P62 POPULATION PHARMACOKINETIC STUDY OF AMINOPHYLLINE IN INDIAN PRETERM NEONATES (≤34WEEKS) WITH APNOEA; A LONGITUDINAL OBSERVATIONAL STUDY

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Background Current dosage regimen of aminophylline is similar in both Appropriate for Gestational Age (AGA) and Small for Gestational Age (SGA) preterm neonates.[1] In contrast with AGA babies, SGA babies handle drugs in different way. However, developing countries like India has significant proportion of Growth Restricted/SGA babies. Hence, there is a need to develop appropriate dosage regimen in this population. Objective of the current study was set to develop and qualify the Population-Pharmacokinetic (PPK) model for aminophylline in premature neonates in Indian population.[2]

Methods Aminophylline-treated neonates with IV loading dose of 5 mg/kg followed by maintenance dose of 1.5 or 2 mg/kg 8th hourly for Apnoea of Prematurity (AOP) were included. Any other conditions for secondary causes were excluded. Blood samples were collected by adopting sparse sample scheme and estimated by LCMS-MS. PPK model was developed with appropriate covariates.[3] Data was analysed by NONMEM vesion 7.3. Non-parametric bootstrap procedure and Visual Predictive Check (VPC) was used to qualify the developed model.

Results One compartment, first-order structured model was fitted to the dataset containing 454 observations from 107 neonates. PPK parameters were represented as model estimated values and variability was depicted as% Co-efficient of variation (%CV). Typical population value of CL was 0.011 L/hour with inter-individual variability (IIV) of 59% and V was 0.332 (L/kg) with 31% IIV. Residual error was found to be 19%. Only postnatal age (PNA) had significant effect on V which was assessed by forward addition and backword elimination regression model.

Conclusion AGA and SGA had no influence on PK parameters. However, PNA showed to have significant influence on V. Developed nomogram based on the qualified model may be effective and safe for aminophylline therapy in preterm neonates with apnoea.

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P63 UPLC/MS/MS ASSAY FOR THE SIMULTANEOUS DETERMINATION OF SEVEN ANTIBIOTICS IN HUMAN SERUM – APPLICATION TO PEDIATRIC STUDIES

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Background Antimicrobials are widely used in children but pediatric dose regimens are not always validated, and PK studies, required to validate dosage, are difficult to conduct in children. Low sampling volume limits the number of PK samples drawn per patient and analytical methods adapted to small volumes are not always available. Due to the wide inter-patient pharmacokinetic (PK) variability in children, particularly neonates, therapeutic drug monitoring is required to adapt dosage to individual patients. In such clinical and analytical context, our aim was to develop a unique, rapid and highly sensitive ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) assay to quantify 7 antibiotics (amoxicillin, azithromycin, cefotaxime, ciprofloxacin, meropenem, metronidazole and piperacillin) in low sample volumes (50 µL) for both routine monitoring and pharmacokinetic studies.

Methods After protein precipitation by acetonitrile, the antibiotics and their associated deuterated internal standard were separated on a Waters Acquity UPLC HSS T3 (100 mm x 2.1 mm; 1.8 µm). The mobile phases consisted of a gradient of ammonium acetate (pH 2.4; 5mM) and acetonitrile acidified with 0.1% (v/v) formic acid (started ratio of 93:7, v/v), run at 0.5 mL/min flow rate (total run time: 2.75 min). Ions were detected in the turbo-ion-spray-positive and multiple-reaction-monitoring modes.

Results This method was linear from 0.1–50 µg/mL. Accuracy and precision were evaluated using Quality Control (2, 10, 35 µg/mL). Validation of the method proved that precision, selectivity and stability were all within the recommended limits.

Conclusion This method has the advantage of a unique, efficient and standardized analytical tool for rapid measurement of 7 antibiotics in low blood volume. It has been successfully applied for routine activity and pharmacokinetic studies in children and neonates.

Disclosure(s) Nothing to disclose.

P64 QUALITY ASSESSMENT FOR THE CONTINUOUS BIOANALYSIS OF ALDOSTERONE: APPLICATION IN AN EUROPEAN PAEDIATRIC STUDY

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Background A validation is crucial to ensure the quality of an analytical method and its results. However, the validation is only a first step, further quality assessment has to be utilised