adverse events of interest requires consideration of how these may present in neonatal/paediatric patients.

Conclusions In order to support the protocol development with regards to neonatal/paediatric drug safety a dual competence in both paediatrics and drug safety is required. This review provides an overview of the practical aspects related to neonatal/paediatric drug safety during protocol development.

Disclosure(s) Nothing to disclose

P12 PUBLIC ANTIBIOTIC AWARENESS CAMPAIGN ORGANISED BY GOVERNMENT SIGNIFICANTLY REDUCED INAPPROPRIATE ANTIBIOTIC USE IN PAEDIATRIC PRIMARY CARE SETTINGS

Serbia, like most other countries in southern Europe, has struggled with high rate of antibiotic consumption. Previous results showed that most of antibiotics were prescribed inappropriately, mainly for influence - like illness. The first short term media antibiotic awareness campaign (AAC) was held in 2011. and 2014. respectively. Shortly after, Ministry of Health, Republic of Serbia in November 2015 has started with public AAC simultaneously across all regions of Republic of Serbia.

Apart from media, the campaign included education, producing national guidelines, as well as regulations. The education goals for public (preschool and school children, parents, pregnant women, students) and healthcare professionals (paediatricians, nurses, pharmacists, etc.) was based on results of analysis of antibiotic consumption in children from 2007 to 2014. which methodology was published previously. Media campaign included public relations activities, press conferences, billboards, printed materials, etc.

In 2017, prescribing rates of antibiotics per 1000 children in primary care settings were decreased by 18% comparing to 2011., after first and by 12% comparing to 2014. when second short term media campaign was performed. After the third, government organised public AAC, prescribing rates of antibiotics per 1000 children in primary care settings were decreased by 6% for only one year (2017 vs. 2016) in all age groups from 2 months up to 17 years. Significant decrease of prescribed rate of antibiotics per 1000 children during 2017. was recorded for indication with policy of delayed or no antibiotic prescription recommended by guidelines. Seasonal oscillations showed that highest prescribing rate during the winter months (I and the IV quarter) of 2017. in line with the lowest prescribing rate during the summer months (II and the III quarter) from 2007. up to 2013.

We can conclude that continuous antibiotic awareness campaign supported by state government is the best way to achieve successful results.

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Disclosure(s) Nothing to disclose

P13 SERIOUS ADVERSE REACTIONS AND OFF LABEL AND UNLICENSED DRUG USE IN CHILDREN – DECADE OF PHARMACOVIGILANCE STUDY IN SERBIA

Background Off label (OL) and unlicensed (UL) drug use in children is a widespread global problem. Previous study showed that only 66% of all available drugs for children is with licence in Serbia. Data on safety of medicines in children remain lacking, so the key intervention for the effective use of medicine is safety monitoring. Therefore, the aim of this study is to evaluate safety implication of OL and UL drug use in children up to 12 years old.

Method We conducted a retrospective study based on reports of suspected adverse reactions (ADRs) collected from 2008. to 2018. by Medicines and Medical Devices Agency of Serbia, using the Medical Dictionary for Regulatory Activities and organized by System Organ Class. Sources of information about medicines including vaccines (license, drug formulation, etc.) are the Summary of Product Characteristics and Serbia’s official drug registry.

Results Within 10 years, we observed 1595 ADRs. Vaccines, antineoplastic and antimicrobial drugs were the most frequently pharmacotherapeutic subgroups involved. Out of total number of observed ADRs, 433 (28%) were serious; 189 of them led to hospitalization, 31 to life threatening conditions and 7 were fatal. More than a half (63%) of serious ADRs were detected in children for the age group of 28 days - 23 months, followed by the age group of 2 to 11 years (34%) and finally by age group of 0 to 27 days (3%). Serious ADRs were detected in boys (55%) as well as in girls (45%). Out of total number of registered only 3% (46) of ADRs were associated with off-label use; 18 of them were serious, 7 led to life threatening conditions and 3 were fatal.

Conclusion This research provided new insight on the factors such as OL and UL use, that might increase the risk of serious ADRs in children.

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Disclosure(s) Nothing to disclose

P14 PHARMACOVIGILANCE IN PEDIATRIC PATIENTS: THE CHALLENGE OF IDENTIFYING NEW SIGNAL

Introduction The importance of reporting adverse drug reactions (ADRs) is well known. However, the reporting rate is very low, and therefore, identifying new signal is challenging.

Objective To create an interventional program in order to improve reporting rate and trying to identify new signal.

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Disclosure(s) Nothing to disclose
Material and methods The interventional program was implemented at the Pediatric Division of Assaf Harofeh Medical Center and included presentations to the healthcare professionals, posters, creating new ADRs reporting methods and alerts.

Results Reporting rate of ADRs during the year before implementation of the program was negligible. During the study period (three months), the reporting rate increased dramatically. A new signal was reported; two neonates with apnea related to IVIG administration in the neonatology department. The distribution of reports was: 50% from the general pediatric department, 26% - pediatric neurology department, 21% and 6%, from the pediatric and neonatal intensive care units, respectively. Steroids and antibiotics were responsible for various ADRs, but not for a new signal.

Conclusion There is one case report in the literature on apnea related to IVIG administration. Adverse reactions in children are a major problem and sometimes can lead to morbidity mortality. Identifying new signal in pediatric patients is not common, and very challenging.

Disclosure(s) Nothing to disclose

P15 LACOSAMIDE MONITORING IN THE SERUM OF CHILDREN WITH REFRACTORY EPILEPSY

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Background Lacosamide is indicated for various types of refractory epilepsy and as adjunctive therapy to other antiepileptic medications. Data on monitoring serum levels of lacosamide in pediatric patients is scarce.

Objective To evaluate the correlation between serum levels of lacosamide and the tolerability in children with refractory epilepsy.

Methods The medical records of 22 children with refractory epilepsy treated with lacosamide at Assaf Harofeh Medical Center were reviewed. Through serum levels of lacosamide was measured using HPLC and correlated with its efficacy and safety.

Results Mean age of the children was 11 ± 4 (3–18) years. Median lacosamide daily dose was 9.3 (6.6–11.9) mg/kg and median plasma concentration was 7.1 (5.9–11.9) µg/ml. The therapeutic range of lacosamide serum concentration is 10 to 20 µg/ml. No change in seizures frequency was reported in 21.4% of children with lacosamide concentrations below 10 µg/ml. However, in 40% of the children, reduction of the seizures frequency was reported when serum concentration was above 10 µg/ml. No serious adverse events were reported during therapy. The prospective part of the study was initiated, and the first patients were recruited.

Conclusion Large studies, preferably prospective, on lacosamide serum monitoring including information on correlation with efficacy and safety are warranted.

Disclosure(s) Nothing to disclose

P16 TOWARDS DETERMINATION OF ENDOGENOUS PRORENIN IN PAEDIATRIC SAMPLES USING A HYBRID APPROACH – IMPACT OF ANTIBODY SELECTION FOR IMMUNOCAPTURE

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Background Since sample volume is limited in children, innovative bioanalytical methods and enrichment procedures are highly required. The analysis of endogenous substances by liquid chromatography coupled to mass spectrometry is a highly specific method because of its selectivity and accuracy. However reliable detection of endogenous substances can only be achieved by a hybrid assay approach combining immunocapture and mass spectrometry. Key element of the immunocapture procedure is the selection of the appropriate antibody for capturing the desired antigen. This study is meant to identify the most suitable antibody that facilitates the development of an hybrid assay approach concerning reliable detection of endogenous prorenin in paediatric samples.

Methods Dynabeads magnetic beads were coupled to three different antibodies from three different vendors (GeneTex, Molecular Innovations, R&D systems). 500 µL human plasma which was spiked with 20 ng recombinant human prorenin (Cayman chemicals). The immunocapture step was followed by protease digestion and a custom-made elution solid-phase extraction protocol. The digest was analyzed by Shimadzu Nexera LC-system coupled with Sciex TripleTOF 6600 mass spectrometer.

Results The analysis of the captured prorenin was performed by the surrogate peptide approach. In this case the surrogate peptide was identified as unique. The comparison of the three available antibodies showed that one antibody did not ensure reliable binding properties in human matrix. Among the two remaining antibodies only one showed sufficient binding capacities to be applied in small sample volumes commonly available in paediatric samples. Using this hybrid approach enabled the enrichment of the required volume by factor of 20.

Conclusion This study identified the most suitable antibody for the immunocapture procedure of the prorenin hybrid approach. This is now followed by further mass spectrometric method development and validation prior to its application in paediatric samples.

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