P77 PEDIATRIC DRUG DATA IN CANADIAN DRUG MONOGRAPHS

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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 dosing 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(s) 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

P78 PHARMACOKINETICS OF INTRAVENOUS AND INTRANASAL NALBUPHINE IN INFANTS

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Background Nalbuphine is a mixed agonist-antagonist opioid analgesic agent frequently used in paediatrics, and licensed for parenteral use only. Intranasal delivery could be a safe, effective and non-invasive alternative, especially in infants in the acute setting. However, pharmacokinetic (PK) data for this route of administration is completely lacking. The aim of this study was to assess PK of nalbuphine in infants 1–3 months after single intravenous (0.05 mg/kg) and intranasal (0.1 mg/kg) application, respectively.

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 ($AUC_{0\text{-Tlast}}$, and $AUC_{0\text{-infinity}}$ for i.v.) was calculated using non-compartmental analysis and was compared between groups using Wilcoxon test. Further parameters derived included maximum concentration (C_{max}), time of maximum concentration (T_{max} for i.n.) and terminal half-life ($t_{1/2}$).

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 $AUC_{0\text{-Tlast}}$ 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). $AUC_{0\text{-Tlast}}$ (i.v.) covered 80 [68–83]% of $AUC_{0\text{-infinity}}$. Median C_{max} 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), $t_{1/2}$2.4 [1.3–2.8] h (i.n.) versus 1.3 [1.1–1.5] h (i.v.) (p=0.021). T_{max} 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%.

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P79 PHARMACOKINETICS OF SUFENTANIL IN CRITICALLY ILL NEONATES

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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 sparse 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.