Disclosure(s) Nothing to disclose

P86 TREATMENT MODALITIES IN PERIPHERAL FACIAL NERVE PALSY IN CHILDREN AND ADOLESCENTS

^{1,2}J Samardžić*, ³B Kukolj, ³M Jovanović, ⁴O Djurić, ⁵J Jancić. ¹Institute of Pharmacology, Clinical Pharmacology and Toxicology, Medical Faculty, University of Belgrade, Belgrade, Serbia; ²Division of Paediatric Pharmacology and Pharmacometrics, University of Basel Children's Hospital, Basel, Switzerland; ³Medical Faculty, University of Belgrade; ⁴Institute of Epidemiology, Medical Faculty, University of Belgrade; ⁵Clinic of Neurology and Psychiatry for Children and Youth, Medical Faculty, University of Belgrade, Belgrade, Serbia

10.1136/archdischild-2019-esdppp.124

Background Bell's palsy is the most common type of peripheral facial palsy in pediatrics. Recent studies strongly support the combined therapy with corticosteroids (CS), antiviral drugs and vitamins B. Our study aims to assess the effectiveness of proposed therapeutic modalities, including the relation between the patients' recovery and their age, etiological factors and applied treatment.

Methods The retrospective analysis involved 88 patients (52 females/36 males), between 18 months and 18 years old; the average age was 11.7 years. Data was obtained from the documentation of patients hospitalized at the Clinic of Neurology and Psychiatry for Children and Youth in Belgrade, from 2000 to 2017. House Brackmann's scale was used for the assessment of disease course and outcome. Pearson's χ^2 test, Friedman's test and general linear model were applied for statistical data processing.

Results The majority of patients were treated with combined CS/vitamins (42.0%) and CS/antiviral/vitamins (17.0%), whereas CS only received 22.7% of patients, all with an appropriate physical treatment. The group of idiopathic paralysis makes 62.5%, while the incidence of symptomatic paralysis is 37.5%; however, the recovery rate between these groups has not been shown ($p=0.309$). Patients received CS therapy were divided into 4 groups: CS only, CS+antiviral, CS+vitamins B, and CS+antiviral+vitamins B. The statistically significant recovery was registered in each group ($p<0.001$); however, no difference was found between the groups in term of recovery rate ($p=0.865$). For the assessment of recovery period in relation to the age, the obtained p value was 0.054, a borderline level, suggesting a faster recovery of children at younger age.

Conclusion The acute one-sided mimic musculature weakness is mostly idiopathic. The effectiveness of the CS therapy was strongly supported, suggesting CS as a core treatment for the Bell's palsy. It has been shown the faster recovery of children at younger age.

Disclosure(s) Nothing to disclose

P87 THE SWISS ASSOCIATION OF PERINATAL PHARMACOLOGY, SAPP: GOALS

L Schenkel*, U von Mandach, The Editorial Board of the SAPP. *Obstetrics, University Hospital of Zurich, Zürich, Switzerland*

10.1136/archdischild-2019-esdppp.125

Background The medicine of pregnant women practices to a targeted personalized approach, tailored to the specific characteristics and needs the implications of interdisciplinary work between healthcare stakeholders. *Perinatal pharmacology*

comprises the impact of substances (drugs, medications and others) in pregnant women, nursing mothers, the unborn child, the premature, the newborn baby and the breastfed baby. Most of the drugs are off-label used. In this field grand challenge for Frontiers in Medicine emphasizes the importance of translational medicine.

Aim The primary goal of SAPP has always been and remains the same: it is the link between medicine and pharmacy, between practice, clinic, research and health authorities, in order to increase the safety of medicines in the population of pregnant and breastfeeding women and their newborns.¹

Methods On December 6, 2007, an interdisciplinary team of 8 physicians and pharmacists founded the Swiss Association of Perinatal Pharmacology, SAPP. It collects and promotes new findings in the field of perinatal pharmacology.

Results Specialists from all areas of perinatal pharmacology work together in a scientific committee to develop and update evidence-based principles for work in everyday clinical practice (hospitals, doctor's surgeries, pharmacies). Today, around 200 members benefit from this, who can orient themselves in regular further training courses and basic documents (monographs of active substances, therapy recommendations based on original literature). The SAPP thus closes the gap resulting from the predominant off-label use and the resulting lack of information on drugs in this population.

Conclusion The primary objective of SAPP has been achieved - it provides guidance for the practitioners in the broad field of perinatal pharmacology and bridges the gap caused by the lack of drug approvals in this population. Long-term survival will be ensured by measures anchored in law.

REFERENCE

1. www.sappinfo.ch

Disclosure(s) Nothing to disclose

P88 THE POTENTIAL IMPACT OF HEMATOCRIT CORRECTION ON EVALUATION OF TACROLIMUS TARGET EXPOSURE IN PEDIATRIC KIDNEY TRANSPLANT PATIENTS

¹A Schijvens*, ¹F van Hesteren, ¹M Cornelissen, ¹C Bootsma-Robroeks, ²R Brüggemann, ²D Burger, ^{3,4}S de Wildt, ¹M Schreuder, ²R ter Heine. ¹Pediatric Nephrology, Radboud University Medical Center, Radboud Institute for Molecular Life Sciences, Amalia Children's Hospital; ²Pharmacy; ³Department of Pharmacology and Toxicology, Radboud University Medical Center, Radboud Institute for Health Sciences, Nijmegen; ⁴Intensive Care and Department of Pediatric Surgery, Erasmus MC Sophia Children's Hospital, Rotterdam, The Netherlands

10.1136/archdischild-2019-esdppp.126

Background Tacrolimus is an important immunosuppressive agent with high intra- and interindividual pharmacokinetic variability and a narrow therapeutic index. As tacrolimus extensively accumulates in erythrocytes, hematocrit is a key factor in the interpretation of tacrolimus whole blood concentrations. However, as hematocrit values in pediatric kidney transplant patients are highly variable after kidney transplantation, translating whole blood concentration targets without taking hematocrit into consideration, is theoretically incorrect. The aim of this study is to evaluate the potential impact of hematocrit correction on tacrolimus target exposure in pediatric kidney transplant patients.

Methods Data were obtained from 36 pediatric kidney transplant patients. 255 tacrolimus whole blood samples were

available, together responsible for 36 area under the concentration time curves (AUCs) and trough concentrations. First, hematocrit-corrected concentrations were derived using a formula describing the relationship between whole blood concentrations, hematocrit, and plasma concentrations. Subsequently, target exposure was evaluated using the converted plasma target concentrations. Ultimately, differences in interpretation of target exposure were identified and evaluated.

Results In total, 92% of our patients had a lower hematocrit (median 0.29) than the reference value of adult renal transplant patients. A different evaluation of target exposure for either trough level, AUC or both, was defined in 42% of our patients, when applying hematocrit corrected concentrations.

Conclusion A critical role for hematocrit in therapeutic drug monitoring of tacrolimus in pediatric kidney transplant patients is suggested in this study. Therefore, we believe that hematocrit correction could be a step towards improvement of tacrolimus dose individualization.

Disclosure(s) All authors declare that they have no conflict of interest. This work was recently accepted for publication in Pediatric Nephrology. We are aware of the statement in the guideline about previously published work, however as we believe that this work suits the aim and topics of the congress very well, we chose to submit this work and will ofcourse leave the final decision to you.

P89

EMICIZUMAB DEVELOPMENT IN PAEDIATRIC PATIENTS WITH CONGENITAL HEMOPHILIA A AND INHIBITORS AGAINST FACTOR VIII

¹C Schmitt*, ²K Yoneyama, ³T Chang, ⁴S Retout, ⁵H -P Grimm, ³GG Levy. ¹F. Hoffmann-La Roche Ltd, Basel, Switzerland; ²Chugai Pharmaceutical, Tokyo, Japan; ³Genentech, San Francisco, CA, USA; ⁴F. Hoffmann-La Roche Ltd, Paris, France; ⁵F Hoffmann-La Roche Ltd, Basel, Switzerland

10.1136/archdischild-2019-esdppp.127

Background Emicizumab, a bispecific monoclonal antibody, bridges activated factor (F) IX (FIXa) and FX, restoring missing FVIIIa function in patients with hemophilia A (PwHA). It has been recently approved for routine prophylaxis of bleeding episodes in PwHA with FVIII inhibitors in all age groups. We herein describe the paediatric development of emicizumab with a focus on dose selection, study design and extrapolation of efficacy.

Methods The dosing regimen for the HAVEN 1 study (adolescents/adults) was selected based on the exposure-response (annualized bleeding rate [ABR]) relationship derived from a phase I/II study in adolescent/adult PwHA. Pharmacokinetic (PK) simulations, with or without maturation of clearance (CL MAT), were performed to guide selection of the dosing regimen for the HAVEN 2 study (paediatrics) aiming to achieve the same target exposure as in HAVEN 1. HAVEN 2 employed a flexible design with possibility for individual- and population-level dose up-titration. Additional PK modeling and simulations together with exposure-response analyses were used to support full extrapolation of efficacy in any age category where no data was available.

Results 1.5 mg/kg/week in HAVEN 1 provided mean trough concentrations of ~50 µg/mL and was associated with a 87% reduction in ABR. Doses of ≥ 1.5 (with CL MAT) and ≥

2.25 mg/kg/week (without CL MAT) were predicted to achieve this target exposure in children. HAVEN 2 began by investigating the same dose as HAVEN 1. Similar trough concentrations of ~ 50 µg/mL were achieved in children and were associated with low ABR. No patients < 1 year were enrolled in HAVEN 2. PK simulations and pharmacological rationale suggested that a different dose for these patients was not warranted.

Conclusions Efficacy of emicizumab in adolescents/adults was demonstrated in HAVEN 1, partially extrapolated to HAVEN 2 participants 1–11 year of age, and fully extrapolated in patients < 1 year.

Disclosure(s) Authors are Roche/Genentech employees

P90

NEUROPSYCHIATRIC DISORDER AND MONTELUKAST: A CASE REPORT AND VIGIBASE® ANALYSIS

^{1,2}I Scholz*, ^{1,3}S Banholzer, ^{1,3}M Haschke. ¹Clinical Pharmacology and Toxicology, Department of General Internal Medicine, Inselspital Bern, Institute of Pharmacology, University of Bern; ²Institute of Pharmacology, University of Bern; ³Institute of Pharmacology, University of Bern, Switzerland, Bern, Switzerland

10.1136/archdischild-2019-esdppp.128

Learning objective Recognize neuropsychiatric symptoms as possible adverse drug reactions (ADR) associated with the leukotriene receptor antagonist Montelukast in children

Clinical Case An 11-year-old boy suffering from asthma presented to his pediatrician with an acute onset of nervousness, restlessness and irritability. The teacher noticed a decline in school performance with a reduced attention span. The patient had been treated with Salbutamol (Ventolin®) and Salmeterol/Fluticasone (Seretide®) for the last few years. A treatment with Montelukast chewable tablets was started four months ago. The ADR was reported to the Regional Pharmacovigilance Centre (RPVC) Bern. The termination of the therapy with Montelukast lead to an amelioration of the symptoms. According to the WHO-UMC Causality Categories,¹ the causality of Montelukast and the described symptoms was classified as 'probable'. The causality of the comedication was considered 'unlikely' as it had been used for several years without complications. After work-up at the RPVC, the case was reported anonymously to the National Pharmacovigilance Center of the Swiss Agency for Therapeutic Products Swissmedic.

Discussion Montelukast is a cysteinyl-leukotriene type 1-receptor antagonist used in the treatment of bronchial asthma in adults and children. Psychiatric disorders such as agitation, psychomotor hyperactivity (including irritability and restlessness), disorders of attention and memory impairment (and others) are listed as known ADRs of Montelukast.²⁻³ The WHO pharmacovigilance database VigiBase® lists a total of 20'897 ADR reports for Montelukast, of which 4'705 (22.5%) refer to nervous system disorders and 6'828 (32.7%) to psychiatric disorders. Within the group of nervous system disorders 256 (5.4%) reports of psychomotor hyperactivity, 232 (4.9%) reports of disturbance in attention and 91 (1.9%) reports of memory impairment were recorded.⁴ The most common symptoms in the group of psychiatric disorders are depression (1'311, 19.2%) and aggressive behavior (1'175, 17.2%). If psychiatric ADRs occur, the risks and benefits of Montelukast should be reassessed.