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, 0.35ng/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

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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 q6h

**Intervention** a single microdose of 14C APAP (3µg/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