Pharmacology II

O-103 SEDATION AND ANALGESIA FOR NEONATES IN NICUS ACROSS EUROPE: THE EUROPAIN SURVEY

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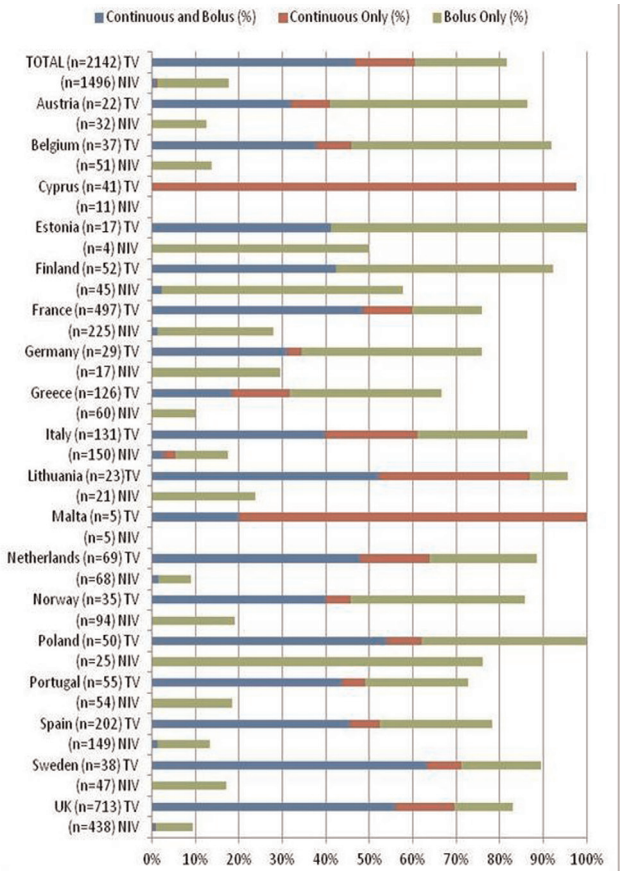
Background Pain and stress induced by mechanical ventilation, invasive procedures, or painful diseases supports the use of sedation/analgesia (S/A) in newborns admitted to Neonatal Intensive Care Units (NICUs). To date, these practices have not been studied at a large scale.

Objective To determine current clinical practices regarding the use of S/A drugs in NICUs across Europe.

Methods This epidemiological observational study on bedside clinical practices regarding S/A collected data for all neonates in participating NICUs until the infant left the unit (discharge, death, transfer) or for up to 28 days. Data collection occurred via an online database for 1 month at each NICU. All neonates up to 44 weeks gestation were included.

Results From October 2012 to June 2013, 243 NICUs from 18 European countries collected data on 6680 eligible neonates. Of these, 2142 received tracheal ventilation (TV), 1496 non-invasive ventilation (NIV) and 3042 only spontaneous ventilation (SV). The median (IQR) gestational age of TV, NIV and SV neonates were 32.1 (28.1–37.4), 33.6 (31.0–36.6) and 37.9 (35.0–39.9), respectively ($p < 0.001$). Overall, more TV neonates [81.5% (n = 1746)] received S/A drugs than NIV neonates [17.8% (n = 266)] and SV neonates [9.3% (n = 282)]; $p < 0.001$. Fig. shows the rate of S/A use by country; table shows S/A drugs used.

Conclusions Most ventilated but few non-ventilated neonates (NIV and SV) receive S/A therapy in European NICUs. Wide variations in S/A use, drugs used, and mode of administration (continuous, bolus, or both) exist among countries.



Abstract O-103 Figure 1 Rate of Analgesia/sedation in 2142 tracheal ventilated neonates (TV) and 1496 Non invasive ventilated neonates (NIV) admitted to NIUC in 18 European countries

Abstract O-103 Table 1 Sedation/analgesia drugs used in TV, NIV and SV neonates neonates

	Tracheal ventilation (n=1746)	Non invasive ventilation (n=266)	Spontaneous ventilation (n=282)
Morphine, *No.(%)*	923 (52.9)	37 (13.9)	56 (19.9)
Fentanyl, *No.(%)*	629 (36.0)	41 (15.4)	24 (8.5)
Sufentanil, *No.(%)*	220 (12.6)	2 (0.8)	5 (1.8)
Midazolam, *No.(%)*	536 (30.7)	16 (6.0)	24 (8.5)
Neuroblocker, *No.(%)*	542 (31.0)	-	-

O-104 TWO YEAR OUTCOMES OF CHILDREN TREATED WITH DEXTROSE GEL FOR NEONATAL HYPOGLYCAEMIA: FOLLOW UP OF A RANDOMISED TRIAL

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Background Neonatal hypoglycaemia is linked to poor developmental outcome. Dextrose gel reverses hypoglycaemia, but its long term effects are unknown.

Aim To determine two year outcomes of children randomised to dextrose or placebo gel for treatment of neonatal hypoglycaemia[1].

Methods At risk babies who became hypoglycaemic (<2.6 mM) were randomised to 40% dextrose or placebo gel. Children were assessed at two years' corrected age for neurological function and general health (paediatrician assessed); cognitive, language, behaviour and motor skills (Bayley III); executive

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