PHARMACOKINETICS OF PROPHYLACTIC AND THERAPEUTIC FLUCONAZOLE IN PRETERM NEONATES

A Engbers*, 1FRB Flint, 1LS Völker, 1KMR Reiss, 1KD Liem, 6PL Degaeuwé, 7P Andriessen, 6IWC Alffenaar, 8SHP Simons, 6CAl Knibbe, 6R Brüggemann, 1Systems Biomedicine and Pharmacology, Leiden Academic Centre for Drug Research, Leiden University, Leiden; 2Department of Paediatrics, Division of Neonatology, Erasmus MC – Sophia Children’s Hospital; 3Department of Hospital Pharmacy, Erasmus Medical Center, Rotterdam; 4BioTherapeutics, Leiden Academic Centre for Drug Research, Leiden University, Leiden; 5Department of Neonatology, Radboud University Medical Center, Nijmegen; 6Department of Paediatrics, Division of Neonatology, Maastricht University Medical Center, Maastricht; 7Department of Neonatology, Maxima Medical Center, Veldhoven; 8Department of Clinical Pharmacy and Pharmacology, University Medical Center Groningen, Groningen; 9Department of Clinical Pharmacy, St Antonius Hospital, Nieuwegein; 10Department of Hospital Pharmacy, Radboud University, Nijmegen, The Netherlands

Introduction Flucanazole is a first choice drug for neonatal cerebral candidiasis and for prevention of candidemia/invasive candidiasis in neonates. Selection of the optimal neonatal dose is difficult and requires solid multiple dose pharmacokinetic (PK) research to guide dosing decisions. We performed a pharmacokinetic study in preterm neonates who received flucanazole prophylactically or as treatment.

Methods Preterm neonates received flucanazole according to local protocol for either prophylaxis or treatment in 5 different hospitals. Samples were collected on multiple occasions with an opportunistic sampling scheme. Patient characteristics were bodyweight, birthweight, postnatal age (PNA), gestational age (GA), postmenstrual age, gender and weight for age. Population PK modelling was performed using NONMEM V7.3.

Results In 44 preterm neonates (median (range) GA 25.3 (24.0–31.3) weeks), 153 plasma samples were collected. Median PNA at treatment initiation was 1 (0–59) day, treatment duration 11 (2–67) days and median PNA during treatment 15 (4–60) days. A one-compartment model described the data best, with an estimated clearance (CL) for a neonate of 0.815 L (RSE 5.9%). Bodyweight was found to influence interindividual variability 21.4%) and volume of distribution of 0.84 kg and PNA of 15 days of 0.0147 L/h (RSE 4.3%, respectively. Maturation of CL was best described by an exponent of 0.184 on PNA (RSE 22.4%), respectively. Maturation of CL was best described by an exponent of 0.184 on PNA (RSE 34.3%).

Conclusion In this pharmacokinetic study on flucanazole in preterm neonates, CL was influenced by both bodyweight and PNA while Vd was influenced by bodyweight only. These findings imply that initial dosing of flucanazole in preterm neonates should be based on bodyweight and that an increase of the dose with 32% during the first week and with 47% during the first month of life could be necessary because of increasing clearance with PNA.

Disclosure(s) Nothing to disclose

DRUG DELIVERY KINETICS OF INTRAVENOUS GENTAMICIN IN A POPULATION OF NEONATES

G Salis*, 1NM Medlicott, 1DR Reith. 1Women’s and Children’s Health; 2New Zealand’s National School of Pharmacy, University of Otago, Dunedin, New Zealand

Background Gentamicin is commonly used in the NICU setting and is often administered via long lines, which increases variability in the rate of administration. We aimed to model drug delivery pharmacokinetic parameters for intravenous gentamicin administered via umbilical venous catheters (UVCs).

Methods Data was modelled from infusion simulations of gentamicin delivery using UVCs with a background flow rate of 0.5 mL/h.1 Different combinations of dose (2 mg, 5 mg) were given by bolus injection over 3–5 minutes, followed by a normal saline flush (1 mL, 2 mL). Gentamicin levels were measured at 5 minute intervals over an hour via high pressure liquid chromatography.

Results Data was modelled from infusion simulations of gentamicin delivery using UVCs with a background flow rate of 0.5 mL/h.1 Different combinations of dose (2 mg, 5 mg) were given by bolus injection over 3–5 minutes, followed by a normal saline flush (1 mL, 2 mL). Gentamicin levels were measured at 5 minute intervals over an hour via high pressure liquid chromatography.

Conclusion This is the first known modelling of gentamicin delivery kinetics. The studies all had high nshrinkage for Ka, therefore the individual estimates of ka may be unreliable. Further studies with a higher number of replicates would provide more valuable data for estimating Ka.

REFERENCE

Disclosure(s) No conflict of interest declared. Funding for research via the Freemasons Society of New Zealand.

EFFECT OF HEMODIALYSIS DOSE (SPKt/V) ON SURVIVAL IN PATIENTS ON MAINTENANCE HEMODIALYSIS SINCE CHILDHOOD – A RETROSPECTIVE ANALYSIS

Gotta*, 3A Atkinson, 3O Marsenic, 3M Pfister. 1Pediatric Pharmacology and Pharmacometrics, University Children’s Hospital Basel (UKBB); 2Hospital Pharmacy, University Hospital Basel; 3Pediatric Pharmacology and Pharmacometrics, University Children’s Hospital Basel (UKBB), Basel; 1Department of Infectious Diseases, University Hospital Bern, Bern, Switzerland; 1Pediatric Nephrology, Yale University School of Medicine, New Haven, CT, USA

Background Hemodialysis (HD) prescription significantly differs between pediatric and adult patients on maintenance HD, resulting in greater difference between prescribed and delivered HD dose.1,2 HD dose targets have formally not been evaluated for children, hence targets are mainly derived from adults (spKt/V >1.4; sp: single-pool model of urea distribution, K: urea clearance, t: duration of HD session, V: urea distribution volume). This analysis aimed to evaluate the relationship between delivered dialysis dose and survival in a large cohort of patients having started HD therapy in childhood.

Disclosure(s) No conflict of interest declared. Funding for research via the Freemasons Society of New Zealand.