higher cost and less than optimum management of infectious diseases.

Objectives To determine the relative likelihood of true allergy in patients suspected to have a penicillin allergy and to investigate the risk factors involved. We hypothesized that the vast majority of self-reported penicillin allergies are less likely to be true allergies when proper immunological work up is performed.

Methods Paediatric patients aged 0–18 years presenting to the ADR clinic at the Children Hospital of Western Ontario (CHWO) with suspected antibiotic allergies were included. A retrospective review of charts was conducted to obtain demographic information and results from allergological and in vitro testing. Subjects were evaluated with a radioallergosorbent test (RAST) or the lymphocyte toxicity assay (LTA) in the in vitro platelet toxicity assay (iPPTA) depending on whether the history was most consistent with an immediate allergy or a delayed hypersensitivity, respectively. Patients with negative RAST or LTA/iPPTA were recommended to undergo confirmatory oral challenge test (OCT).

Results Ninety subjects were identified including 75 with possible penicillin allergy and 10 with suspected allergy to a non-penicillin antibiotic. Five subjects presented with a mixed allergy. Based on the results from RAST, in vitro testing and OCTs, the prevalence of a true allergy in the penicillin group was 6.25% vs. 66.67% in the non-penicillin group (p<0.001). Patients presenting with severe reactions were more likely to be truly allergic (p<0.01). In-patients were more likely to present with non-penicillin allergies and were subsequently more likely to have a true allergy (p<0.001).

Conclusions True allergy is very rare in patients with suspected penicillin allergies and can be determined with a proper work-up including OCT. Shorter protocols for the evaluation of these patients would be beneficial.

Disclosure(s) Nothing to disclose

Background Little is known about the pharmacokinetics (PK) of acetaminophen during different stages of pregnancy. The aim of this study was to develop a physiologically based pharmacokinetic (PBPK) model to predict acetaminophen PK throughout pregnancy.

Methods PBPK models for acetaminophen and its metabolites were developed in non-pregnant and pregnant women. Physiological and enzymatic changes in pregnant women expected to impact acetaminophen PK were considered. The models were developed in non-pregnant and pregnant women. Physiological and enzymatic changes in pregnant women expected to impact acetaminophen PK were considered. The models were validated using goodness-of-fit-plots and through comparison of predicted PK profiles with in-vivo PK data. Predictions were performed to illustrate the concentrations at steady state (C_{ss-mean}), used as indicator for efficacy of acetaminophen achieved following 1000 mg q6h. Furthermore, as measurement for potential hepatotoxicity, the molar dose fraction of acetaminophen converted to NAPQI was estimated.

Results PBPK models successfully predicted the PK of acetaminophen and its metabolites in populations of non-pregnant and pregnant women. Predictions resulted in lowest C_{ss-mean} in the third trimester (4.5 mg/L), while C_{ss-mean} was 6.7, 5.6 and 4.9 mg/L in non-pregnant, first and second trimester populations, respectively. Assuming a constant increased activity of CYP2E1 throughout pregnancy, the molar dose fraction of acetaminophen converted to NAPQI was highest during the first (11.0%), followed by second (9.0%) and third trimester (8.2%), compared to non-pregnant women (7.1%).

Conclusion Risk for drug related hepatotoxicity in pregnant women might be increased as more NAPQI is produced during pregnancy compared to non-pregnant women, especially in late pregnancy.
METHADONE DOSING STRATEGIES IN PRETERM NEONATES CAN BE SIMPLIFIED

1T van Donge*, 2J Samiee-Zafarghandy, 1M Pfister, 1G Koch, 1M Kalani, 4A Bordbar, 1S van den Anker, 1Pediatric Pharmacology and Pharmaceutics, University Children’s Hospital Basel (UKBB), Basel, Switzerland; 2Department of Pediatrics, McMaster University, Ontario, ON, Canada; 3Certara LP, Princeton, NJ, USA; 4Department of Pediatrics, Iran University of Medical Sciences, Tehran, Islamic Republic of Iran; 5Intensive Care and Department of Pediatric Surgery, Erasmus MC Sophia Children’s Hospital, Rotterdam, The Netherlands; 6Division of Clinical Pharmacology, Children’s National Health System, Washington, DC, USA

Aims A dramatic increase in newborn infants with neonatal abstinence syndrome has been observed and these neonates are frequently treated with complex methadone dosing schemes to control their withdrawal symptoms. Despite its abundant use, hardly any data on the pharmacokinetics of methadone is available in preterm neonates. Therefore we investigated developmental pharmacokinetics of methadone and evaluated current dosing strategies and possible simplification in this vulnerable population.

Methods A single center open-label prospective study was performed to collect pharmacokinetic data after a single oral dose of methadone in preterm neonates. A population pharmacokinetic model was built to characterize developmental pharmacokinetics of methadone and to assess the effects of weight and age on clearance and volume of distribution. In addition, simulation techniques were applied to evaluate reported dosing scenarios, investigate methadone exposure levels and examine the feasibility of simplified dosing recommendations.

Results In total, 121 methadone concentrations were collected from 31 preterm neonates. The median weight and gestational age amounted 1.6 kg and 32 weeks, respectively. A one-compartment model with first order absorption and elimination kinetics best described the data for (R)- and (S)-methadone. Clearance was observed to be higher for the (R)-enantiomer as compared to the (S)-enantiomer (0.244 versus 0.167 L/h).

Target exposures, based on simulations, can be maintained target exposure to control withdrawal symptoms in preterm neonates. A simplified methadone dosing strategy can maintain target exposure to control withdrawal symptoms in preterm neonates.

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