function; and vision (clinical examination and global motion perception). Primary outcomes were neurosensory disability (cognitive, language or motor score below -1 SD or cerebral palsy or blind or deaf) and processing problem (executive function or global motion perception worse than 1.5 SD). Data are mean (SD), n (%), or relative risk (RR), 95% confidence interval.

**Results** 184 children were assessed; 90/118 (76%) randomised to dextrose and 94/119 (79%) to placebo gel. Mean birth weight was 3093 (803) g and gestation 37.7 (1.6) wk. 67 children (36%) had neurosensory disability (1 severe, 9 moderate, 57 mild) with similar rates in both groups (dextrose 35 (39%) vs placebo 32 (34%), RR 1.14, 0.78–1.67). Processing difficulty was also similar in both groups (dextrose 8 (10%) vs placebo 16 (18%), RR 0.52, 0.23–1.15).

**Discussion** Neurosensory disability is common amongst children treated for neonatal hypoglycaemia. Treatment with dextrose gel does not change the incidence of disability or processing problems.

## REFERENCE

1 Harris DL, *et al*. Dextrose gel for neonatal hypoglycaemia (the Sugar Babies Study). *Lancet* 2013;382:2077–83

# Pharmacology, Pharmacokinetics, Pharmacodynamics

## O-105 PROSPECTIVE EVALUATION OF REMIFENTANIL DURING INSURE IN PRETERM NEWBORNS: UNPREDICTABLE EFFECTS AND SIDE EFFECTS

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**Background and aims** Premedication for neonatal intubation should provide fast and adequate sedation with a minimum of side-effects. Aim of this study was to evaluate effect and safety of remifentanil as premedication during INSURE in preterm neonates.

**Methods** Remifentanil was prospectively studied using increasing dosages (Table 1). Outcome measures were adequate sedation, defined as adequate sedation score, good intubation conditions and absence of side-effects, and duration of respiratory depression. To exclude degradation or dilution errors as explanation for observed variability in response, pharmaceutical analysis was performed after simulated preparation.

**Abstract O-105 Table 1** Protocol of remifentanil for the 2 study periods

| | Period 1 (n = 5) | Period 2 (n = 9) |
|---|---|---|
| **Site of administration** | Intravenously | Intravenously |
| **Period of administration** | In 30 seconds | In 30 seconds |
| **Starting dose** | 1 µg/kg | 2 µg/kg |
| | | Dose 2: 3 µg/kg |
| | Dose 2: 1 µg/kg | Dose 3: 4 µg/kg |
| **Repeated doses** | Dose 3: 1 µg/kg | Dose 4: 5 µg/kg |
| **Sedative in case of failure** | Propofol 1–2 mg/kg | Propofol 1–2 mg/kg |

**Results** The study was terminated after inclusion of 14 patients. A dose of 1 ug/kg did not provide adequate sedation in 80% of patients. Higher dosages also resulted in inadequate sedation in 89% of patients and were frequently associated with chest rigidity (36%). Duration of respiratory depression was reported in 6 patients, with a median of 18 min (mean 16.5 min, range 5 seconds to 30 min). Pharmaceutical analysis showed a concentration of the active substance of 80 to 112% of the expected concentration, indicating adequate stability and preparation.

**Conclusion** Remifentanil intravenously over 30 seconds frequently not provides adequate sedation and has a high risk of chest wall rigidity in preterm neonates. Also, duration of respiratory depression is quite long for use during INSURE.

## O-106 POPULATIONPHARMACOKINETIC MODEL OF THE ANTIMICROBIAL EXCIPIENT METHYL PARABEN ADMINISTERED IN ROUTINE CLINICAL PRACTICE TO NEONATES

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**Introduction** Parabens are widely used as antimicrobial preservatives in medicines given to neonates. Some concerns have been raised about the potential of paraben toxicity. To date there have been no studies of the circulating concentrations of methyl paraben (MPB) in babies. This study aimed to describe the relationship between dose of MPB administered and circulating concentrations using a population pharmacokinetic model.

**Methods** Neonates in 4 UK and 1 Estonian neonatal units who were prescribed paraben-containing medications were recruited with parental consent. Parabens were assayed in timed, dried blood spots using LCMSMS. The limit of quantification was 20ng/mL.

**Results** 180 babies provided 841 samples of which 382 (45%) were below the limit of quantification. The mean (range) of observed blood MPB concentrations was 28.4 (10–874) ng/ml. The final kinetic model for MPB included first order absorption and two compartment disposition. Clearance was related to postnatal age (PNA). The model parameters are shown in the Table.

**Discussion** Routine use of MPB as an excipient in medicinal formulations does not lead to markedly high circulating blood concentrations of MPB in neonates. We cannot exclude accumulation from these data. These findings will contribute to safety

**Abstract O-106 Table 1**

| Parameter | Estimate | % Relative Standard Error |
|---|---|---|
| Clearance if PNA <21 days (L/hr) | 0.57 | 9.57 |
| Clearance if PNA ≥21 days (L/hr) | 0.88 | 7.19 |
| Central volume (L/1.6kg) | 1.84 | 7.55 |
| Peripheral Volume (L) | 12.2 | 12.0 |
| Residual (proportionate) Error (%) | 44.5 | 4.7 |