157 SURVEY ON USE OF CAFFEINE IN APNOEA OF PREMATURITY IN NEONATAL UNITS ACROSS ENGLAND

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Background Apnoea of prematurity (AOP) is a significant clinical problem in premature infants and is almost universal in infants < 1000 g at birth. Caffeine has emerged as the methylxanthine of choice to treat AOP. Although it is commonly used, there is no unified consensus or guideline on its use in NNUs in England.
Aim To study the current practice of caffeine use in AOP at NNUs in England.
Methods A telephonic survey of level 3 and level 2 units in England was conducted, using a standardised questionnaire, over November and December, 2011.
Results Out of 52 units surveyed, 48% were level 3 units. All units used caffeine for treatment of AOP (base 60% and citrate 40% of units). 92% of units have written guidelines on caffeine use. Caffeine was started by 47% of units based on gestational age, regardless of symptoms.[IS3] All units used a loading dose, which varied between 5 and 25mg/kg (median of 10mg/kg) for caffeine base and 15 to 20mg/kg (median of 20mg/kg) for citrate. The maintenance dose varied between 2.5–6mg/kg/day (median of 5mg/kg/day) for base and 5–12mg/kg/day (median of 5mg/kg/day) for citrate. Caffeine levels were routinely performed by 7% of units. Caffeine was discontinued between 30 to 36 weeks gestation.
Discussion Our survey depicts that practice of caffeine use varies significantly across NNUs in England. The results from this survey could be used as a footing for further data collection, for formulation of a uniform guideline maximising the utilisation of this extensively studied drug.

158 A SYSTEMATIC REVIEW OF PHARNMACOKINETICS (PK) OF DOBUTAMINE FOR USE IN NEONATES AND CHILDREN

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Background Dobutamine has been used off-label in newborns and children for treating haemodynamic insufficiency for over 20 years. As preparation for a large randomised study to achieve Paediatric Use Marketing Authorisation for dobutamine in newborns we performed a structured literature review of PK data.
Methods Structured searches were conducted using the electronic databases Medline and Embase. Search terms included dobutamine, infant, newborn, paediatric/pediatric, prematurity, child, infant, low birth weight infant, preschool child, school child, adolescent, pharmacokinetics, clinical pharmacology. Data was extracted based on pre-defined criteria decided by the team.
Main results Six of eleven papers emerging from this search met our inclusion criteria. These reported dobutamine PK data in a combined total of 70 children (age range 0 days-22 years, 13 newborns, 27–42 weeks gestation), with infusion rates ranging from 0.5–20 μg/kg/min. Five papers found that the infusion rate was positively correlated to plasma dobutamine concentration. Dobutamine clearance rates showed great variability between individuals (range 35.1–482.2 mL/kg/min). Four papers found that clearance did not vary with infusion rate, suggesting first order kinetics, although one paper (n=12) showed a significantly negative relationship (p<0.001) of dobutamine clearance to steady-state plasma concentration (dobutamine dosage 2–15 μg/kg/min).
Conclusions The current dobutamine PK data is difficult to interpret due to inhomogeneity and variability of patients' age and conditions, dobutamine dosages and study designs. High quality prospective PK data -especially in newborns- is urgently required prior to our large randomised study.

159 PHARMACOKINETICS (PKS) OF LEVOSIMENDAN (LEVO) AND INTERMEDIATE METABOLITES (OR-1855 AND OR-1896) IN NEWBORNS UNDERGOING CARDIOVASCULAR SURGERY WITH CARDIOPULMONARY BYPASS (CPB)

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Background and aims LEVO is a novel inodilator developed to treat heart failure. Biotransformation of LEVO in the intestinal tract gives rise to intermediate metabolites with prolonged beneficial haemodynamic effects. There are no data on LEVO PKs in neonates. We aim to investigate LEVO and intermediate metabolites PKs in newborns undergoing CPB.
Methods Eleven infants received step-wise dose increase of LEVO (0.10, 0.15, 0.20 mg/k/min) delivered as i.v. continuous infusion, starting before CPB up to 48h post-surgery. Eleven blood samples per subject were collected up to day 14 post-infusion started. Samples were quantified by HPLC-MS/MS. Non-compartmental methods were used for PK parameters. Median (IQR) values are reported.
Results Area under the curve (AUC, ng*h/mL) OR-1855 plasma concentration [1717.10 (930.38–3756.41)] was 2.3- and 8.2-fold higher than LEVO [742.10 (527.23–1046)] and OR-1896 [209.78 (99.54–275.36)], respectively. LEVO clearance (CL, L/h/k) was 0.67 (0.44–1.0). OR-1855 maximum concentration (Cmax, ng/ml) was 5.2-fold higher than OR-1896 [18.5 (10.44–33.25) vs. 3.58 (2.94–4.38)]. OR-1896 and OR-1855 Cmax were respectively achieved 2h before and 120h after LEVO infusion stopped. LEVO CL increased and AUC decreased with postnatal age, explaining 66.23% (p=0.023) and 34.51% (p=0.047) of their respective variance. LEVO AUC and pre-surgery antibiotics explained 38.89% (p=0.016) and 26.68% (p=0.035) of OR-1855 AUC variance, respectively. Use of additional diuretics to furosemide explained 27.21% (p=0.025) of OR-1896 AUC. No other covariates influenced LEVO or metabolites PKs.
Conclusions This study describes the pharmacokinetic profile of LEVO and intermediate metabolites in newborns as well as covariates explaining a significant part of their variance.

160 LONGTERM OUTCOME AFTER LIVER TRANSPLANTATION: PSYCHOSOCIAL AND COGNITIVE ISSUES

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Psychosocial outcome in liver transplanted children was primarily investigated in terms of health related quality of life (HRQOL). In children this multidimensional construct additionally accentuates domains like school, family, and peers as well as physical and cognitive-emotional development.

Although organ transplantation is lifesaving, recipients trade a terminal illness for a chronic syndrome with good organ function in most cases, however. Nevertheless, restoration of organ function does not involve return to a normal life. It is characterized by fear of organ failure and complications, side effects of the medication, developmental deficits, and psychiatric comorbidities. Liver transplanted children show a poorer HRQOL compared with the healthy population, equal to or better than in children with other chronic diseases. Factors