Background Little is known about the short and long-term therapeutic management of asthmatic children. The aim of this study was to assess the prescribing patterns of antiasthma drugs in primary care.

Methods This is a retrospective cohort study performed between January 2011 and December 2017 using the EGB (Echantillon Généraliste de Bénéficiaires) database, a 1/97th sample of the French national healthcare insurance system. Claims data for all individuals aged from 5 to 18 years' old who had received at least one antiasthma drug in the study period without any delivery in the previous 24 months and with 24 months of follow-up after first delivery, were analysed.

Results A total of 7,680 children and adolescents (68.6% aged 5–11, 31.4% aged 12–18 years) were delivered at least one antiasthma drug (ATC code R03) during study period. The majority (66%) did not redeem another prescription in the following year (occasional users), whereas 18.4% redeemed prescriptions twice (low users) and 15.6% ≥ 3 times (high users). Most users (67%) were delivered only one class of R03 per dispensing in the first year and short-acting β2-agonists (SABAs) were the most frequently dispensed drugs. However, 33.4% of users were not prescribed SABAs. During the second year, only 27% of first-year users redeemed R03 prescriptions: 15.8% among occasional users, 35.5% of low users and 67.4% of high users. Among low and high first-year users who redeemed R03 drugs during the second year, 39.7% did not use inhaled corticoids alone or in association to LABAs.

Conclusions A high proportion of children and adolescents that used antiasthmatic drugs, even on a regular basis, were not prescribed these drugs in the long term. This finding may correspond either to the widespread use of antiasthma drugs in indications other than asthma or to an important undertreatment of asthmatic children and adolescents.

Disclosure(s) Nothing to disclose
hours. Physiologic parameters were monitored and pain scores assessed.

Results The median fentanyl concentrations were 0.18, 0.15, 0.15 and 0.57, 0.37, 0.35 μg/mL at 15–31 minutes, two and four hours and the half-lives were 1.6 to 20.5 or 4.1 to 32.6 hours for the low and high dose groups, respectively. A significant correlation was seen between weight at study inclusion and half-life (Spearman’s r = -0.9, p < 0.001), volume of distribution (r = -0.8, p < 0.01) and clearance (r = -0.9, p < 0.01) in the low dose group (n=9). Pain assessment results were not correlated to pharmacokinetic variables. Fentanyl was well tolerated.

Conclusion The inter-individual variation of fentanyl pharmacokinetics is large in preterm infants and the dose of 0.5 mg/kg seems too small for skin-breaking procedures.

Disclosure(s) Nothing to disclose

P51 A COMBINED EXPERIMENTAL APPROACH TO ASSESS INTESTINAL DRUG ABSORPTION IN EARLY CHILDHOOD

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Background Drug transporters and metabolizing enzymes located in the epithelial lining of the intestine limit or enhance systemic drug exposure. During child development, the abundance and activity of these transporters and enzymes - determining how fast and how much of a drug is being absorbed into the circulation - changes from birth to adolescence. As most drugs given to children are taken by mouth, the aim of this project is to study the abundance and activity of transporters and metabolizing enzymes, involved in the intestinal absorption of drugs.

Methods The ex vivo Ussing chamber with pediatric small intestinal tissue is applied to evaluate intestinal drug absorption and metabolism.1 Transport and metabolism of a selection of drug molecules is assessed across these tissues by sampling the donor and receiver compartment at different intervals and sample analysis by LC-MS/MS. Viability, functionality and integrity of the tissues are monitored using electrophysiological parameters (dP, R, I). Ussing chamber experiments are combined with a targeted proteomics approach to quantify drug transporter and metabolizing enzyme abundance in these tissues.

Results An Using chamber method has been successfully set up using both adult and pediatric intestinal tissue. To date samples from three children of different ages have been evaluated and show promising results. Tissue from the same patients has been stored for proteomics analysis.

Conclusion The Using method presents an innovative, feasible approach to study active intestinal transport in children. Further studies are now underway to elucidate age-related variation in intestinal transport and metabolism.

REFERENCE


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P52 LOW AND ERRATIC EXPOSURE OF ORAL ACETAMINOPHEN IN CRITICALLY ILL CHILDREN DETERMINED WITH A 14C MICROTRACER STUDY: A CASE FOR IV ACETAMINOPHEN FOR ACUTE PAIN MANAGEMENT?

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Background Despite being the most commonly used analgesic and antipyretic, oral APAP bioavailability has not been determined in children.

The aim of this study is to compare exposure after oral vs iv APAP using the PK data of the first pediatric oral bioavailability 14C microtracer study.

Methods Design Bioavailability microtracer population PK study Participants patients < 6 yrs old in the pediatric ICU who received 15 mg/kg iv APAP 46h Intervention a single microdose of 14C-APAP (3 μg/kg) given orally at the same time as a therapeutic iv dose Data collection Blood was sampled 8 times up to 24 h post-dose Data analysis Population PK analysis using NONMEM. Based on the model, exposure after oral vs iv was compared by simulating the concentration-time profiles and Css (targeted: 10 mg/L ± 20% deviation).

3 doses were simulated: 15 mg/kg q6h oral and iv and 22.5 mg/kg oral q6h. 1000 simulations were performed and the percentage of patients reaching the targeted mean Css of 10 mg/L±20% were compared.

Results Oral bioavailability was 72% (range: 11–91%). After 15 mg/kg APAP, the median simulated oral Css was subtherapeutic (6.5 mg/L), but therapeutic (10 mg/L) for IV dosing (15 mg/kg). Patients were 2.5 times less likely to reach therapeutic plasma concentrations with 15 mg/kg oral vs iv APAP.

With the maximal recommended oral doses of 22.5 mg/kg 6 h aimed to overcome the 72% bioavailability, median mean Css were therapeutic but overexposure and underexposure were more common than with iv (37 vs 32% Css< 8 mg/L and 30 vs 21% Css>12 mg/L).

Conclusion Compared to IV, the usual (15 mg/kg) oral APAP doses result in low systemic exposure with subsequent risk of therapeutic failure. When oral doses are increased to overcome the low bioavailability, underdosing still occurs and overdosing was observed in patients with high bioavailability. IV