Background Optimal drug therapy in children relies on availability of pediatric-specific information. European and American legislative initiatives have resulted in advancement of pediatric pharmacotherapy data. We aim to describe the quality and quantity of pediatric information in drug monographs of New Active Substances (NASs) approved by Health Canada.

Design/Methods Canadian drug monographs of NASs approved by Health Canada, from January 2007 until December 2016, were systematically reviewed for pediatric-specific information. Pediatric-specific information defined as: pediatric indication, dosing, pediatric-friendly dosage forms, and pediatric safety data.

Results Over the period of the study, Health Canada approved 281 NASs. Of all the non-biologic NASs (205, 74%), 39 (19%) were approved for use in pediatric patients. The number of drugs with pediatric approval was lowest in 2008 (1, 8%) and highest in 2016 (8, 32%), following no specific pattern. Neonates had the lowest rate of drug approvals through all pediatric age groups (4, 2%). All drugs with pediatric approval had pediatric-specific dosage information with the majority of them presenting pediatric safety data (79%). Pediatric friendly formulation was only available in 20% (8) of drugs with pediatric approval. Studies in pediatric populations were the source of pediatric information in 59% (23) of drugs with pediatric approval.

Conclusion Less than 20% of the NASs approved by Health Canada for use in adults contain pediatric approval. Neonatal populations remain a therapeutic orphan, with severe lack of dosing and safety information. Safe and effective pediatric pharmacotherapy requires well-conducted pediatric research to enhance pediatric drug data. Canadian children are in need for legislative initiatives to promote pediatric drug development.

Disclosure(s) Nothing to disclose

Methods We conducted a prospective, single centre, open-label pharmacokinetic study in infants 1–3 months undergoing sepsis workup in the emergency unit. Included infants received alternating nalbuphine as 0.05 mg/kg intravenous bolus or as 0.1 mg/kg intranasal spray. PK samples were taken at 3 predefined time points (15, 30 and max. 240 min post-dose before discharge). Area under the concentration-time curve (AUC0–Tlast and AUC0–infinity for i.v.) was calculated using non-compartmental analysis and was compared between groups using Wilcoxon test. Further parameters derived included maximum concentration (Cmax), time of maximum concentration (Tmax for i.n.) and terminal half-life (t1/2).

Results A total of 31 patients were included in the analysis. Median age was 55 days (interquartile range 38–63) in the intranasal (N=20) and 42 (37–76) days in the iv group (N=11). Median AUC0–Tlast was 7.6 (5.4–10.4) mcg*h/L following intranasal versus 7.9 (6.0–14.7) mcg*h/L for iv administration (p=0.46). AUC0–Tlast (i.v.) covered 80 ±83% of AUC0–infinity. Median Cmax was 4.5 [3.5–5.6] mcg/L (i.n.) versus 6.5 [5.3–15.9] mcg/L (i.v.) (p=0.014), t1/2 1.6 [1.3–2.8] h (i.v.) versus 1.3 [1.1–1.5] h (i.v.) (p=0.021). Tmax occurred 37 [32–65] min after intranasal administration.

Conclusion This first PK study of intranasal nalbuphine in infants suggests that 0.1 mg/kg i.n. dosing provides similar exposure as 0.05 mg/kg i.v. in infants in terms of AUC, and hence intranasal bioavailability close to 50%.

Disclosure(s) Nothing to disclose

Background Sufentanil is a potent synthetic opioid increasingly used as an analgesic drug for pain treatment in critically ill neonates. Clinical studies concerning the pharmacokinetics (PK) of sufentanil administered as a bolus or continuous infusion in neonates are scarce and a population model has been developed for critically ill children beyond the newborn period. The aim of our study was to determine the PK of sufentanil in critically ill neonates treated with continuous sufentanil infusion for pain management (prophylactic and therapeutic use).

Methods Eight term neonates (birth weight 2.60–4.30 kg; postnatal age 2–96 h) were treated with sufentanil (initial bolus 0.1–0.5 µg/kg i.v. administered for 5 minutes followed by continuous infusion 0.1–0.5 µg/kg per hour i.v.). Sufentanil plasma concentrations were determined using a UPLC-MS/MS assay. Totally 159 sufentanil concentrations were measured (8–27 measurements per patient). Individual sufentanil PK parameters were calculated in a two-compartmental PK model with first-order elimination kinetics based on individual demographic and clinical data and observed sufentanil plasma levels using MWPharm++ software (MediWare, Prague, Czech Republic). The sufentanil population PK model was individualized to maximize fitting of the simulated PK profile curve with observed concentration points. The fitting was performed using Bayesian method.
Results Median (IQR) sufentanil central and total volume of distribution, clearance, and distribution and elimination half-life were 4.7 (4.2–5.2) L/kg and 11.8 (9.9–14.2) L/kg, 0.552 (0.415–0.671) 1/h/kg, and 0.0264 (0.0260–0.0264) h and 15.7 (13.4–19.2) h, respectively.

Conclusion We observed similar sufentanil PK parameters (preliminary results) as described previously in literature. However, further studies with more patients are needed.

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P80 OBJECTIVE PHARMACODYNAMIC EVALUATION OF DOXAPRAM IN PRETERM INFANTS

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Background Pharmacodynamic evaluation is challenging in neonatal clinical care, and often based on subjective human interpretation of clinical signs and the available ‘snapshot’ of physiological parameters. High frequency data (≥ 1Hz) of bedside patient monitors provide the opportunity of continuous and objective drug evaluation.1 This study investigates the predictive value of continuously available vital and ventilatory parameters to evaluate doxapram therapy. Doxapram is a respiratory stimulant to avoid mechanical ventilation and adverse outcomes of hypoxemia in preterm infants.2

Methods Preterm infants admitted to a level III NICU centre who received doxapram therapy were eligible for inclusion. Stored vital and ventilatory parameters were retrospectively analysed. Multivariate analysis was performed to identify variables that influenced therapy failure (intubation or death) or success. Variables with a p value < 0.1 in univariate analysis were included in the multivariate analysis. Additionally, the ΔSpO2/FiO2-ratio was calculated by subtracting the median SpO2/FiO2-ratio 1 day after therapy from the median SpO2/FiO2-ratio 1 day before therapy.

Results The first episode of doxapram treatment was analysed in a total of 61 preterm infants with a median postnatal age at therapy start (PNA) of 3.0 weeks (IQR; 2.0–3.6). The success rate of doxapram therapy was 57%. Out of all parameters, the SpO2/FiO2-ratio showed to be the most indicative for therapy outcome. The predictive model included the ΔSpO2/FiO2-ratio, the PNA, the administration of a loading dose at start, and intubation within 24 hours before the start of doxapram (area under the curve of 0.828). The ΔSpO2/FiO2-ratio was inversely associated with therapy outcome (OR 0.26, CI 95% 0.07–0.83; p = 0.03).

Conclusion The ΔSpO2/FiO2-ratio between 1 day before and 1 day after start of the therapy is predictive of failure or success of doxapram therapy. The use of physiological data shows potential in the pharmacodynamic evaluation of doxapram therapy.