION

CRYPTOSPORIDIUM INFECTION AND ITS IMPACT ON CHILDHOOD MORBIDITY AND MORTALITY

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Background

Cryptosporidium is an intracellular protozoan that has long been recognized as a cause of diarrheal disease, particularly among children under 5 years of age. *Cryptosporidium* is the second leading cause for all diarrhea-associated deaths in children under age 5 worldwide, second only to rotavirus. The Global Burden of Disease Study (GBD) estimates the years of life lost and the years lost to disability associated with diarrhea etiologies, including c*ryptosporidium*. There is increasing evidence that childhood diarrhea may have long-term consequences including impaired physical growth and cognitive development, sequelae that are not currently captured in the GBD framework.

Methods

Here, we describe the current GBD results for c*ryptosporidium* and expand our results to assess the burden of symptomatic, subclinical, and asymptomatic infection on childhood non-fatal, long-term outcomes. We performed a systematic review and meta-analysis of the effect of c*ryptosporidium* infection on childhood growth and cognition.

Results

Our results show that *cryptosporidium* infection is associated with physical growth stunting. C*ryptosporidium* infection was associated with a 0.08 decrease of height-for-age z-score. There was no association between cryptosporidium and cognition.

Conclusions

Our findings will improve our estimates of the burden from *cryptosporidium* and call for continued reductions in childhood morbidity and mortality relating to diarrhea.

Systematic Review Registration (Please input N/A if not registered)

N/A

ESP16-0551
26. OTHER

GIANOTTI-CROSTI SYNDROME DUE TO EPSTEIN-BARR VIRUS (EBV) INFECTION
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Title of Case(s)

Gianotti-Crosti syndrome due to Epstein-Barr virus (EBV) infection; a case report in Paediatrics

Background

Gianotti-Crosti Syndrome (GCS); is a viral exanthema of childhood. The exanthema is typically symmetrical erythematous papular or vesiculopapular eruption. GCS is benign in nature, managed with supportive care only. Herein we describe the case of GCS caused by EBV infection in a five-year-old male patient; presented with symmetric red papular rash over elbows and knees, petechial rash over lower limbs, associated with abdominal pain and diarrhoea. Related case reports and articles were reviewed and used to support this case report.

Case Presentation Summary

A 5 years old male, Previously healthy admitted with 2 days history of bloody diarrhoea and 2 weeks history of abdominal pain with itchy rash. no other symptoms.

Physical examination was remarkable apart from symmetrical itchy erythematous maculopapular rash over elbows and ankles.

The provisional diagnosis was Henoch-Schönlein purpura (HSP). other differential diagnoses were considered and ruled out including presence of rectal polyp. Regarding his chronic constipation , it was treated with laxative. While patient was admitted the possibility of GCS was raised. His was clinically improving with supportive case and was discharged home. Investigations done showed; monocytosis. Urine was normal.HBV and CMV titters were negative. EBV's PCR and antibodies was positive (IgM and IgG). Patient was retrospectively diagnosed as GCS (based on clinical presentation and high EBV titters).

Patient was followed up in the outpatient clinic, his rash resolved 5 weeks after the initial presentation, abdominal pain was fluctuating mostly due to his chronic constipation.

Learning Points/Discussion

GCS can be misdiagnosed with long list of other diagnoses and EBV should be considered as the cause of GCS even with atypical presentaion.

ESP16-0069
26. OTHER

DEEP NECK INFLAMMATION AS A PRESENTATION OF KAWASAKI DISEASE

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Title of Case(s)

Deep Neck Inflammation as a Presentation of Kawasaki Disease

Background

Kawasaki disease (KD) is typically a self-limiting condition that is a common cause of pediatric vasculitis (1) and the leading cause of pediatric acquired heart disease (2) .

There is currently no laboratory test for diagnosing KD. Rather, diagnosis is performed with reference to established clinical criteria (5) . Unfortunately, atypical manifestations of KD appear to be on the rise (1) , decreasing the likelihood of timely diagnosis and appropriate treatment. Herein, we report an unusual case of KD: a 5-year-old boy who presented with fever and right side cervical lymphadenitis

Case Presentation

A 5-year-old boy known presented with an 8-days history of fever and neck pain with swelling. P/E revealed highly febrile child with bilateral firm cervical lymphadenopathy with right side anterior cervical lymph node measuring 4x4 cm. The patient was treated as a case of acute bacterial lymphadenitis with no improvment noticed in the next 72 hours. Patient started to have red cracked lips with conjunctivitis after 4 days of antibiotics.

Blood tests revealed WBC of 10,000/mm3 and CRP of 280 mg/L, ESR of 135 mm/hr.

On the fifth day of admission the patient was started on IVIG and high dose aspirin treating atypical Kawasaki disease.

The patient clinical condition significantly improved after the first of IVIG and aspirin

Background

The clinical manifestations of KD can be diverse and the diagnosis is based on demonstrating characteristic clinical signs and excluding other febrile diseases.

Case Presentation Summary

5 years old male presented with acute cervical lymphadenopathy and progressed to have atypical kawasaki diseas with good repsonse to IVIG and high dose aspirin

Learning Points/Discussion

Deep neck inflammation can be the first manfestaion of Kawasaki disease

ESP16-0072
26. OTHER

THYROID ABSCESS: RARE DISEASE IN PEDIATRICS WITH RARE ORGANISM

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Title of Case(s)

Thyroid Abscess: RareThyroid Abscess: Rare Disease in Pediatrics with Rare organism Disease in Pediatrics with Rare organism

Background

•Though thyroid abscess is rare clinical entity, the diagnosis can be made if the examiner has a high index of suspicion. USG of the thyroid can help in the decision making of the treatment. Incision and drainage followed by antibiotics can give complete clearance of the disease, decreasing the morbidity. Because this disease entity is rapidly progressive and often delayed in its presentation, early recognition and intervention are necessary to curtail the morbid potential of the complications of this process.•We believe that this is the first reported case of thyroid abscess in pediatrics due to H.Influenza

Case Presentation Summary

•A 5 years old female presented to the ED with 3 days history of fever and painful neck swelling that was preceded with one month history of cough and rhinorrhea
P/E revealed febrile child with tachycardia. She was having tender, mobile, non fluctuant, circumscribed swelling in the left lobe of the thyroid which moved on deglutition but not on protrusion of the tongue. The mass measured 3 x 3 cm with overlying skin erythema. Multiple small anterior and posterior cervical lymph nodes were felt in the left side. Rest of the examination was unremarkable.
US scan showed left thyroid abscess measuring 2.6 x 2 cm with well defined 2,5 mm wall. Several predominantly left cervical lymph nodes are present.
Provisional diagnosis of Acute Suppurative Thyroiditis with abscess formation was made and the patient was successfully treated with IV antibiotics and Incision and drainage.
Culture from the fluid growed Haemophilus influenza.

Learning Points/Discussion

•Thyroid abscess is rapidly progressive disease. Early recognition and intervention are necessary to prevent complications.

ESP16-0073
26. OTHER

IS A NEGATIVE BLOOD CULTURE ENOUGH TO RULE OUT BACTERIAL MENINGITIS (BM) IN INFANTS 0-90 DAYS OF AGE?

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Background and Objective

•Lumbar Puncture is a crucial part of sepsis work up in infants < 90 days •As pediatritians we face many Diagnostic and theraputic challenges if parents refuse the procedure.
Diagnostic challenges:
– Parental refusa
l–The technical difficulties, e.g dry tap
Therapeutic challenges
–What is the organism–What kind of antibiotics
–Meningitic doses of antibiotics
–Duration of therapy
–Need to repeat LP or not
Hypothesis:
• It has been previously hypothized that the spread of bacterial organism to the CNS in younger age group (< 3 months) is always hematogenic.
Therefore, some experts believed that in the presence of a negative blood culture, CSF studies may not be needed.
Objectives:
Primary: Study the rate of positive blood cultures in BM among infants 90 days and younger
Secondary: Study the relevance of common inflammatory markers (i.e: WBC in CSF and serum, and serum CRP) in BM

Methods

•Retrospective study
Population:– All infants 90 days and younger with positive CSF culture – Positive CSF was deemed as a real growth in the following scenarios:•All gram negative bacteria•Common gram positive bacteria known to cause meningitis such as GBS•Staph growth in patients with VP shunts•Other gram positive with pleocytosis suggestive of meningitis
Locations: Tawam Hospital
Duration: between June 2008 to may 2013

Learning Points Discussion

CSF culture is the gold standard in diagnosing BM
Negative blood culture can not rule out BM
Normal serum WBC, Serum CRP and CSF WBC can not rule out meningitis
High rate of CSF culture contamination in Tawam during the study period

ESP16-0074
26. OTHER

EPIDEMIOLOGY OF BRONCHIOLTIS- EXPERIENCE AT TAWAM HOSPITAL

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Background and Objective

•Bronchiolitis is a common reason for hospital admission. Among all viruses that can cause bronchiolitis,RSV is the leading cause of LRTI in infants worldwide
The aim of the study was to determine the epidemiological and clinical characteristics of infants hospitalized with bronchiolitis in Tawam Hospital.

Methods

•Retrospective study all infants admitted with acute bronchiolitis over a 3-year period (November 2008 - December 2011).

DemographicsNumber (%) unless stated otherwise	
Number of infants	362
Number of admissions	381
Mean (range) time of admission after onset of symptoms	3 days (0-6)
Mean age (range)	5.8 months (0.1-59)
Preterm	41 (14%)

Learning Points Discussion

In our study we found that 362 infants were admitted with bronchiolitis . Fifty two percnet of these cases were shown to have laboratory proven evidence of RSV infection . A Prevoius studies have shown that RSV is the manin causative agent of bronchiolitis , as a study done in Greece in 2002 showed that 636 infants were admitted with bronchiolitis , 61 % had RSV and the rest were attributed to other viruses(1)•As the course and mangament of brcohiolits vary based on the severity of illness, among the cases admitted with bronchiolitis, 42% required oxygen, 87% received bronchiodilators,30% recieived antibioiotcs due to related bacterial infection •In our study complications associated with bronchiolitis include apneas in 4.5%, cardiac complications in 1% and encephalopathy in 1 infant . Regarding PICU admissions due to complications or severe respiratiry distress , 10% of the patintes were admitted to PICU . Comparing this to the previous study the rate of admission to PICU was 6% thought the number of patient s were higher. These measures raise challenges and costs when it comes to management of bronchiolitis and it complications.

ESP16-0268
26. OTHER

DISSEMINATED SALMONELLOSIS AND BCGITIS LYMPHADENITIS IN A PATIENT WITH INTERLEUKIN-12P40 DEFICIENCY

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Title of Case(s)

"DISSEMINATED SALMONELLOSIS AND BCGITIS LYMPHADENITIS IN A PATIENT WITH INTERLEUKIN-12P40 DEFICIENCY"

Background

According to our available data, we believed this is the first reported case in our institute.

Case Presentation Summary

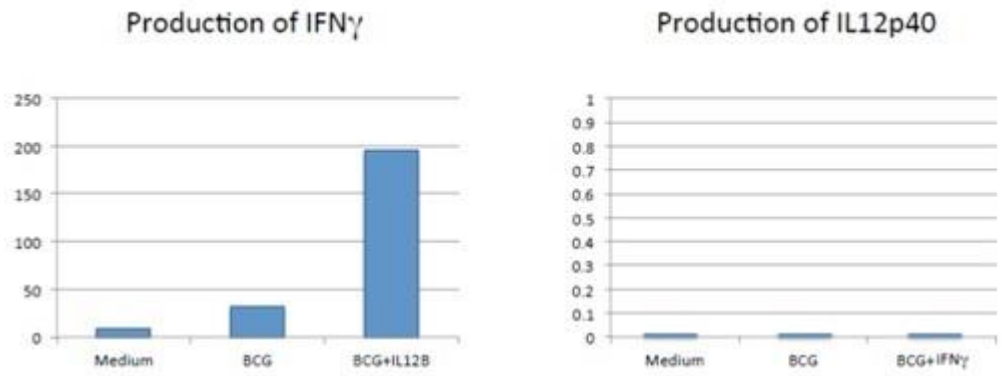
Interleukin (IL)-12p40 deficiency is a very rare genetic etiology of Mendelian Susceptibility to Mycobacterial Disease.
Patients with IL-12p40 are susceptible to infection caused by,Bacille Calmette Guérin vaccines,environmental mycobacteria and Salmonellosis.

In this case report, an 18 month-old boy with absence of IL-12p40 production is suffering from recurrent dissemination with Non–Typhoid Salmonella (NTS), persistent fever, swelling, tender,discharge from left axillary lymph node,oral candida, severe chest infection, recurrent gastroenteritis ,septicemia with generalized lymphadenopathy and hepatosplenomegaly and PPD was negative.The patient is a product of apparently healthy family,parents are not consanguinity,he received all vaccinations,with 5 siblings two of them are twins and one of those twins had a similar problem.

At age of 36 months, the parents discontinued medications soon admitted to ICU and intubated. The culture was positive for group D (NTS), from the left axilla, spleen biopsy and blood. Fine needle aspiration showed no granuloma. NTS sensitive to ampicillin, cefotaxime, ciprofloxacin and cotrimoxazole. Mycobacterium tuberculosis complex, polymerase cell reaction and culture for acid fast bacilli and all serological tests were negative.

Radiologically: bilateral multiple necrotic lymph nodes extending down to the mandibular area,huge anterior mediastinal necrotizing and lower lobe infiltration.

Samples were sent to France, showing absence of IL-12p40 production.Treated according to (NTS) sensitivity and Anti Tuberculosis for one year and there are remarkable improvement with prophylactic.



Laboratory of Human Genetics of Infectious Diseases

Stimulation with a combination of IL-12 plus BCG increased IFN-F levels in the whole blood of IL-12p40-deficient patient.

The whole-blood cells of patients stimulated with live BCG alone or BCG plus exogenous recombinant IFN-F produced no IL-12p40

Learning Points/Discussion

Interferon may have been a useful adjunct to antimicrobial therapy in his case. However the family refused to use gamma interferon since the patient improved in all conventional treatment.The patient currently doing well attending school with regular follow up.

ESP16-0746
26. OTHER

PASTEURELLA MULTOCIDA MENINGITIS IN A NEONATE: NOT MAN'S BEST FRIEND

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Title of Case(s)

***PASTEURELLA MULTOCIDA* MENINGITIS IN A NEONATE: NOT MAN'S BEST FRIEND**

Background

Pasteurella multocida is a well-recognised cause of infection after cat and dog bites. Neonatal infection is very uncommon and is frequently not associated with trauma. We describe a case of *Pasteurella multocida* neonatal meningitis associated with licking by a pet dog.

Case Presentation Summary

A previously healthy 13-days old female neonate was admitted with history of lethargy and decreased feeding for less than 24 hours. A full septic workup was performed and empiric Amoxicillin, Cefotaxime and Gentamycin treatment started. CSF showed Gram negative coco-bacilli. Growth on SBA and Chocolate agars but not MacConkey agar and negative Oxidase test were against *Haemophilus* species. API, Malditof and 16srDNA sequencing identified the organism as *Pasteurella multocida*. A more detailed history revealed that the pet dog had frequently licked the parent's hands and the baby's head. Examination revealed healed scalp electrode wounds on the baby. MRI brain demonstrated leptomeningeal enhancement with bilateral subdural collections. Cefotaxime was continued for a total of 14 days. Hearing and developmental follow-up were normal.

Learning Points/Discussion

Pasteurella infection in neonates may occurs without animal bites and following seemingly innocuous contact with pets. Parents should be advised to keep dogs and cats away from neonates and to practice good hand hygiene.

ESP16-0377
26. OTHER

THE HIDDEN ASPECT OF FEBRILE CONVULSION

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Title of Case(s)

The hidden aspect of febrile convulsion

Background

5 y 6 mo old presented to ER with a generalized tonic and clonic seizure5 y 6 mo old presented to ER with a generalized tonic and clonic seizure

Case Presentation Summary

She had associated fever, diarrhea, vomiting and abdominal pain of 24 hours prior to admission. Seizure lasted for 10 minutes and was followed by post ictal depression for 15 minutes.

Past medical History :

Complex febrile convulsions up to 10 episodes since age 6 months. Normal EEG and brain MRI. Patient controlled by Kepra. Negative family history of epilepsy and normal psycho-motor development. No perinatal or neonatal problems.

Admission lab work up: WBC 21,400 with 86% neutrophils, CRP 181. Electrolytes and blood glucose were normal.She was started on Rocephine and discharged on suprax within 24 hours. Stool culture grew Shigella Sonnei.

Learning Points/Discussion

Shigella gastroenteritis may lead to convulsion in patient controlled on anti-seizure medication

ESP16-0712
26. OTHER

BRAIN ABSCESS MIMICKING BRAIN TUMOR IN A PATIENT WITH CONGENITAL HEART DISEASE

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Title of Case(s)

Brain abscess mimicking brain tumor in a patient with congenital heart disease

Background

Brain abscess continues to be a serious, life threatening neurological infection among children despite advances in diagnosis and management. Congenital heart disease is one of the most common causes of brain abscesses in children. The clinical signs and symptoms of brain abscesses are nonspecific that can interfere with many other disease, such as brain tumors. Herein, we report a patient with brain abscess mimicking brain tumor, he was diagnosed with L-transposition of great arteries and ventriculer septal defect when he was 3 months of age.

Case Presentation Summary

A four year old boy was admitted with complaints of fever, projectile vomitting, seizure and impaired consciousness. He was entubated for respiratory failure and low Glascow coma score. Leucocyte count and C-reactive protein level were high. Computed tomography (CT) of brain revealed a mass, 5x6 cm in diameter, located in right thalamus with a midline shift, suggesting brain tumor. Brain abscess was also suspected because of the history of congenital heart disease, fever and elevated acute phase proteins. Diffusion-weighted MR imaging confirmed the diagnosis of brain abscess. Drainage of the abscess was performed. Abundant leucocytes and gram positive diplococci were observed in gram stain smear, unfortunately no bacteria yielded. He showed gradual improvement, after c*ombined* antibiotic therapy with vancomycin, ceftriaxone and *metronidazole.*

Learning Points/Discussion

The differential diagnosis of brain abscess from brain tumor is extremely difficult. Brain abscess may progress and can be lethal if appropriate treatment is delayed. Physicians must never forget the possibility of brain abscess in a patient with congenital heart disease. Differential diagnosis should be done as soon as possible considering clinical and radiological features for effective and early therapy.

ESP16-0887
26. OTHER

ACUTE LOWER CRANIAL NERVE INFECTIOUS MULTINEVRITIS IN A 10 YEAR-OLD BOY.

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Title of Case(s)

Acute lower cranial nerve infectious multinevritis in a 10 year-old boy.

Background

Combination of dysphagia, dysphonia and dysarthria is due to lower brainstem lesion such as stroke, tumor, degenerative diseases or rhombencephalitis. It can also result from lower cranial nerve involvement, usually when they are together in the jugular foramen and mainly due to ischemia after carotid artery damage.

Case Presentation Summary

A previously healthy 10 year-old boy was seen to the neurological outpatient clinic for sudden onset of dysphonia. The medical history revealed a hyperactivity status treated with Methylphenidate. A right side palatal hypotonia, dysphagia, dysphonia and right tongue weakness was observed. Neurological examination confirmed right side IX, X, XI and XII cranial nerve involvement

No other neurological deficit was noticed. Brain MRI iwas normal. CSF examination was normal, including protein level, absence of white and red blood cell, and normal CSF glucose when compared to blood glucose level. Early electromyography confirmed acute peripheral tongue involvement.

Blood analysis disclosed normal sedimentation rate, normal C-reactive protein level and normal white blood cell count. A titer of 5.321 RU/ml (Normal value< 1.1) of Borrelia Burgdorferi M Immunoglobulin was found and confirmed with Western blood test. IgG were normal

Patient was then IV treated with Ceftriaxone 100 mg a day for 7 days, and then reduced to 50 mg a day for the next 21 days. Neurological examination remained normal after ten days.

Learning Points/Discussion

The originality of this case is the involvement of lower cranial nerves neither in the brainstem nor in the CSF but in their extra-cranial portion when they are together in the foramen jugular. It is an exceptional case of unilateral cranial mutinevritis, here due to Lyme disease.

ESP16-0136
26. OTHER

JOB SATISFACTION OF PEDİATRİC İNFECTİOUS DİSEASE SPECİALİSTS IN TURKEY

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Background

Job satisfaction(JS) is usually defined a collection of feelings or affective responses associated with the job situation. JS is related with labor productivity and performance. Specialists' mental health is likely to be preserved to the high demands of medical practice by enhancing job satisfaction

Methods

This cross-sectional study was conducted on 82 of 62 pediatric infectious disease specialists in March 2015 in Turkey (response rate: %75). A questionnaire including sociodemographic variables and the Minessota Satisfaction Questionnaire short form, a 5-point Likert-type scale of 20 items with a score range 20-100 was used.

Results

The mean age of 62 pediatric infectious disease specialist was 38.9 ± 8.4 years of whom %66.1 was female , %33.9 was male and %83.9 was married . The mean levels of job satisfaction of participants were 71 ±10.3 for general, 44.2 ± 7.2 for intrinsic and 25.8 ± 5.7 for extrinsic job satisfaction. Specialist job satisfaction was moderate .There was a significant difference between age and intrinsic job satisfaction (p:0.03).The lowest intrinsic satisfaction was found in 30-40 age group. In addition to this a significant relationship between hospital level and general job satisfaction was determined (p=0.02). Pediatric infection disease specialists working at university hospital had a higher general job satisfaction. Also extrinsic job satisfaction in university hospital score was higher than state hospital (p=0.048).

Conclusions

This study is a one of the very few study with job satisfaction of specialists and especially leads to investigate the factors of job satisfaction among subdivision of pediatrics. Pediatric disease specialist enjoyed a moderate level of job satisfaction.

Determining factors that increase job satisfaction and making improvements on issues may provide better health services for both of doctors and patients.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0203
26. OTHER

THE ATTİTUDE OF PARENTS TO THE EARACHE OF THEİR CHİLDREN: MULTİCENTER QUESTİONNAİRE STUDY, PEDIOTAL-I

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Background

Acute otitis media(AOM) is characterised by presence of middle ear effusion with otalgia(earpain) that one of the major symptoms.This study aims to share the experience of parents' attitude to earpain of their children

Methods

Multicenter descriptive questionnaire study was conducted on 16 center from different geografic location of Turkey with 1830 parents (father or mother) that had 5-years -old and under-agedchildren between June 2015 and August 2015.The questionaire including sociodemographic variables and the attitudes of parents to ear pain was formed as 20 questions.

Results

The mean age of mothers and fathers were 30,7±5,6years and 34,3 ±6,0years respectively. 50,5% of participants' child/children had earache before and 30,1% had AOM previously. When the question ''what do you do when your child has earache'' was asked,99%of parents stated of taking his/her child to the hospital and/or seeking medication. Also the 82,9% of participants stated of taking his/her child that had earache to the hospital in the first 24 hours. The drug choices of parents for ear pain were 27,9% only paracetamol,16 % only ibuprofen,46,4% paracetamol oribuprofen without preference. The parents' also used variety of herbal and folk remedy such as breast milk,olive oil ,glycerine,herbal product for

earache and percentacages were 16,8 %, 5,4 %, 8,1 % , 3,6 % respectively . 17,3 % of parents might use non-pharmacologic therapies (e.g:onion juice,garlic, applecider vinegar,almond oil,thyme oil)for earache.

Conclusions

This study highlights the ear pain is taken serious by parents and is thought that the ear pain must be treated immediately. The parents have known different systemic analgesic and used them but some of parents have thought that those are not succesfull enough and they have used variety of folk remedy that might be harmful .

ESP16-0606
26. OTHER

SIFD (SIDEROBLASTIC ANAEMIA, IMMUNODEFICIENCY, PERIODIC FEVER, DEVELOPMENTAL DELAY) SYNDROME: A NOVEL PERIODIC FEVER SYNDROME

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Title of Case(s)

SIFD (Sideroblastic anaemia, immunodeficiency, periodic fever and developmental delay) syndrome: a novel periodic fever syndrome

Background

SIFD syndrome is a rare mitochondrial disorder that needs to be considered in infants presenting with congenital sideroblastic anaemia (CSA), B cell immunodeficiency, periodic fever and developmental delay for which the causative gene, TRNT1, has recently been identified. Prognosis without treatment is poor with early onset neurological impairment and death from septic-like episodes. There is limited anecdotal evidence for treatment with anti-cytokine agents and haematopoietic stem cell transplant (HSCT).

Case Presentation Summary

A female infant presented at birth with CSA requiring 3 weekly blood transfusions. From 4 weeks old she presented every 3-4 weeks with febrile episodes lasting 4-5 days, associated with gastrointestinal disturbance (vomiting, diarrhoea, abdominal cramps), raised inflammatory markers (CRP, ESR) and neutrophilia. Extensive microbiology and virology investigations were negative. Immunology investigations showed hypogammaglobulinaemia and CD19 lymphopenia. Cytokine analysis during one episode showed high IL-1β, IL-6 and TNFα. TRNT1 mutation was confirmed. She was treated with IV fluid rehydration, broad spectrum antibiotics, 3 weekly replacement intravenous immunoglobulin and prophylactic penicillin V. Subcutaneous anakinra reduced the frequency and severity of the febrile episodes. Three months following initially successful HSCT she developed Norovirus PCR positive gastroenteritis followed by encephalitis and renal failure leading to her death at the age of 19 months.

Learning Points/Discussion

We would like to share this case to increase awareness of this rare disorder. A key feature of this condition is recurrent sepsis-like episodes in which an uncontrolled cytokine storms may play a key part, for which anti-cytokine therapy may play a role. HSCT may be curative for some aspects of this syndrome but experience of its use in SIFD syndrome is extremely limited.

ESP16-0716
26. OTHER

CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF KAWASAKI DISEASE - A SINGLE CENTER 8 YEARS OF EXPERIENCE

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Title of Case(s)

CASE SERIES

Background

Kawasaki disease (KD) is an acute febrile disorder, characterized by multisystem vasculitis, affecting predominantly medium-sized arteries, particularly the coronary artery, most commonly occurring in children under 5 years of age. Coronary artery aneurysms (CAA) develops in 15%–25% of untreated Kawasaki disease children, and it is the leading cause of acquired heart disease in developed countries.

Case Presentation Summary

24 children with a mean age of 3,12 years and a sex ratio M:F 3.42: 1 were diagnosed to have Kawasaki disease during the study period.Diagnosis was established based on the AHA diagnostic criteria for Kawasaki disease. The ages ranged from 5 months to 13 years; 7 children were less than 1 year, 2 were more than 5 years and 15 were between 1 to 5 years old.All patients were received human immunoglobulin (2g/kg); a single case has disease recrudescence and a second dose of IGIV was administrated, he developed CAA**.** EchographicCAA was found in 4 children. We did not identify recurrence of disease.

Learning Points/Discussion

KD is the second most common vasculitic illness of childhood after Henoch Schönlein purpura, with increasing incidence in the last years. Unfortunately, KD is still undiagnosed or misdiagnosed childhood disease. Although the cause of Kawasaki disease is unknown, recent studies highlight the association between genetic risk factors and infectious agent as triggers of an inflammatory response which leads to host immune dysregulation.

ESP16-0373
26. OTHER

CAN VIRAL ENCEPHALITIS BE A COMPLICATION OF BACTERIAL PNEUMONIA?

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Title of Case(s)

Can viral encephalitis be a complication of bacterial pneumonia?

Background

10 months old girl admitted for management of her bilateral lower lobe pneumonia. She was started on rocephine and Klacid with no clinical improvement

Case Presentation Summary

.

On day 3, she became somnolent and progressed into stage 2 coma. Physical exam revealed hepatomegaly. Laboratory work up : WBC 3150 with 49% neutrophils, 47% lymphocytes ,platelets 231.000, alpha fetoprotein 21.85 (nl < 7), ferritin 5,OOO , SGPT 800, LDH 2,200 and D- Dimers 3.99 . Cerebral CT scan showed encephalitis. LP was negative. CT of chest revealed bilateral basal pneumonia extending to the upper lobes.

Blood culture was negative; CMV IGM negative.,herpes PCR negative Patient was transferred to ICU for nasal CPAP . Antibiotics were switched to vancomycin and acyclovir. Bone marrow biopsy was in favor of a viral infection but did not confirm herpetic inclusions. 24 hours later, patient improved markedly.

Past medical history: 36 weeker with no perinatal or neonatal problems. 2 previous bronchiolitis .

Took Klacid and orelox 3 weeks before admission because of fever 39 with no focus ; since then patient was having one fever peak up to 39 daily till she presented to our pediatric clinic. She was diagnosed to have bilateral acute otitis media and given 3 IM injections of rocephine prior to admission.

Learning Points/Discussion

Progression from pneumonia to encephalitis
Worsening pneumonia on antibiotics
Viral encephalitis as a complication of bacterial pneumonia?

ESP16-0520
26. OTHER

SERUM LEVELS OF Ca2+ AMONG BULGARIAN CYSTIC FIBROSIS PATIENTS WITH LONG LASTING ANTI-INFLAMMATORY TREATMENT

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Background

Background:

Long lasting anti-inflammatory treatment is obligatory for severe cystic fibrosis (CF) patients, especially for those, positive for sputum Ps. Aeruginosa (PA). Cases with bone metabolism abnormality and bone fractures among them are also often seen lately.

Aim:

To assess the serum levels of Ca2+ among severe CF patients according to their body mass index (BMI), sputum flora data, lung function (FEV1) and frequency of antibiotics and corticosteroids uses.

Methods

The serum levels of Ca2+ were measured in 44 CF patients (27 males and 17 females; 12 up to 12 years, 9 between 13 -18 years and 17 adults) and in 43 aged and sex matched healthy controls. The CF data were compared to age, sex, BMI, PA sputum content, frequency of antibiotics and corticosteroids uses and lung function tests (spirometry).

Results

We found significantly decreased levels of serum Ca2+ in CF patients with bone fractures, comparing to those without (p= 0.03). We did not find a significant difference in levels of serum Ca2+ between CF and controls in total (p=0.25) and between age and sex matched subgroups. We found significant differences in serum Ca2+ among young CF (up to 12y) according to their BMI (p=0.012). A significant difference in CF serum Ca2+ levels according to sputum PA and frequency of antibiotic and corticosteroid uses also has not been found .

Conclusions

Conclusion:

Long lasting antibiotics and corticosteroids treatment in severe CF patients does not influence dramatically the levels of serum Ca2+ and is not a reasonable explanation for CF impaired bone metabolism and bone fracture cases.

ESP16-0164
26. OTHER

PARENTAL BELIEFS AND PRACTICE OF SPIRITUAL METHODS FOR THEIR SICK CHILDREN AT A TERTIARY CARE HOSPITAL OF PAKISTAN

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Background

Complementary and alternative medicine (CAM) is “a group of diverse medical & health care systems, practices, and products that are not generally considered to be part of conventional medicine”. We are reporting the parental beliefs and practices for use of spiritual methods in the treatment and early recovery of their children.

Methods

It is cross-sectional, descriptive study with convenience sampling of parents/caregivers of sick children admitted in Children Hospital Multan. A trained interviewer collected data on a pro forma that was analyzed with SPSS-16.

Results

1280 forms were analyzed. The majority of respondents were mothers 1053 (82.4%), belonged to Multan 817 (63.8%) and not educated 754 (58.9%). The respondents belonged to lower-socioeconomic background in 420 (32.8%), to middle class in 601(47%) and to upper class in 259 (20.2%). The grandmothers/mothers advised spiritual method in majority 605(85.9%). The parents used spiritual methods in 704(55%) children in the form of Taveez, Dam, Threads, Nazar wattoo and Clothes. The economic status and education have inverse relation with the use of CAM. The 809 (63.2%) respondents believed that it is only the drug that would heal the disease, while 575 (44.9%) believed that spiritual methods have a 25-50% role in healing. The 1269(99.1%) respondents believed that allopathic drugs are needed for healing while only 0.9% considered otherwise.

Conclusions

The people believe CAM is contributory factor towards healing and does not interfere with allopathic treatment.

ESP16-0925
26. OTHER

PERICARDIAL TAMPONADE AS A MANIFESTATION SYSTEMIC JIA I(SJIA)MIMICKING INFECTIVE PERICARDITIS

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Title of Case(s)

Pericardial tamponade as a manifestation Systemic JIA (sJIA)mimicking infective pericarditis

Background

Systemic JIA (sJIA)is the most common cause of autoinflammatory fever. Sometimes it can present with pericardial effusion mimicking infective pericarditis without the presence of typical rash and arthritis. Unrecognised sJA with pericardial effusion has potentiality to be complicated by deadly macrophage Activation Syndrome(MAS) as well as pericardial tamponade.

Case Presentation Summary

We have seen 3 cases of sJIA who presented with pericardial effusion in the last 1 year.All these 3 patients presented with almost similar features of high spiking quotidian fever not responding to conventional broad spectrum antibiotics,neutrophillic leucocytosis, very high ESR and CRP .Chest X ray revealed cardiomegaly which was later confirmed as pericardial effusion by echocardiography.There was no evidence of arthritis and rash at the time of presentation.All these cases initially managed with broad spectrum antibiotics considering infective pericarditis, but later on all of them complicated by MAS,pericardial tamponade and needed pericardial drainage,mechanical ventilation, ICU admisiion and immunesupresive therapy.2 of them survived while one succumbed.All of them later on developed typical evanscent rash and arthritis in the course of the disease.

Learning Points/Discussion

Pericardial effusion in the background of PUO and high inflammatory markers may be a manifestation of sJIA even in the absence of typical rash and arthritis.They are frequently misdiagnosed as pyopericardium and treated with antibiotics.Early identification and prompt treatment with immunesupressive therapy like Steroid and Cyclosporine is life saving.

ESP16-0634
26. OTHER

FEVER OF UNKWOWN ORIGIN – STILL CHALLENGING TO APPROACH

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Title of Case(s)

Fever of unkwown origin – Still challenging to approach

Background

Kikuchi Fujimoto's disease (KFD) or histiocytic necrotizing lymphadenitis is especially rare in paediatrics. Although it is a self-limited and benign disease, its differential diagnoses are vast and includes lymphoma, infections and auto-immune diseases.

Case Presentation Summary

9-years old, previously healthy male, was admitted with painful, bilateral, cervical and supra-clavicular lymphadenopathies for the last five weeks. They progressively enlarged and fever and weakness appeared on the last three weeks. On examination there was also cheilitis, an erythematous macular rash and splenomegaly (12,5 cm).

Etiologic investigation revealed leukopenia with neutropenia (0,61 x 10^9/L), thrombocytopenia (99 x 10^9/L), low CRP and ESR values and high lactic dehyrogenase value (629 U/L). The serology for CMV were positive (IgM and IgG, high avidity, no seroconvertion. Negative viral load)
Other infections were excluded. ANA (1/80) was positive, and remained positive on second evaluation (1 month later).
Echocardiogram revealed no alterations.
Lymph node excisional biopsy showed histiocytic necrotizing lymphadenitis compatible with KFD. Bone marrow was normal.
The patient remained febrile for a total of 6 weeks, and corticoid therapy was initiated with resolution of fever and lymph node enlargement.

Learning Points/Discussion

Persistent lymph node enlargement with a prolonged fever requires a careful differential diagnosis, which should include KFD. KFD is a benign, self-limited disease and in the majority of cases no therapy is required. For persistent disease steroids are used with a favorable outcome.

ESP16-0553
26. OTHER

EOSINOPHILIC COLITIS IN CHILDREN

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Background

Eosinophilic colitis, which is a rare form of eosinophilic gastrointestinal diseases, occurs as primary and secondary allergic eosinophilic colitis of the gastrointestinal tract infection, inflammatory bowel disease, celiac disease, vasculitis, or the treatment.The aim of the study was the clinical picture analysis, taking into account comorbidities and endoscopic picture in children with eosinophilic colitis.

Methods

The test group consisted of 43 children diagnosed with eosinophilic colitis hospitalized in the Gastroenterology Unit in Katowice. Testing for food allergies, celiac disease, inflammatory bowel disease, gastrointestinal diseases and parasitic diseases was performed in the group of children and the analysis was carried of the intensity of eosinophilic infiltration of the colon mucosa with the severity of clinical symptoms, endoscopic picture, the presence of IBD, food allergy.

Results

Half of the tested children suffered from isolated eosinophilic colitis but rest of them had eosinophilic infiltrate with inflammatory bowel disease more often, however, the Crohn disease. Endoscopic image was uncharacteristic, and the grade III in the Whitington scale was predominant in the histopathological examination, in most cases located in the entire large intestine. The higher level of total IgE was found in less than half of the patients and it did not correlate with the severity of eosinophilic infiltration. It was shown that the severity of eosinophilic infiltration correlated with exacerbation of clinical symptoms, endoscopic image, the presence of inflammatory bowel disease.

Conclusions

The higher concentration of total IgE in less than half of the patients with eosinophilic colitis indicates the need for improving allergy diagnosis also in terms of IgE - independent allergy . The presence of the higher levels of antibodies of ASCA and ANCA indicates the need of further observation for the occurrence of IBD.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0639
26. OTHER

PRIMARY CUTANEOUS ASPERGILLOSIS IN A PRETERM INFANT. IS THERE A ROLE FOR VORICONAZOLE?

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Title of Case(s)

PRIMARY CUTANEOUS ASPERGILLOSIS IN A PRETERM INFANT

Background

Primary cutaneous aspergillosis (PCA) is rare in premature infants. Liposomal amphotericin-B is recommended, but other antifungal, such as voriconazole, have been reported.

Case Presentation Summary

A newborn was delivered at 24 6/7, 550g. After NICU admission, mechanical ventilation, umbilical catheters, antibiotic and parenteral nutrition were started. Hyperglycaemia, thrombocytopenia and neutropenia developed. Cultures were sterile, but antibiotics were continued. From birth, the infant's skin was very thin. On day 4, two erythematous skin lesions with elevated edges, central ulceration and exudate were observed in the neck. There was no probe placement or tape removal. The skin lesions extended, and the respiratory condition worsened with infiltrates on chest-X-ray. *A. fumigatus* and *A. nidulans* were isolated on skin cultures. Serum galactomannan antigen was >10. A presumptive diagnosis of IA (invasive aspergillosis) was established, and liposomal amphotericin-B was initiated without response. Abdominal and cerebral ultrasound were normal. Bronchoalveolar lavage and chest-CT were not performed because of the critical condition. Blood cultures were negative. Due to clinical worsening, intravenous voriconazole 3mg/kg/12h was added. Two days after signs of shock were presented, with kidney and liver failure. Drug trough levels were toxic (voriconazole:30mcg/mL and vancomycin:18mcg/mL) and they were discontinued. At this time, the skin lesions had considerably improved. However, on day 22, the patient died. There was no evidence of primary immunodeficiency.
Necropsy found intestinal perforation, but no evidence of IA. Coagulase-negative *Staphylococcus* and *Enterococcus faecalis* were isolated in liver/spleen biopsies, peritoneal, pleural and ascitic fluids, and blood culture. Environmental samples from the NICU were negative.

Learning Points/Discussion

PCA can occur in preterm infants, and it´s important to rule out IA. Further studies are needed to establish the appropriate dosage and duration of voriconazole.

ESP16-0771
26. OTHER

NEUROLOGICAL COMPLICATIONS IN PREMATURE INFANTS

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Background

Depending on the duration and severity of intrauterine hipoxic ischemic brain injury, newborns, premature infants especially, may have neurological complications, which may have unfavorable long-term prognosis. This paper aims to present the neurological complications that can occur in premature infants, risk factors for their appearance, and the diagnosis and evolution.

Methods

The study was conducted over a period of 3 years and were included premature infants with gestational age below 37 weeks, born at the Maternity Bega Timisoara.

Results

From the total of 6,640 newborns in this period, 565 were premature babies. One of the risk factors is low birth weight, 483 preterm having a weight under 2500 g. Other risk factors are: gestational age below 32 weeks (32%), Apgar score below five (21%), associated mother pathology. From the total number of premature infants, 191had intraventricular hemorrhage, 184 preterm presented hypoxic-ischemic encephalopathy, 10 premature developed periventricular leukomalacia and 3 cases have developed hydrocephaly.

Conclusions

Neurological complications may affect subsequent psychomotor development. Risk factors that may influence neurological complications are : the degree of cerebral hipoxic ischemic injury , gestational age below 32 weeks, Apgar score less than 5, associated mother pathology. The most common disorders are intraventricular hemorrhage and hypoxic-ischemic encephalopathy. Evolution of the disease depends on the promptness of initiating therapy, and associated pathology. The diagnosis of hypoxic-ischemic brain injury is based in basically on antenatal history and physical examination.

ESP16-0680
26. OTHER

SOCIODEMOGRAPHIC DETERMINANTS OF KNOWLEDGE, PREVALENCE AND INCIDENCE OF MENINGITIS INFECTION IN CHILDREN IN PAKISTAN

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Background

Meningitis in infants and children is one of the most dangerous causes of infection worldwide due to its high morbidity and mortality, especially in low income countries. This study was performed to identify the knowledge, socio-demographic determinants, prevalence and incidence, etiological types and nutritional status of the pediatric meningitis patients.

Methods

A cross-sectional and questionnaire based observational study was conducted in Punjab province of Pakistan. 310 pediatric meningitis patients attending tertiary hospital in Punjab, Pakistan were selected for the study. The variables studied were age, sex, nutritional status, residence, etiological type, duration of hospital stay and fatality rate. All obtained data were analyzed using descriptive and inferential statistics. The research tool was also piloted on 15 healthcare providers in a different hospital before start of the study. A p-value < 0.05 was considered statistically significant.

Results

More than 57% of the cases were infants and about 24% were below three years of age. The majority of the cases were male (50.83%), illiterates (49.17%) and rural (71.88%) by residence. For 67.84% of meningitis cases the hospital stay was between 3-5 weeks. The overall fatality rate was 27.66%. Incidence rate was higher in rural pediatric patients (67%) compared with urban pediatric patients (33%).

Conclusions

It was concluded that fatality rate of meningitis and prevalence of under-nutrition was quite high in rural pediatrics even in this era of modern medicine. This showed socio-economic factors were directly related with the incidence rate, knowledge, fatality rate and prevalence of the pediatric meningitis in Punjab, Pakistan.

ESP16-0061
26. OTHER

HEMOLYTIC UREMIC SYNDROME IN A CHILD WITH A DIARREAL DISEASE - CASE PRESENTATION

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Title of Case(s)

Hemolytic uremic syndrome in a child with a diarrheal disease – Case presentation

Background

Hemolytic uremic syndrome is a severe complication secondary to an infection. It is most frequently described in patients with acute diarrheal disease of various etiologies. Children develop this condition more frequently than adults

Case Presentation Summary

We present the of a 3 year old girl admitted in the 9th Pediatric Department of the National Institute of Infectious Diseases "Prof. Dr. Matei Bals" with the diagnosis of hemolytic uremic syndrome secondary to an acute dysentery-like gastroenterocolitis.
Clinical examination upon admission suggested an acute bacterial diarrheal disease. The workup showed: leukocytosis with neutrophilia, inflammatory syndrome, slight anemia and thrombocytopenia. 24 hours after admission, the child presented intense abdominal pain, vomiting, lack of appetite and persistence of dysentery-like stools and subsequently oligoanuria. Further workup revealed severe anemia and thrombocytopenia and stools cultures isolated Escherichia coli. The diagnosis of hemolytic uremic syndrome is established and the child was started on peritoneal dialysis. Evolution was favorable under complex treatment (antibiotic, pathogenic, intravenous fluids, and peritoneal dialysis), with resuming of diuresis and normalization of laboratory workup.

Learning Points/Discussion

Hemolytic uremic syndrome represents a severe complication which can have favorable evolution in the presence of a correct diagnosis and treatment. In our case, the child was not left with sequelae, as diagnosis was quickly established and treatment was instituted promptly.

ESP16-0815
26. OTHER

IMMUNOLOGICAL ALTERATIONS OF PROGRESSIVE OSSEOUS HETEROPLASIA IN AFFECTED IDENTICAL TWINS WITH A DISCORDANT CLINICAL PHENOTYPE

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Title of Case(s)

"Immunological alterations of progressive osseous heteroplasia in affected identical twins with a discordant clinical phenotype"

Background

Progressive osseous heteroplasia (POH) is a rare genetic disorder in which extra-skeletal bone forms within skin and muscle tissue. Ectopic bone formation begins in deep layers of skin and gradually moves into other tissues such as skeletal muscle and tendons. We present the cases of two genetically identical children whose phenotypical expression was totally different, and we wondered why.

Case Presentation Summary

Objective. Based on the close connection between the skeletal system and the immune system (osteo-immune system), the present study aimed to analyze the eventual immunological alterations in POH in two monochorionic and phenotypically discordant twins, with almost asymptomatic *versus* severe clinical course.

Methods. Flow cytometry analysis of peripheral blood immune populations and serum cytokine determination by a multiplex high throughput assay was used.

Results. Major immune cell fractions were altered in both twins, mainly B-CD5+ cells and TCR Yδ+ T cells. Cytokine signaling displayed a strong osteoclastic inhibition, by preponderance of IL-4, IL-10 and IFN-γ cytokines. This pattern was almost similar in both twins. Also an unexpected constant low level of IGF-1 was found in the patient with worse outcome from birth. Analytical and biochemical parameters of bone metabolism reflected large differences between patients.

Learning Points/Discussion

Genetic alterations leading to POH and producing profound bone metabolism alterations, also generate remarkable alterations of the immune system that are not necessarily dependent on the causal genotype, supporting the very close relationship between skeletal and immune systems. However, the immunological alterations found do not reflect the clinical course and cannot explain the vast discordance existing between these genetically identical twins.

ESP16-0134
26. OTHER

NAİL MATRİX ARREST İN THE COURSE OF HAND, FOOT AND MOUTH DİSEASE(HFMD): FOUR CASES OF ONYCHOMADESİS

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Title of Case(s)

Nail matrix arrest in the course of hand, foot and mouth disease(HFMD): Four Cases of Onychomadesis

Background

HFMD is contagious clinical disorder and comparatively common in children. Onychomadesis is defined as proximal nail plate separation with the temporary arrest in the activity of the nail matrix.

Case Presentation Summary

Case 1: A 11-year-old boy previously treated forALL,was referred to pediatric infection clinic(PIC) for nail changes. There was no history of trauma or skin disorder. Howeverhis parent noticed that he developed fever to 40 ^{0}C for 2 days and maculopapular rash eruption of oralcavity, palms, soles and glutealregion for 1 week.After 3 weeks with rashes disappeared nail changes were observed in finger nails and toenails. Onychomadesis secondary HFMD was diagnosed on examination and from history andthe other systems were normal. Nails recovered on following without anytreatment.

Case 2: A 21-month-old previouslyhealthyboy was referred to PIC for nailchanges without any trauma or skin disorder. Past history was noticed that he run a fever to 38,6 ^{0}C for 2 days and pruritic vesicular eruption of oral cavity, palms and soles.Varicella serology was negatif for acute infection. After 2 weeks vesicular eruptions were removed, finger andnail changes were seen. Onychomadesis secondary HFMD wasdiagnosed on examination and fromhistory. Nails recovered withno treatment.

Case 3 and 4: A 21-month-old and a 7-year-old previouslyhealthyboys were admitted to PIC for nail changes. There wasno history oftrauma or skin disorder. It was noticed that HFMD were diagnosed in both of patients before. After 4 weeks with eruptions disappeared nail changes were observed and onchomadesis was diagnosed according toHFMD. No treatment was given , nails recovered on following.

Learning Points/Discussion

The history of HFMD is needed to ask as one of the reasons in a patient with onychomadesis

ESP16-0033
26. OTHER

EFFECT OF ANTENATAL TAURINE SUPPLEMENTATION ON PIRB EXPRESSION IN FETAL RAT BRAIN WITH INTRAUTERINE GROWTH RESTRICTION

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Background

To explore the expression of paired immuonglobin-like receptor B(PirB) in fetal rat brain tissue with intrauterine growth restriction (IUGR) and the influence of antenatal taurine on its expression.

Methods

Eighteen pregnant rats were randomly divided intio 3 groups:normal control group,IUGR models group(IUGR group) and the IUGR +antenatal taurine supplement group(taurine group)（n=6. IUGR models were induced by low protein diet throughout gestation period. Three fetal rats were randomly selected from each nest and were sacrificed to obtain the brains.The PirB positive cell counts were detected by immunohistochemistry ,the PirB protein contents were deteceted by Western Blot and the level of mRNA expressions of PirB gene were detected by Real time-PCR.

Results

Control group, IUGR group, taurine group: 1）the PirB positive cell counts in the three groups were respectively 18.40±1.52，66.17±3.66，21.17±2.71; 2）the PirB protein semi-quantitative analysis results respectively 0.05，0.31，0.09; 3）the level of PirB mRNA $2^{-\Delta\Delta CT}$ numerical respectively 1（0.87，1.15），0.08（0.06，0.11），1.22（0.97，1.55）.Compared control group and taurine group with IUGR group, PirB positive cell counts were lower than that of IUGR group, PirB mRNA and protein expression were lower than that of IUGR group. The differences of comparing IUGR group with taurine group were statistically significant（$p<0.05$）.

Conclusions

The results of this study shows that the expression of PirB in fetal rat brain tissues was higher in IUGR groups than that in controls while antenatal taurine can significantly decrease its expression, which suggested that antenatal taurine may play a protecting role by inhibiting the expression of PirB in fetal brain tissues（This work was supported by the National Natural Science Foundation of China (81471087).

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0253
26. OTHER

MOLECULAR HYDROGEN AMELIORATES NECROTIZING ENTEROCOLITIS BY DECREASING OXIDATIVE STRESS VIA NRF2 SIGNALING PATHWAY IN RATS

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Background

Necrotizing enterocolitis (NEC) is most common acquried gastrointestinal and surgical emergency and acts as a leading cause of death among preterm infants. Hypoxia/reoxygenation injury causes serious intestine complications. Molecular hydrogen (H2) has been shown to be effective in protecting various cells and organs against oxidative stress injury.

Methods

In vitro studies were carried out in an antimycin A or menadione stimulated cell model treated with or without H2, to determine the potential protective effects of hydrogen against oxidative injury and explore the underlying mechanisms. In vivo study, NEC was induced in newborn rats, and hydrogen saturated formula was used as a therapeutic way to treat NEC pups.

Results

Our study revealed that H2 activated Nrf2 and downstream cytoprotective protein expression. H2 inhibited antimycin A induced cell apoptosis. Also, H2 increased Nrf2 activation and Nrf2 shRNA abolished the protective effect of H2 on antimycin A-induced cellular ROS production. A rat model of NEC indicated that H2 significantly attenuates ischemia/reperfusion intestine injury in vivo.

Conclusions

In conclusion, the inhibitory effects of H2 on the apoptosis and cytotoxity of oxidative-stimuli cells, which take effect by activating the Nrf2 antioxidant pathway, might lead to an improvement in the prevention and treatment of NEC.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0832
26. OTHER

ENTECAVIR IN HEPATITIS B INDUCED MEMBRANOUS NEPHROPATHY

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Title of Case(s)

Entecavir in Hepatitis B induced membranous nephropathy

Background

We report a case with Hepatitis B virus (HBV) induced membranous nephropathy (MN) treated successfully with entecavir**.**

Case Presentation Summary

A 7-years-old boy presented with 1st episode of generalized anasarca, nephrotic-range proteinuria, hypoalbuminemia, microscopic hematuria and hypertension. He had serum cholesterol -385 mg/dL, normal renal and liver function tests, negative anti-nuclear and anti-neutrophilic cytoplasmic antibodies; normal C3 levels; HBsAg and HBeAg positive (ELISA), quantitative HBsAg 27906.7 IU/mL (normal<0.05); HBV-DNA (rt-PCR) 54360903 IU/ml (linear range of assay = >20-<1.7x 10^8); negative serology for hepatitis-C and HIV. Family screening for Hepatitis B and C were negative. For HBV related glomerulopathy, he was started on prednisolone (2mg/kg/day for 4 weeks), enalapril and lasilactone. He failed to attain remission, was labelled as steroid resistant nephrotic syndrome and percutaneous renal biopsy was performed.

Light microscopy showed diffuse global basement membrane thickening with focal segmental sclerosis. Direct immunoflourescence showed capillary loop positivity for IgG, C3, kappa and lambda (2 to 3+) consistent with membranous pattern. Electron microscopy showed presence of transmembranous and epimembranous immune complex deposits with effacement of foot processes.(See Fig.) A diagnosis of MN secondary to HBV infection was made.

Child was started on Peg Interferon 2b (50 microgram / week) for 16 weeks. He failed to attain remission (nephrosis persisted although blood pressure stabilised) and seroconversion (Repeat HBsAg and HBeAg were positive; Quantitative HBV –DNA was 11524620 IU/ml). Oral therapy with Entecavir (0.5 mg daily) was started then and child attained remission as well as seroconversion after 3 months of therapy. He maintained his seroconversion status at 6 and his recent 12 months followup visit.

Learning Points/Discussion

Entecavir seems a promising drug for HBV-related glomerulopathy especially in interferon resistant cases.

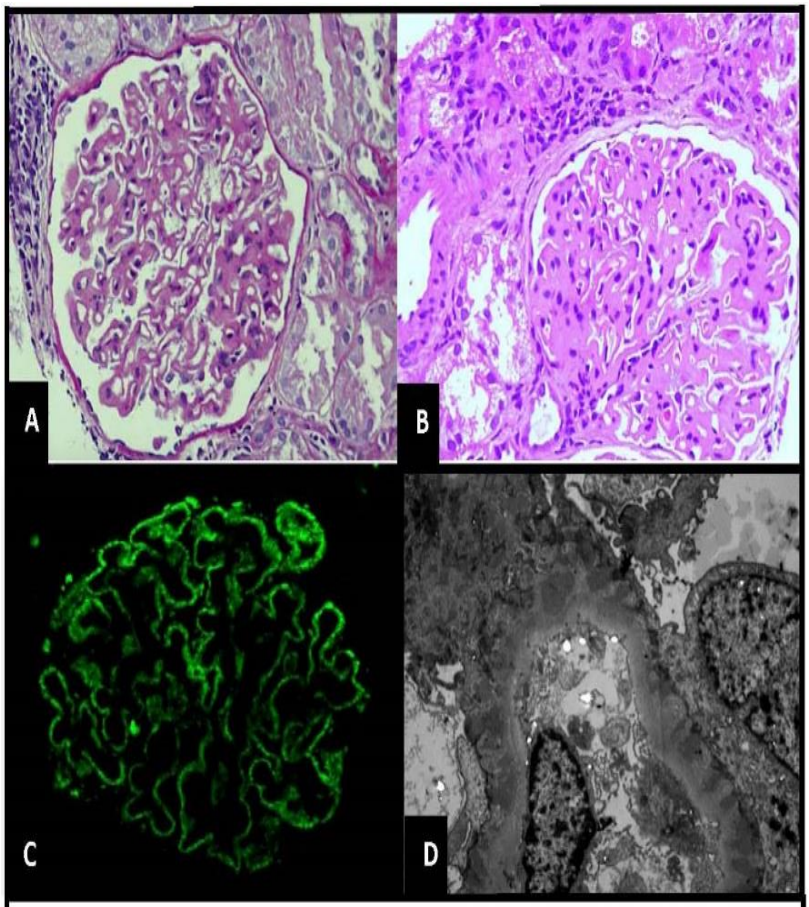

Fig 1: (A) PAS and (B) H&E stain show diffuse global basement membrane thickening; (C) capillary loop positivity for IgG, (D) EM photo-Transmembranous and epimembranous immune complex deposits with laying down of basement membrane between the deposits.

ESP16-0442
26. OTHER

OCULAR TOXOPLASMOSIS IN IMMUNOCOMPETENT CHILDREN

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Background

Congenital and acquired Toxoplasma gondii infection sometimes result in acute posterior uveitis. Eye infection may follow a relapsing course, with gradual vision decrease or even blindness, when lesions affect fovea. Typical cases of ocular toxoplasmosis are recognised by fundoscopy. Current therapies lack evidence for effectiveness and do not prevent relapse.

Methods

We evaluated 34 immunocompetent children (23 girls, 9 boys) aged 0 to 18 years (mean 7.4±5.5) with ocular toxoplasmosis diagnosed by ophthalmologic examination (fundoscopy with color fundus photography, fluorescein angiography) and positive serum anti-Toxoplasma IgG ELISA (DiaSorin, Italy). Examinations were repeated ever 6 months for mean 18 months. In nine children with documented congenital toxoplasmosis eye infection was diagnosed in the first year of life, in other twenty five – between the 2nd and the 18th. The former group and all children with active lesions were treated with oral pyrimethamine and sulfadiazine plus systemic corticosteroid for 6-12 months.

Results

Ocular toxoplasmosis presented as necrotizing retinitis, secondary choroiditis, sometimes retinal vasculitis, vitritis and subsequent scarification. We ascertained 64% (22/34) recurrence rate in 1 to 5 years; one relapse in 16 children, two in 5, three in 1. Bilateral lesions were found in 44% (15/34) children, central localization in 82% (28/34), multifocal lesions in 32% (11/34). Serum anti-Toxoplasma gondii IgG ranged from 20 to 1170 U/l. Acute eye infection was accompanied with higher mean antibody titers (178 U/l) than levels at the time of remission (90 U/l); p=0.0016.

Conclusions

Ocular toxoplasmosis in immunocompetent children requires long-term follow up as infection persists and relapses in spite of anti-parasite treatment. We suggest regular checkups of fundoscopy and specific serum antibody titer in all anti-Toxoplasma positive children. Increase in serum anti-Toxoplasma IgG may predict ocular recurrence.

ESP16-0283
26. OTHER

READABILITY ASSESSMENT OF ONLINE PATIENT MATERIALS RELATING TO PAEDIATRIC PNEUMONIA

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Background

The internet is a widely-used resource for parents who seek medical information. Many have wrong expectations of care due to low quality educational materials online. Previous research has stated that the content of patient information materials should not surpass a reading level of 12-13 years old. Thus, we undertook a comparative readability assessment of patient-centred materials relating to pneumonia in children

Methods

Materials were downloaded from 7 websites in January 2016: National Health Service (NHS), Child Development Institute, Stanford Children's Hospital, Boston Children's Hospital, Seattle Children's Hospital, AboutKidsHealth and HealthyChildren.The text was processed and formatted in Microsoft Word. Names of bacteria, viruses and drugs were excluded to limit bias. A readability assessment was undertaken on the remaining text using 6 quantitative formulas: Automated Readability Index, Coleman-Liau Index, SMOG Index, Gunning-Fog score, Flesch-Kincaid Grade level and Flesch-Kincaid Reading Ease using Readability Studio (Oleander Software).

Results

The edited and original texts shared identical mean readability scores. NHS Choices had the highest mean readability score (14±2). AboutKidsHealth had the lowest mean readability score (9.0±2). ANOVA analysis demonstrated no statistical difference between the readability when comparing websites ($p>0.05$). The mean Flesch-Kincaid Reading Ease score was 51, which compares to a reading level of >16 years old. The overall mean readability score was 11.7, which compares to a reading level of >16 years old too

Conclusions

The mean readability scores of patient resources are considerably higher than the recommended level of 12-13 years old. Simpler and clearer materials would be more suitable to the general public in the UK and internationally

ESP16-0421
26. OTHER

MOTHERS' KNOWLEDGE AND ATTITUDES TOWARDS CHILDREN'S VACCINATION

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Background

Sufficient immunization coverage among children depends on parents' knowledge and attitudes towards vaccination and their intentions to vaccinate their children. Aim of the study was to evaluate mothers' knowledge and attitudes towards children's vaccination.

Methods

The questionnaire was handed out to randomly selected postpartum mothers in the Hospital of LUHS Kaunas Clinics from March until June of 2014. In total, 300 women were surveyed.

Results

The mean age of the respondents was 29.51±5,589 years. 63% of them had higher education. The main sources of information about children's vaccination indicated by the women were the doctor, internet and mass media. 88.2 % of the mothers thought the disease, which the child was being vaccinated from, was dangerous, 55.9 % thought that vaccines protected from them efficiently. 77.7 % of the respondents thought that the benefits of vaccines was greater than the risks, and only 56.7 % answered that vaccines were safe. 36.3 % of mothers had good knowledge about immunization, 41.3 % - average and 22.3 % - poor. The mothers with higher level of education also had better knowledge ($r=0.189$, $p<0.0001$). 72.7 % of the mothers were the most worried about adverse reactions caused by the vaccines. 75 % of the mothers, whose knowledge was evaluated as good, had never refused or had doubts about having their child immunized ($r=-0.216$, $p<0.0001$). The mothers with better knowledge were less likely to worry ($r=0.211$, $p<0.0001$).

Conclusions

1. One third of mothers had good knowledge about immunization.

2. The mothers with higher level of education had better knowledge about vaccination.

3. Mothers, whose knowledge was evaluated as good, less often refused, had doubts or were worried about their children imunization.

ESP16-0934
26. OTHER

A CASE OF ORAL ERYTHEMA MULTIFORME DUE TO MYCOPLASMA PNEUMONIAE INFECTION IN A PAEDIATRIC PATIENT

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Title of Case(s)

A case of oral erythema multiforme due to Mycoplasma pneumoniae infection in a paediatric patient

Background

Erythema multiforme is an acute mucocutaneous disorder. Its etiology most commonly involves infections and drugs. Oral erythema multiforme is an underrecognised form of the disease. It is characterized by oral ulcerations, which have typical characteristics of erythema multiforme but are not accompanied with skin lesions.

Case Presentation Summary

An eleven year-old girl was admitted due to the eruption of oral blisters 24 hours ago, which subsequently broke leaving painful ulcers. Seven days before admission, the patient suffered from a respiratoty tract infection, for which she was put on antibiotic treatment with clarithromycin. A small consolidation on the left lower lobe was revealed on chest X-ray. On examination, the child had low fever and mild wheeze was present. Extensive oral ulcerations with unclear boundaries, which were covered by pseudomembranes and were localized on the lip, mouth floor and buccal mucosa, as well as hemorrhagic crusting of the lips were noted. The patient was put on treatment with oral prednisolone and topical anesthetics. The oral lesions quickly improved. IgM antibodies for Mycoplasma pneumoniae were found to be positive. The acute manifestation of the lesions, their localization and their quick improvement established the diagnosis of oral erythema multiforme due to Mycoplasma pneumoniae infection.

Learning Points/Discussion

HSV and Mycoplasma pneumoniae are the most common infectious causes of erythema multiforme. The acute manifestation and the localization of the lesions in the non-ceratinized oral mucosa is the basis for the differential diagnosis of oral erythema multiforme from other entities, characterized by oral ulcerations, such as herpetic gingivostomatitis and bullous pemphigoid. In the event of recurrences, a biopsy might be needed to ensure the diagnosis.

ESP16-0370
26. OTHER

C. DIFFICILE SEVERE CASES IN ICU- DIAGNOSTIC METHODS

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Title of Case(s)

C. difficile severe cases in ICU- diagnostic methods

Background

Clostridium infections are becoming a public health issue and are increasingly encountered in pediatric hospitals, mostly due to antibiotic overuse. There is a constant search for new treatments.

Case Presentation Summary

We have monitored all cases admitted between 2011 and 2015 in the pediatric departments of the National Institute of Infectious Diseases “Prof Dr Matei Bals” with the diagnosis of C. difficile colitis. Patients were aged between 0-14 years and presented severe forms of diseases and other comorbidities. Between January 2011 and December 2015, 1425 had gastrointestinal sepsis. In 57 patients, diagnosis was established through a positive C. difficile PCR, most of them presenting severe forms of disease. No deaths were registered.Most affected age group was 3-5 years. Patients with the most severe forms of illness all had comorbidities.Fecal microbiota transplantion was performed in 2 patients with multiple relapses after treatment with vancomycin. All other patients benefited from standard treatment.

Learning Points/Discussion

Clostridium difficile infection represents an important cause of morbidity and mortality in Romanian hospitals and the number of cases is on an exponential rise. Limitation of antibiotic treatment is a first step in preventing C. difficile infection.

Although PCR testing is costly, we consider it highly important because of the fact that it can reveal ribotypes implicated in acute infection and it can guide selection of adequate therapy, bearing in mind that the most frequent ribotype in Romania is 027 (65-80 %) which is resistant to fidaxomicine.

ESP16-0371
26. OTHER

THE MOLECULAR DIAGNOSIS OF SEVERE BACTERIAL SEPSIS IN CHILDREN BETWEEN 2011-2015

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[2]National Institute for Infectious Diseases- "Prof. Dr. Matei Bals", Pediatric, Bucharest, Romania
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Title of Case(s)

The molecular diagnosis of severe bacterial sepsis in children.

Background

In children, bacterial sepsis is a not a very common condition but often accompanied by severe complications that can leave sequelae. Sometimes can be life-threatening and requires a complex and quickly set treatment.

Case Presentation Summary

We conducted a 5 years study from Jan 2011 to Dec 2015 on 2851 children admitted in our pediatric intensive care unit of National Institute of Infectious Diseases for severe forms of SIRS and bacterial sepsis. Positive diagnosis of sepsis was established on clinical and laboratory criteria . As well as classical cultures, we found causal agents through PCR anf Plex ID. We watched the correlation of data obtained by hemocultures, CSF cultures versus PCR and the clinical evolution of the patients.

In the 60 months of study, 265 children met the clinical and biological criteria for severe bacterial sepsis. 68% of patients came from other hospitals, reason for which we consider that the etiology is most likely nosocomial pathogens. Sex distribution was approximately equal to boys and girls. Considering age distribution, children in group 3-5 years of age prevailed.

We obtained 163 hemoculture positive results (61%) and 112 obtained by molecular methods. The data were correlated with conventional methods of diagnosis.

The seat is the distribution of cases etiology was as follows: N. meningitides-7 cases, Streptococcus pneumoniae-39 cases, Staphylococcus spp - 2 cases, Acinetobacter baumanii-1 case, Ps aeruginosa 1 case, Mycobacterium tuberculosis-5 cases, 57 Clostridium difficile,

Learning Points/Discussion

Bacterial sepsis in children is a serious condition resulting in 24 deaths (14%) in our study. It requires a quick etiologic diagnosis and establishment of appropriate emergency treatment.

PCR is an effective and rapid diagnosis method, identifying casual agent in 42% of cases.

ESP16-0499
26. OTHER

YERSINIA ENTEROCOLITICA INFECTION AS DIFFERENTIAL DIAGNOSIS IN SEVERE BACTERIAL INFECTIONS- CASE PRESENTATION

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Title of Case(s)

Yersinia infections

Background

Yersinia enterocolitica is a Gram negative, facultative anaerobe bacillus that belongs to the family Enterobacteriaceae.

Human yersiniosis is frequently associated most with acute enterocolitis, terminal ileitis, mesenteric lymphadenitis, reactive arthritis, pseudoappendicitis and even severe sepsis, especially in infants.

Case Presentation Summary

We present the case of a 10 year old boy hospitalized in the Pediatric Department of the National Institute of Infectious Diseases ”Prof Dr Matei Bals” during 10-26 June 2015 for the investigation of a prolonged febrile illness.

The child’s medical history revealed the fact that the onset was 31 days prior to admission, with high fever, abdominal pain and vomiting. He was hospitalized in a territorial clinic with the diagnosis of acute meningitis. He received antibiotic treatment but evolution was unfavourable with persistence of fever and onset of hepatosplenomegaly.

In the absence of a diagnosis the child was admitted in our clinic, where the diagnosis of acute meningitis was excluded. Through multiple interdisciplinary consultations, other illnesses (rheumatic, haematological, parasitic) were excluded.

Laboratory investigations revealed pancytopenia, important inflammatory syndrome, and a positive serology for Yersinia spp., and abdominal ultrasound and MRI scan showed mesenteric adenopathies.

As a result of antibiotic, pathogenic and symptomatic treatment, the patient had a favourable evolution, with the cessation of fever and the reduction of hepatosplenomegaly after 10 days of hospitalization.

At the subsequent revaluations at 1, 3 and 6 months, the patient did not present any signs or symptoms, and has since been classified as cured.

Learning Points/Discussion

Yersinia infections can be polymorphic in presentation and quite often can imitate others serious illnesses, as it was in this case. We regard this infection as a potential differential diagnosis in cases of prolonged febrile illnesses.

ESP16-0917
26. OTHER

ACUTE FEVER IN CHILDREN UNDER FIVE HOSPITALIZED AT DR. SOETOMO HOSPITAL SURABAYA

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Background

In children under five year, fever is a common illness accounted as 10-20% of healthcare visits annually. In developing country like Indonesia, infectious diseases are common causes of fever. This study aimed to describe diagnosis and associated laboratory findings in children under five year with fever.

Methods

Prospective study was conducted at dr. Soetomo Hospital from 2008 to 2009. Subjects were children aged 28 days to <60 month hospitalized with acute fever (axillar temperature ≥38°C). All subjects underwent blood examination and culture, and Chest X Ray (CXR) if needed. We collected demographic, clinical and laboratory data.

Results

Eight hundred sixty three children with temperature ≥38°C were included. Most (85.6%) subjects were 3 months-3 years old. Leukocytosis found in 210 (24.3%). Final diagnosis mostly were Pneumonia Clinical Syndrome/ PCS (36%), acute pharyngitis (21%), acute diarrhea (16%) and sepsis (11%). The most common findings in blood culture were *Staphylococcus* 127 (14,7%) and *Pseudomonas* 19 (2.2%). In 311 PCS patients, common CXR result were patchy infiltrat (64%), consolidation (3.5%) and air bronchogram (2.5%). Twenty one (2.4%) patients died due to respiratory failure(1.8%) and sepsis(0.002%)

Conclusions

Most common diagnosis in children who came with acute fever were PCS, acute pharyngitis and acute diarrhea. *Staphylococcus* spp. is the most common findings in blood culture.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0495
26. OTHER

CLINICAL AND MICROBIOLOGICAL CHARACTERIZATION OF STAPHYLOCOCCUS AUREUS SKIN AND SOFT TISSUE INFECTIONS

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Background

The epidemiology of *Staphylococcus aureus* (SA) rapidly changed in the last years with the diffusion of community-associated methicillin-resistant SA (CA-MRSA) clones and SA producing Panton-Valentine Leukocidin (PVL-SA). This study analyzes epidemiologic, clinical and microbiological characteristics of SA isolated from skin and soft tissue infections (SSTI) of pediatric patients attending a third level hospital.

Methods

All pediatric patients (aged < 18 years) with SA SSTI observed at Meyer Children's University Hospital from December 2012 to November 2015 were included in the study.

Results

A total of 89 (median age 95 [IQR: 19,5-142] months) patients were included in the study. Thirty-nine (43,8%) patients were admitted to hospital (median lenght: 8 [IQR 6-12] days), and 2 (2,2%) to intensive care units. Fifteen (16,9%) patients needed surgical intervention. Twenty-two (24,7%) strains were MRSA (3 SCC*mec* III, 12 SCC*mec* IV and 6 unidentified) and 47 (52,8%) out of 89 were PVL-SA. PVL presence were more frequent in MRSA than MSSA (34% vs 14,3%, OR 3,097, 95%CI 1,079-8,885, p=0,031). Table summarizes risk associated to PVL acquisition.

Variable	PVL-positive (47) n° (%)	PVL-negative (42) n° (%)	OR	95% CI	p
Male	25 (53,2)	22 (52,4)	1,017	0,655-1,579	0,939
Foreign	13 (27,7)	17 (40,5)	0,526	0,231-1,366	0,202
Family history	20 (42,6)	1 (2,4)	30,370	3,847-239,786	<0,001
Previous injury	2 (4,3)	8 (19)	0,189	0,038-0,947	0,027
Previous surgery	2 (4,3)	6 (14,3)	0,267	0,051-1,401	0,099
Previous hospitalization	3 (6,4)	9 (21,4)	0,250	0,063-0,996	0,038
Nosocomial infection	0 (0)	8 (19)	0,810	0,699-0,937	0,002
Recurrent infections	26 (55,3)	7 (17,1)	6,014	2,221-16,285	< 0,001

Conclusions

Half of SA strains isolated in SSTI produced PVL. Presence of PVL is significantly associated to presence of recurrent infection, family history of SSTI and MR.

Clinical Trial Registration (Please input N/A if not registered)

N/A

ESP16-0726
26. OTHER

AN EVALUATION OF DOCTORS AND MEDICAL STUDENTS' ATTITUDES AND BELIEFS OF PAEDIATRIC VACCINATIONS IN UNITED KINGDOM (UK)

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Background

Doctors and medical students now have decreased exposure to Vaccine Preventable Diseases as successful vaccination programs have decreased their prevalence. This combined with the media's negative portrayal of vaccines may cause misconceptions and misinformation. The aim of this survey was to explore doctors and students' attitudes and beliefs of paediatric vaccinations and identify their training needs.

Methods

Doctors from two UK hospitals, General Practitioners (GPs) from four London boroughs and students from three medical schools participated by completing an anonymous, cross-sectional, internet-based survey from 14 April 2015 to 14 July 2015. Data were analysed qualitatively for themes and sub-themes. Ethical approval was obtained from King's College, University of London.

Results

60 doctors (including 18 GPs) and 109 students participated. Overall, the majority of doctors (34/52 (65.3%)) and students (32/89 (67.4%)) agree/strongly agree that parental refusal to vaccinate their child is a form of neglect. 26/52 (50.0%) of doctors and 41/89 (46.1%) students disagree/strongly disagree that unvaccinated children should be excluded from school. 51/52 (98%) of doctors and 85/89 (95.5%) of students disagree/strongly disagree that multiple vaccines weaken a child's immune system. 50/52 (96.1%) of doctors and 83/89 (93.3%) of students disagree/strongly disagree that natural immunity is better than vaccines.

Lack of parental knowledge and the media were perceived as major barriers to vaccination in developed countries whereas in developing countries, main barriers were perceived to be access to healthcare, infrastructure, parental knowledge and cost.

Conclusions

This study identifies attitudes of doctors and students in UK towards children's vaccines and the findings form a platform upon which to develop interventions to integrate into formal educational curriculum. Recommendations include developing up-to-date core competencies with individualised Continuing Medical Education (CME) activities and specific communication skills training.

ESP16-0731
26. OTHER

AN EVALUATION OF DOCTORS' KNOWLEDGE OF PAEDIATRIC VACCINATIONS IN UNITED KINGDOM (UK)

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Background

Doctors have decreased exposure to Vaccine Preventable Diseases (VPDs) as successful vaccination programs have decreased their prevalence. This combined with the media's negative portrayal of vaccines may cause misconceptions and misinformation. Doctors are trusted sources of information; their knowledge can influence parental acceptance of vaccinations. The aim of this study was to explore doctors' knowledge of paediatric vaccinations, highlight knowledge gaps, identify training needs and make recommendations for future training.

Methods

Vaccination knowledge of doctors from two UK hospitals and General Practitioners (GPs) from four London boroughs was assessed by an anonymous, self-administered, cross-sectional, internet-based survey from 14 April 2015 to 14 July 2015. Questions addressed vaccine guidelines, schedules, administration, handling, contraindications and adverse events. Analysis included comparison of proportions with the use of descriptive statistics. Ethical approval was obtained from King's College, London.

Results

60 doctors participated including 18 GPs. The mean knowledge score was 6.9/10 (69%) and the most correctly answered questions were whether vaccinations can be administered to an afebrile child with an Upper Respiratory Tract Infection (URTI), and whether vaccinations cause autism. Both of these questions were correctly answered by 54/56 (96.4%) of UK doctors. The most poorly answered question overall was related to a child who has come from abroad without any medical records and was answered incorrectly by 29/56 (51.2%) of doctors.

Conclusions

This study identifies gaps in knowledge amongst doctors in UK and the findings form a platform upon which to develop educational interventions which can be integrated into formal educational curriculum. Recommendations include developing up-to-date core competencies and individualised Continuing Medical Education activities. Teaching methods used in various institutions should be compared to determine effective teaching strategies. Specific communication skills training should also be promoted.

ESP16-0652
26. OTHER

EPIDEMIOLOGY, CLINICAL CHARACTERISTICS, LABORATORY FINDINGS AND SEVERITY OF RESPIRATORY SYNCYTIAL VIRUS ACUTE LOWER RESPIRATORY INFECTION IN MALAYSIAN CHILDREN, 2008-2013.

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Title of Case(s)

Epidemiology, Clinical Characteristics, Laboratory Findings and Severity of Respiratory Syncytial Virus Acute Lower Respiratory Infection in Malaysian children, 2008-2013.

Background

Although there is wealth of data on burden of Respiratory Syncytial Virus(RSV) acute lower respiratory infection(ALRI), there are still gaps in the body of evidence of the disease among children in low- and middle-income nations. This is particularly true in the setting of Malaysia because there has also not been any recent large case series on RSV ALRI originating from this upper middle-income country.

Case Presentation Summary

Retrospective data on demographics, clinical presentation, outcomes and laboratory findings of 450 children admitted into Tuanku Jaafar Hospital in Seremban, Malaysia from 2008 to 2013 with documented diagnosis of RSV ALRI were collected and analysed.

Most admissions were children less than 2 years old(85.8%;386/450). Commonest symptoms were fever(84.2%;379/450), cough(97.8%;440/450) and rhinorrhea(83.6%;376/450). The median age among febrile patients(n=379) was 9.0 months with interquartile range(IQR) of 4.0-19.0 months whereas the median age among those who were pyrexial (n=71) was 2 months with IQR of 1-6 months(p value <0.001). Although antibiotics were started for 58.9%(265/450) of the subjects, only 1.5%(4/264) of blood cultures were positive for pathogenic bacteria. 15.3%(69/450) needed intensive care and case fatality rate was 1.6%(7/450). Younger patients, those with history of prematurity, chronic comorbidity and thrombocytosis were of higher risk of severe RSV ALRI.

Learning Points/Discussion

Infants less than 6 months old with RSV ALRI tend to be afebrile at presentation. Younger age, history of prematurity, chronic comorbidity and thrombocytosis are predictors of severe RSV ALRI among Malaysian children. Antibiotics should not be started inappropriately for children diagnosed with RSV ALRI especially if they are more than 90 days old and not admitte to intensive care unit.

ESP16-0654
26. OTHER

RHEUMATIC FEVER REDUX

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Title of Case(s)

THE REBOUND PHENOMENON RETURNS

Background

Post-streptococcal acute rheumatic fever and subsequent chronic rheumatic heart disease remains an enigmatic and deadly scourge upon human health. The near-disappearance of these conditions from historical centres of medical scholarship in the developed world belies a major ongoing global contribution to morbidity and mortality. With decreasing familiarity, divergences from classical 'textbook' presentations may not be recognised and the basis for management recommendations forgotten.

Case Presentation Summary

We present a case of ARF in a nine-year-old boy of Samoan descent with an atypical protracted four-month course and repeated episodes of rebound clinical and laboratory signs of inflammation upon withdrawal of anti-inflammatory therapy. The initial episode occurred in temporal relation to S. pyogenes skin infection. There was no history of recent pharyngitis. Presentation was with fever, severe migratory arthralgia, and a cardiac murmur. Investigations found elevated inflammatory markers, first-degree heart block, and echocardiography showed aortic and mitral rheumatic valvulitis. Arthralgia rapidly improved after starting aspirin. Penicillin secondary prophylaxis was instituted.

Over four months there were three distinct episodes of clinical rebound, with migratory arthritis, and raised inflammatory markers. Each episode occurred within approximately two weeks of withdrawal or reduction of anti-inflammatory therapy (initially aspirin, later naproxen). Anti-inflammatory therapy was finally ceased after four months, without further rebound. Cardiac signs and imaging were static through this four-month period and improved at follow-up twelve months later.

Learning Points/Discussion

1. The continuing impact of ARF and RHD
2. Touch upon areas of uncertainty, controversy, and promise in regards to the pathogenesis, diagnosis, management and prevention
3. Describe the 'rebound phenomenon', a potentially confusing clinical syndrome of ARF

4. The rationale for anti-inflammatory therapies in rheumatic fever and differing indications and regimens advocated in current and historical guidelines

ESP16-1016
26. OTHER

A STUDY OF VARICELLA GANGRENOSA IN CHILDREN HOSPITALIZED AT CLINIC FOR INFECTIOUS DISEASES AND FEBRILE ILLNESSES, UNIVERSITY CLINICAL CENTRE LJUBLJANA IN A 10 YEAR PERIOD

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Background

Background: *Varicella* gangrenosa (VG) is a descriptive term for a variety of conditions that occur as a rare complication of *Varicella* and manifest themselves as a gangrene of the skin and deeper tissues.

Methods

Methods: Using a computer database and patients discharge documents we analyzed the data of children diagnosed with VG at Clinic for Infectious Diseases and Febrile Illnesses, University Medical Centre Ljubljana in a period of 10 years (January 2006 - December 2015).

Results

Results: In the evaluated period of time 354 children were admitted to our hospital because of *Varicella* complications and 5 (1,41%) of them were diagnosed with VG. All 5 children (2 boys, 3 girls) were between 6 months and 3 years of age (median age: 23 months) and were admitted between fourth and seventh day of their disease. Upon admission all of them presented with local edema and several necrotic *Varicella* lesions, predominantly on the face and back. Results of the laboratory tests at admission showed elevated CRP (median: 128 mmol/l) and median value of leukocytes 13,8 10^9/l. They all received antibiotic treatment with flucloxacillin and 3 (60%) of them were given acyclovir intravenously. Other supportive therapy included potassium supplements (80%), erythrocyte transfusion (60%), diuretics (60%), humane albumins (40%), platelet transfusion (20%), fresh frozen plasma (20%) and IVIG (20%). In 60% the vesicular smear was positive for *S. aureus*, blood cultures remained negative in all of our cases. Three out of five patients needed to be transferred to PICU and two out of five were in need of surgical treatment.

Conclusions

Conclusion: All of our patients were treated in accordance with the guidelines from accessible literature and made a full recovery with minimal scar tissue formation.

ESP16-0116
26. OTHER

NEW DELHI METALLO-β-LACTAMASE (BLANDM-1) PRODUCING MICROORGANISMS: A THREAT TO CHILDREN

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Background

New Delhi Metallo-β-lactamase-1 (NDM-1) is a type of Metallo-β-lactamase named after the city of origin “New Delhi”. The organisms acquiring blaNDM-1 gene are resistant to multiple classes of antibiotics including β-lactams and carbapenems too. This leaves very limited options for the treatment of such infections. NDM-1 producing pathogens also can lead to morbidity and mortality particularly in children. Therefore this study was planned to determine the frequency of blaNDM-1 gene in Gram-negative rods from ≤5 years of children.

Methods

One hundred carbapenem resistant clinical isolates were collected from different children hospitals. These isolates were reconfirmed on the basis of their colony morphology and biochemical tests (API 20E and 20NE). Antimicrobial susceptibility was done according to CLSI 2011. Carbapenems resistant isolates were analyzed for MBLs producers by double disc diffusion method and carbapenemases as per CLSI 2011 guidelines. These positive microbes were further analyzed for *bla*$_{\text{NDM-1}}$ gene using specific primers in PCR technique.

Results

Out of 100 carbapenem resistant isolates >90% were found to be resistant against commonly use antibiotics including carbapenems except polymixin B. Among these 89 were carbapenamase and MBLs producers. Out of these 89 organisms, 32 (36%) were *bla*$_{\text{NDM-1}}$ producers. The predominant microbes which contain *bla*$_{\text{NDM-1}}$ genes were *K. pneumoniae* (n=12) followed by and *E. cloacae* (n=10) and *P. aeruginosa* (n=6). These 32 isolates reported as high drug resistant and most effective drug was polymixin B which showed sensitivity of 44% against *bla*$_{\text{NDM-1}}$ producer organisms.

Conclusions

The spread of *bla*$_{\text{NDM-1}}$ gene among Gram-negative rods is an alarming threat particularly in hospitalized neonates. A national multicenter survey should be carried out to combat this serious problem.

Clinical Trial Registration (Please input N/A if not registered)

NA

ESP16-0658
26. OTHER

RECRUITING CHILDREN WITH SUPPURATIVE LUNG DISEASES TO CLINICAL TRIALS: EXPERIENCE FROM AN AUSTRALIAN MULTI-CENTRE VACCINE TRIAL

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Background

There is increasing attention on the potential for vaccines to reduce acute exacerbations of chronic lung diseases in children however clinical trials are scarce. We describe the challenges of recruiting children to such a trial and the lessons learned for future research.

Methods

An Australian multi-centre, double-blind randomized controlled trial evaluating the efficacy of a 10v pneumococcal-Protein D conjugate vaccine in preventing acute exacerbations in children with suppurative lung diseases. The required sample size was 262 children and participation involved 5 clinical visits and fortnightly contacts over 14 months. Research nurses recruited through clinics in tertiary pediatric hospitals in liaison with attending physicians and clinic staff.

Results

Over a 2.5-year period, 975 children were screened and 75 enrolled resulting in a major amendment to the protocol’s primary endpoints. Of those not enrolled, 52% were ineligible, 32% refused and 8% were not enrolled for other reasons. The major reasons for ineligibility were being clinically ineligible 78 %) and current/planned involvement in another clinical trial (21%). 5 children have not completed the study due to withdrawal of parent consent.

Conclusions

Vaccines trials in children are complex given lengthy eligibility criteria, the duration of study participation and demanding requirements of participants and their families. In children with complex medical histories and frequent need for tertiary health care, these issues will influence the available pool of potential participants for vaccine trials. Future studies will require large numbers of sites and detailed consideration of eligibility requirements in order to meet primary objectives.

Clinical Trial Registration (Please input N/A if not registered)

Clinical Trial Registration: ACTRN12612000034831

ESP16-0590
26. OTHER

SALMONELLA ENTERICA SSP ARIZONAE INFECTION IN A 2-YEAR-OLD GIRL: A CASE REPORT AND REVIEW OF THE LITERATURE

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Title of Case(s)

Gastroenteritis from *Salmonella enterica ssp arizonae*

Background

Salmonella enterica ssp arizonae is an uncommon human pathogen with serious infections reported in immunocompromised hosts. *Salmonella enterica ssp arizonae* infections have been well described in patients from the southwestern United States, whereas in Europe only a few cases have been reported. Patients with this infection usually have a history of contact with reptiles, ingestion of rattlesnake products or travel abroad. We present a case of gastroenteritis caused by *Salmonella enterica ssp arizonae* and a review of the literature.

Case Presentation Summary

A 2-year-old Greek girl presented to our hospital with fever, diarrhea and signs of mild dehydration. A stool culture yielded *Salmonella enterica ssp arizonae*. The patient was not immunocompromised and the immunological tests did not reveal any immunodeficiency. She was treated with intravenous fluids and recovered completely.

Learning Points/Discussion

The prevalence of human infection due to *Salmonella enterica ssp arizonae* is probably underestimated, as the gastroenteritis that it causes is usually benign. However, this pathogen should be considered in the differential diagnosis of patients with severe gastroenteritis who have a history of contact with reptiles or ingestion of snake meat preparations. Young children and immunocompromised persons are at increased risk. Therefore, immune dysfunction should always be investigated when *Salmonella enterica ssp arizonae* is isolated. In Greece only two cases have been reported, the likely route of transmission remaining unclear.

ESP16-0622
26. OTHER

EBOLA VIRUS DISEASE; A PAEDIATRIC CASE REPORT AND REFLECTIONS FROM SIERRA LEONE

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Title of Case(s)

Lessons Learnt: Management of a four year old girl with Ebola Virus Disease in Sierra Leone

Background
West Africa is just emerging from the world's worst outbreak of Ebola Virus Disease. With mortality rates of up to ninety percent reported in infants and evidence emerging to support unique physiological differences in how children handle the virus we should take this opportunity to reflect on our knowledge and experiences in this epidemic to improve case management and prevent future outbreaks.

Case Presentation Summary
Four year old MK arrived at Kerrytown's Ebola Treatment Centre by ambulance with a history of fever, fatigue, joint, and muscle pains in addition to profound nausea and diarrhoea.

Her serum PCR confirmed the presence of the Ebola virus in her blood therefore she was admitted to the 'red zone' where her IV fluid resuscitation and ongoing care were complicated by the unique challenges of working in an Ebola Treatment Centre.

Initial blood results revealed a microcytic anaemia with a low platelet count and raised liver enzymes, characteristic of the disease. The significance of ongoing fevers and bloody diarrhoea proved difficult to interpret with limited diagnostic tools available and a high endemicity of pathogens causing both dysentery and fever. Guided by the World Health Organisation's Ebola Case Management Protocols, MK received broad-spectrum antimicrobials and nutritional supplementation to which she responded well. Her discharge was carefully prepared to ensure that the risk of onward transmission of the virus was minimised.

Learning Points/Discussion
This report describes the unique challenges of managing paediatric Ebola in the context of an outbreak. A discussion is stimulated on what can be learnt from these experiences to improve management of acute paediatric cases and the emerging complications presenting in survivors

ESP16-0363
26. OTHER

EPINEPHRINE VERSUS DOPAMINE AS FIRST LINE INOTROPE IN NEONATAL SEPTIC SHOCK: A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

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Background

The choice of vasoactive drugs in neonatal septic shock is not evidence based. We compared Epinephrine and Dopamine in neonatal septic shock to study reversal of shock in first 45 minutes of treatment.

Methods

This double-blinded, randomized controlled trial was conducted in level-III NICU in North India. We enrolled 40 neonates with fluid refractory septic shock in two gestational age strata- ≤$30^{6/7}$ and ≥$31^{0/7}$ weeks. Epinephrine or Dopamine was initiated at 0.2 or 10 µg/kg/min, respectively. Neonates were assessed after 15 minutes. If shock persisted, Epinephrine or Dopamine was hiked to 0.3 or 15 µg/kg/min respectively from 16-30 minutes and thereafter to 0.4 or 20 µg/kg/min from 31-45 minutes. Neonates were reassessed at 30 and 45 minutes. Our main outcome was reversal of shock by 45 minutes after starting study drug, which was defined as systolic and diastolic blood pressure >5^{th} centile and capillary filling time <3 sec and left ventricular output ≥150 mL/kg/min.

Results

Proportion of neonates achieving 'reversal of shock' by 45 minutes [5 (25%) vs 6 (30%), (p=0.6)], hemodynamic stability anytime during therapy [10 (50%) vs 6 (30%), (p=0.3)], or death within 28 days of life [14 (70%) vs 16 (80%), (p=0.7)] were comparable in Epinephrine and Dopamine groups, respectively. The change in heart rate, blood pressure and acid-base variables from baseline to 45 minutes of therapy was comparable. More neonates in ≤$30^{6/7}$ weeks stratum achieved hemodynamic stability in Epinephrine group [5/9 (56%)] compared to Dopamine group [0%], (p=0.03).

Conclusions

Epinephrine (0.2-0.4 µg/kg/min) and Dopamine (10-20 µg/kg/min) had comparable efficacy and safety in neonatal septic shock. More neonates ≤$30^{6/7}$ weeks achieved hemodynamic stability with Epinephrine.

Clinical Trial Registration (Please input N/A if not registered)

CTRI/2015/10/006285

ESP16-0831
26. OTHER

USE OF RANITIDINE ASSOCIATED WITH INFECTIONS IN NEWBORNS HOSPITALIZED IN AN NEONATAL INTENSIVE CARE UNIT

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Background

The inhibition therapy of gastric acid secretion with ranitidine is off-label prescribed in newborns admitted to neonatal intensive care units (NICU). There are some evidences showing that the suppression of gastric acidity in neonates predisposes to infections and increases the risk of necrotizing enterocolitis (NEC). This study aimed to compare the rates of hospital neonatal infections and NEC among preterm infants hospitalized in NICU exposed or not to treatment with ranitidine.

Methods

A prospective longitudinal observational study was conducted with consecutives infants observed in a NICU from August 2014 to October 2015. The rates of infection, NEC and death to all enrolled subjects exposed or not to ranitidine were recorded.

Results

A total of 300 infants were enrolled, of whom 115 had received ranitidine and 185 had not. There were no differences regarding the main demographic and clinical characteristics between the two groups (Table 1). Forty-eight (41.7%) of the 115 infants exposed to ranitidine and 49 (26.5%) of the 185 not exposed were infected (RR= 1.6, 95%CI 1.1-2.2, p=0.006). Sepsis rate was higher in the group exposed to ranitidine than in those not treated (24.3% vs. 3.8%). There was no significant association between the use of ranitidine and NEC (p=0.36). Mortality rate was significant higher in infants receiving ranitidine (16.5% vs. 8.6%). The risk of death was 4.1-fold higher in infants with infection (p<0.001).

Conclusions

Ranitidine use was associated with an increased risk of infections and mortality, but not with NEC. The use of ranitidine in neonates must be better evaluated and used only with real necessity.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-0172
26. OTHER

COMMON PRACTICE OF TOPICAL EMOLLIENTS AMONG THE YOUNG KIDS IN A DEVELOPING COUNTRY

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Background

Emollients are moisturizing treatments applied directly to the skin to reduce water loss and cover it with a protective film. However, all types of emollients are not good for skin especially for those young kids. Thus, we ought to understand the common practice and knowledge of the caregivers regarding the use of emollients.

Methods

In this cross sectional study, we took interviews of randomly selected 100 caregivers of <5 years children those were admitted at Dhaka Hospital of International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) in September, 2015. Predefined questionnaires were used to collect data on socio-demographic characteristics and practices of topical emollients to their children.

Results

All the caregivers (100%) use some kinds of emollients for their kids where 40% participants were from very low income group and 58% from low income. Among all, 60 (60%) used round the year whereas 40 (40%) only in winter. Application of emollients by the caregivers up to two times were frequent compared to those more than two times (80% Vs 20%). Seventy four (74%) caregivers used mustard oil and rest 26(26%) used the commercially available products. Without any evidence, 54 (54%) caregivers believed that the usages of emollients protected their kids from cold and 44(44%) believed that it was good for the skin.

Conclusions

The results of our study suggest that mustard oil was the most popular emollient among the caregivers with false belief of their benefit which underscore the importance of counseling of the caregivers to amend their current practice in order to avoid potential risk of adverse skin reactions of kids. However, randomized controlled clinical trial with larger sample may require consolidating or refuting our speculation.

ESP16-0488
26. OTHER

A RARE CONDITION: JUVENILE RECURRENT PAROTITIS OF TWO MONTH OLD BOY

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Title of Case(s)

A RARE CONDITION: JUVENILE RECURRENT PAROTITIS OF TWO MONTH OLD BOY

Background

Juvenile recurrent parotitis (JRP) is a rare, nonobstructive, non-neoplastic, nonsuppurative parotid inflammation characterized by recurrent episodes in young children. Herein, we report a case of two-month-old boy with of repeated episodes of the parotid gland swelling.

Case Presentation Summary

A 2-month-old boy admitted to hospital with a swelling near the left ear. On intra-oral examination, there was no evidence of any swelling or lesion. Extra-oral examination showed a swelling in the left preauricular region with mild erythema. He had no fever. His medical history revealed 2-3 similar episodes of swelling on same side of his face. Ultrasound of salivary gland showed a normally sized left parotid gland,with heterogeneous echogenicity and increased blood flow when compared to right parotid gland. Ampicillin-sulbactam was started for suspected infectious parotitis and continued for 7 days. After treatment, swelling of the parotid gland reduced and the patient was discharged without any sequelae.

Learning Points/Discussion

Juvenile recurrent parotitis affects commonly children. Antibiotics, analgesics, massage and hydration may be helpful in reducing the symptoms and attack frequency. Although presenting symptoms usually begin between the ages of 3 to 6 years, it should kept in mind that JRP can be occuredin younger children.

ESP16-0223
26. OTHER

FACTORS ASSOCIATED WITH MORTALITY OUTCOMES IN NEONATAL SEPTICEMIA IN SRINAGARIND HOSPITAL, THAILAND

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Background

Neonatal septicemia is a major cause of infant death worldwide. early detection and management of the factors associated with neonatal mortality outcomes are necessary to prevent life-threatening complications and death.
The objective of this study was to determine the risk factors for mortality in neonatal septicemia.

Methods

This is retrospective case- control study was conducted in Srinagarind Hospital, Khon Kaen, Thailand. the study considered the demographics, laboratory results, and clinical features for a total of 133 patients during the period May 2005- September 2010. Thirty four out of these patients died from their condition.

Results

Investigation of neonatal and maternal demographics found that the use of a central line catheter, low Apgar scores, comorbidity , VLBW (<1500 grams), prematurity, EOS, PROM, and delivery in other hospitals, were all significantly associated with fatality. Laboratory results showed that hyperglycemia, thrombocytopenia, hyponatremia, and acidosis were significant contributors to fatality. Among all clinical features, apnea, jaundice, lethargy, and poor feeding, were significantly associated with fatality. Gram-negative and mixed gram negative/ gram- positive bacteria were frequently isolated from dead septicemic neonates. *E. coli* was most common bacteria isolated from dead septicemic neonates (23.8%) followed by *Klebsiella* spp. (20.6%), *Enterobacter* spp.(20,6%), *Acinetobacter* spp. (17.6%), and *Pseudomonas* spp. (14.7%).

Conclusions

Early detection and management of these associated factors are necessary to prevent severe life threatening complications and death in neonatal septicemia. strict infection control measures remain the mainstay in the management of the multidrug resistant bacterial infections in neonates.

Clinical Trial Registration (Please input N/A if not registered)

ESP16-1032
26. OTHER

PREVENTING AND CONTROLLING INFECTIOUS DISEASES AFTER NATURAL DISASTERS

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Title of Case(s)

PREVENTING AND CONTROLLING INFECTIOUS DISEASES AFTER NATURAL DISASTERS

Background

Contaminated drinking water as a result of natural disasters -flood and landslides is a common cause of infectious diseases with the children.The study involves 5 populated rural areas from one region Tetovo-Macedonia affected by flood and landslides on August 3, 2015. Affected were part of the 2826 residents of the Shipkovitsa, 3977 Great Rechica, 8353 Small Rechica the 2899 from the Poroj and Tetovo which counts 52,915 inhabitants. More than 30% of them are children Floods and landslides were with tragic consequences that killed 6 people including 1 child.

Case Presentation Summary

Results: In flood and landslides on August 3, 2015 were affected residents of 5 villages from the Tetovo region of Macedonia, with a total of 70 970 inhabitants, of which 30% are children 21 291.Floods and landslides killed 6 people including 1 child. Immediately after the natural disaster preventive measures were taken to reduce the occurrence of an infectious disease. Prohibit the use of drinking water, the population was divided bottled water and water tanks. The inhabitants were trained about some hygienic and epidemiological measures. Flooded houses were cleaned and disinfected. Dead livestock was remove and terrain was clean. Due to the timely take measures from the competent authorities' diarrhea and vomiting symptoms appeared only 35 people- 0.05%, and hepatitis A later appeared only 5 people.

Learning Points/Discussion

Conclusion: Preventive measures are very important part in reducing the risks of infectious diseases with timely activities before disaster stricken. Education the inhabitants with epidemiological measures are also the most important part from the competent authorities.

ESP16-0544
26. OTHER

PNEUMATOSIS oF THE INTESTINE AS A COMPLICATION OF ACUTE DIARRHOEA

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Title of Case(s)

Pneumatosis of intestinal wall as a complication of acute diarrhea.

Background

Pneumatosis of intestinal wall is the most often described in the course of necrotic enterocolitis in premature infants and during graft versus host reaction. There is not a lot works about this complication in the course acute diarrhea.

Case Presentation Summary

The aim of the study was evaluation of the course and analysis factors affecting on occurrence of pneumatosis of intestine in the course of acute diarrhea.

Patients and method. 10 children, aged from 7 months to 6 years, 5 girls and 5 boys, treated in Department of Paediatrics in Katowice, in the years 2011-2015 due to acute diarrhea were analysed. Ultrasonography of the abdomen in which we have found pneumatosis of intestine was done in all children. Gestational and labour history, clinical symptoms and results of the laboratory tests were evaluated.
Results. Bloody diarrhea has dominated in the clinical picture in 8/10 examined children (80%).Burdening gestational and labour history was observed in 5 patients. NEC in history was found in 2/10 children. Rotavirus infection was diagnosed in 7/10 patients. Klebsiella pneumoniae was cultured in the stool of 3/10 children. We diagnosed IgE-dependent food allergy (on cow`s milk protein and egg`s protein in older group) in 4 children and deficiency of immunoglobulins in 2 children. We ordered in all patients antibiotic therapy, total parenteral nutrition, with improvement of general condition, disappearance of symptoms and pneumatosis of intestine in ultrasonography examination.

Learning Points/Discussion

We present rare cases of complication of acute diarrhea - intestinal pneumatosis, which we have observed the most often in the youngest children (age below 6 months). The risk factors were burdening gestational and labour history, low birth body mass and coexistence of food allergy.