Results Seven prospective observational studies containing pharmacokinetic data regarding the use of IV fentanyl in 208 neonates up to and including a postconceptional age of 44 weeks were included. Studies included 30 (15%) term and 173 (85%) preterm with GA (min, max) of 23–42.3 weeks and postnatal age (min, max) of 1–71 days. Postnatal age and gestational age were identified as covariates of importance contributing to the interindividual pharmacokinetic variability of IV fentanyl. One study applied a population pharmacokinetic model to recommend gestational age and postnatal age-based dosing.

Conclusions Pharmacokinetic data of IV fentanyl in neonates, although limited, is available and can be applied to the use of this drug in neonatal patients. This data needs to be presented in the prescription labelling for enhanced knowledge translation and to achieve optimal safety-efficacy balance in use of this drug. Future research on pharmacokinetics-pharmacodynamic relationship of IV fentanyl in the neonatal population will pave the way toward an individualized approach to therapeutic dosing among these vulnerable neonates.

38 ACCURACY OF ANTIBIOTIC CONCENTRATIONS IN DRUG DISPENSING: A RISK FOR LOW DOSES IN NEONATES

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Introduction Antibacterial therapy plays a crucial role in neonatal infections. Antibacterial efficacy is closely related to the actual dose given to the neonates. Thus, we aimed to evaluate the factors affecting actual dose of intravenous antibiotics in the dispensing process to ensure the precision therapy in neonates.

Methodology Meropenem, cefoperazone/sulbactam and piperacillin/tazobactam with two drug strengths were used as representative drugs to evaluate three different drug dispensing methods. Method A was once dilution method, in which the drug powder was dissolved by a small volume of 5% glucose and then diluted once to a certain concentration. Method B was the same with method A except that the volume of 5% glucose used to dissolve the drug powder was doubled. Method C was double dilution method, in which the drug powder was dissolved by 5% glucose and then diluted twice to a certain concentration. The drug concentration was measured by high performance liquid chromatography. The relative error (RE) of the drug concentration was used to evaluate the accuracy of the preparation.

Results A total of 648 drug concentrations were measured. The average of RE absolute value of the drug concentrations obtained by method B was 1.4% with small drug strength, and 6.7% with large drug strength, respectively. The RE absolute value of drug concentration obtained by method A and C was larger than that by method B. The average of RE absolute value of the drug concentrations obtained by method A was 7.8% with small drug strength, and 15.6% with large drug strength, respectively; and the values obtained by method C was 4.5% with small drug strength, and 6.9% with large drug strength, respectively.

Conclusion The factors affecting actual dose of intravenous antibiotics in the dispensing process were the volume of solvent and the drug strength, as well as the dilution times for drugs with poor stability. Method B was more suitable for neonatal drug dispensing because of its high accuracy and simple operation.

39 POPULATION PHARMACOKINETICS OF MEROPENEM IN NEONATAL AND PEDIATRIC EXTRACORPOREAL MEMBRANE OXYGENATION: A RETROSPECTIVE PILOT STUDY (PRELIMINARY ANALYSIS)

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Introduction Meropenem is a broad-spectrum antibiotic commonly used to treat serious infections in the pediatric population treated with extracorporeal membrane oxygenation (ECMO). It is known that ECMO may affect the drug's pharmacokinetics (PK) by altering the drug's clearance (CL), volume of distribution (Vd), and protein binding. There are limited data on ECMO influence on PK of meropenem in neonates and children undergoing ECMO. Therefore, the aim of this study was to describe PK of meropenem in critically ill neonates and children undergoing ECMO.

Methodology Data from therapeutic drug monitoring (TDM) were available from 25 (14 female, 11 male) critically ill patients (median (interquartile range, IQR), body weight (BW): 5 (3.28–13.50) kg; postnatal age (PNA): 124 (15–1008) days) treated with meropenem (average intermittent dose of 20 mg/kg or continuous infusion), of whom 15 received veno-venous (VV) or veno-arterial (VA) ECMO. Meropenem levels ranged between 0.68 and 67 mg/L. Population PK analysis was performed using NONMEM V7.3.0. The following covariates were tested: maturation variables: BW, PNA; disease status: laboratory values, including serum creatinine, serum urea, serum albumin, total bilirubin, blood pH, aspartate transaminase, and alanine transaminase; concomitant therapy: use of diuretics, inotropes, as well as use of continuous renal replacement therapy; ECMO variables: on/off ECMO, duration of ECMO treatment, ECMO flow rate.

Results According to the model, PNA is a covariate for both CL and Vd, while BW is a covariate of CL. ECMO and CRRT have no significant impacts on the PK parameters. In a one-compartment model, CL and Vd for a typical child of median BW (5 kg) at median PNA (124 days) are 0.459 L/h (RSE = 22.7%)) and 1.76 L (47.3%), respectively. The coefficients of variation for inter-individual variability (IIV) for CL