maternal and fetal acetaminophen concentrations were compared with those observed in the literature. umbilical cord data at birth.

Results The 3 different approaches to predicted acetaminophen PK in the umiblical vein were found to yield broadly similar results. Acetaminophen exposure was similar in maternal blood compared to venous umbilical cord blood. Prediction of the median dose fraction of acetaminophen converted to its metabolites (f_m) revealed higher maternal acetaminophen-glucuronide formation clearance and sulphate formation compared to that in the fetal liver ($f_{m_glucuronide}$52.2 vs 0% and $f_{m_sulphate}$30.4 vs 0.8%, respectively) and higher fraction of acetaminophen converted to the reactive metabolite N-acetyl-*p*-benzoquinone-imine (f_{m_NAPQI}, 6.5 vs 0.06%) in pregnant women compared to their fetus.

Conclusion No differences were observed in the 3 approaches for integration of placental drug transfer. Differences in acetaminophen biotransformation to its metabolites between pregnant women and their fetuses were quantitatively predicted.

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P67 IMPACT OF ENANTIOMER-SPECIFIC MATURATIONAL CHANGES IN PHARMACOKINETICS ON THE RACEMIC KETOROLAC TARGET TROUGH CONCENTRATION

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Introduction Ketorolac is a racemic drug with analgesic effects specific to its S-enantiomer. This study aimed to describe enantiomer-specific maturational pharmacokinetics (PK). Simulations were performed to describe how S-ketorolac exposure in infants differs from adults, and how this affects the adult racemic analgesic trough threshold EC_{50} ($EC50_{thr-adult}$, 0.37 mg/L) in infants ($EC50_{thr-infant}$)when the same S-target is applied.

Methods A population PK analysis (NONMEM 7.3) was performed based on 1020 plasma samples from 5 studies including 80 patients (adults, children, infants) following single intravenous ketorolac administration.

Results S-ketorolac PK was best described with a 2-compartment model in infants and 3-compartment model in adults, while R-ketorolac PK was best described with a 2-compartment model in all. S-ketorolac clearance [mean population value: 3.45 L/h/56 kg] and central volume of distribution (V1) [4.27 L/56kg] increased exponentially with bodyweight (0.75, 0.59 respectively). R-ketorolac clearance [0.93 L/h/56kg], peripheral volume of distribution (V2) and inter-compartmental clearance (Q) increased exponentially with bodyweight (0.62, 1.20, 0.76 respectively), V1 [4.11 L/56kg] linearly with bodyweight. Simulations revealed $EC50_{thr-adult}$ (0.37 mg/L) contained 0.048 mg/L S-ketorolac as mean in typical adults (BW 48.6–99.6 kg), while $EC50_{thr-adult}$ contained 0.032–0.036 mg/L S-ketorolac in typical infants (BW 5.3–10.6 kg). To reach adult S-enantiomer concentration (0.048 mg/L) in typical infants (BW 5.3–10.6 kg), $EC_{50thr-infant}$ should be 0.49–0.46 mg/L, respectively.

Conclusion Enantiomer-specific maturational PK of ketorolac were described. Subsequent simulations displayed differences in proportion of S- and R-ketorolac on the racemic threshold EC_{50}. A The same S-ketorolac concentration necessitates a higher $EC50_{thr-infant}$ to $EC50_{thr-adult}$.

Disclosure(s) Nothing to disclose

P68 SIGNIFICANT ORAL DRUG USE IN CRITICALLY ILL CHILDREN: RATIONAL THERAPY OR A BLACK BOX?

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Background The disposition of orally prescribed drugs in critically ill children may be affected critical illness in in addition to age, resulting in erratic effects and safety. We aimed to study oral drug prescribing in the neonatal and pediatric intensive care unit (NICU and PICU).

Methods A one-year retrospective cohort study of all drug prescriptions, including route of administration for all children admitted to the NICU and PICU of the Erasmus MC-Sophia's children's hospital.

Results 1723 children with 2091 unique admissions received per admission (median [IQR]) 5 (3–10) drugs; 1 (0–2) orally and 3 (1–7) intravenously (IV). During mechanical ventilation 15% and 75% of drugs were given orally and IV, respectively. In non-ventilated patients, 27% of drugs were given orally and 60% IV. The 5 most frequently orally prescribed drugs were: vitamin K, spironolactone, oral probiotics, amphotericin B (prophylaxis) and trimethoprim.

Discussion Critically ill infants receive a considerable proportion of drugs orally. Considering that critical illness may significantly impact intestinal drug absorption, this may expose them to an increased risk of ineffective or unsafe drug therapy.

Disclosure(s) Nothing to disclose

P69 PHARMACOKINETICS OF A CONTINUOUS INFUSION OF PIPERACILLIN/TAZOBACTAM TO CHILDREN USING AN ELASTOMERIC PUMP (POPPET STUDY): PILOT DATA FROM DOUBLE LUMEN CENTRAL LINES

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Background Piperacillin/Tazobactam is the first-line antibiotic for the treatment of febrile neutropenia in the UK. There is