(Spearman's 0.151, p=0.0377) between QTc-Bazett and plasma phosphate.

Conclusions QTc-Bazett intervals are not significantly different between former preterm and/or ELBW cases and term-born controls, and we rejected a potential prolongation >10 ms in cases. When prescribing QTc prolonging drugs, pharmacovigilance practices in this subpopulation should be similar to the general public.

D) Session 6: Drugs in Special Populations and Settings II: Pharmacology of ECMO and other Extracorporeal Devices

11 MICRODOSED YOHIMBINE AS CYP2D6 PROBE DRUG IN PEDIATRIC HEART PATIENTS AGED 6 MONTHS TO 6 YEARS

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Introduction A safe and effective drug therapy for children requires a fundamental understanding of the role of ontogeny in the pharmacokinetics (PK) and pharmacodynamics of drugs. Age-associated developmental changes in body composition and organ function are dynamic and profoundly affect the response to medications, requiring age-dependent dose adjustments. CYP2D6 is involved in the metabolism of psychotropic drugs as well as beta blockers. The maturation of CYP2D6 during early infancy has been described by being present at 1 week of age, increasing to 20% of adult activity by the age of 1 month, and reaching adult capacity by 3–5 years of age. In addition, genetic polymorphisms can contribute to variations in the expression of CYP2D6 activity, thus suitable probe drugs are evaluated for phenotyping. Yohimbine is a plant-derived indole alkaloid and alpha-2 receptor antagonist. It is metabolized to 11-OH-yohimbine by CYP2D6. The objective of this analysis was to characterise CYP2D6 activity by means of a yohimbine microdose in young children.

Methodology A single-center, open label, fixed-sequence clinical trial primarily evaluating a microdosed anticoagulant cocktail (EudraCT 2019-001759-38) was conducted in children aged 6 months-6 years (body weight >7 kg) after congenital heart surgery. Yohimbine (25 µg p.o.) was used as probe drug to determine CYP2D6 activity. Plasma concentrations over 12 h were quantified by UHPLC-MS/MS. The PK of 14 patients were compared with data of 10 healthy adult volunteers who had received 50 µg Yohimbine p.o. in a previous study.

Results The mean age of the 14 children (6m/8f) was 1.9 (0.5–4.9) years and mean body weight was 10.9 (7.2 –18.2) kg. All patients received concomitant treatment per standard of care. Oral clearance was 167 (95% CI 147–326) mL/min, Volume of distribution was 16.8 (95% CI 13.4–31.9) L. T1/2 was 1.2 (95%-CI 1.0–1.4) h. Cmax was 2757 (95% CI 2028–5249) pg/mL. AUC0-inf was 2500 (95% CI 53–10100) h*pg/mL. PK profiles were similar to those in adults.

Conclusion This small cohort delivers first, preliminary information on the PK of Yohimbine in young children up to 6 years of age. The application of a 25 µg microdose together with highly sensitive analytical methods is a safe and effective methodology to assess CYP2D6 activity in vulnerable pediatric populations. Yohimbine seems to be a suitable candidate as probe drug for CYP2D6 phenotyping in children, which should be evaluated in a larger cohort.

12 MEDICAL CANNABIS FOR CHILDREN WITH AUTISTIC SPECTRUM DISORDER: IS THERE A DIFFERENCE BETWEEN THOSE TREATED WITH CANNABIS AS MONOTHERAPY VS THOSE TREATED WITH CANNABIS AND CONCOMITANT CONVENTIONAL MEDICATIONS?

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Background Use of medical cannabis in pediatrics is increasing. A number of trials have investigated the efficacy and safety of medical cannabis for the treatment of co-morbid symptoms in children with ASD (Autistic Spectrum Disorder). Many of these children are treated with conventional medications.

Objective To compare the efficacy of cannabis monotherapy vs cannabis with concomitant conventional medications in children with ASD.

Methods Children with ASD were treated with cannabis oil at Shamir Medical Center. They underwent evaluation with trained speech therapist (ADOS) and psychologist (WPPSI). Parents and teachers filled questionnaires (Vineland, Conners, sleep, eating) at baseline and after 6 months of treatment.

During biweekly telephone follow-up, dosage was adjusted as per parents' report, which included physical and behavior parameters- appetite, anxiety, aggression, sleep and compulsive behavior.

Laboratory values, efficacy and dosage of medical cannabis were compared between both groups of children.

Results Out of 81 patients, 30 received concomitant medications. Cannabis dose did not differ significantly between both groups. There were no significant differences in the laboratory values for both groups. Parents of children with cannabis monotherapy reported a significant improvement in aggressive behavior (p=0.027), anxiety (p=0.023) and coping with changes (p=0.036). In the group of patients with concomitant treatment, there was a significant improvement in sleep quality (p=0.029).

Conclusions Medical cannabis is probably effective in reducing co-morbid symptoms in children with ASD. However, whether treatment with cannabis as monotherapy is superior to treatment with conventional drugs for co-morbidities warrants further investigation.