5 had above the sorbitol level (0.9g and 2.1 gram/kg respectively). Three patients received above the propylene glycol limit (52.6mg, 30mg and 190mg/kg), and at least one patient was getting 14.4mg/kg of hydroxybenzoates.

Conclusion When the information regarding quantities of excipients in medicines are available and calculated PICU patients are receiving significant amounts of excipients, some above the recommended safe limits.

1639 ADVERSE DRUG REACTIONS ASSOCIATED WITH CIPROFLOXACIN IN NEONATES

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[1]KA Kuruvilla, [1]V James, [2]M Subramani, [2]B Mathew. *[1]Child Health & Neonatology; [2]Clinical Pharmacology, Christian Medical College & Hospital Vellore, Vellore, India*

Background Ciprofloxacin is used in many nurseries in developing countries. Data on drug concentrations and side effects of ciprofloxacin in neonates is limited.

Aims To study adverse drug reactions(ADR) associated with ciprofloxacin in term and preterm neonates and correlate them with drug levels.

Design Babies of 3 gestational age(GA) groups were enrolled: 37 (gp1), 32–36 (gp2) and 28–31(gp3) weeks. Ciprofloxacin was administered twice daily at 10mg/kg/dose IV. Lab parameters were done at baseline, day 3 and day 7, including peak and trough drug levels. Using Naranjo algorithm, babies who developed new symptoms after starting ciprofloxacin were classified into definite, probable, possible or doubtful ADR. Drug levels were correlated with ADR.

Results 165 babies receiving ciprofloxacin were enrolled. Predominant ADR were jaundice(79%), rash(23%), hyponatremia(28%), anaemia(15%) and hypokalemia(5%). Using Naranjo algorithm, ProbableADR were cardiac arrhythmia, mucosal ulceration, renal failure and seizures. PossibleADR were rash, elevated liver enzymes, feed intolerance and leucopenia. ADRs were self-limited and treatable.

The mean (SD) trough and peak values of ciprofloxacin for the entire study population was 3.57(1.88) and 11.67 (3.66), respectively. Mean (SD) trough drug levels were gp 1–2.84 (1.54), gp 2–3.80 (1.9), gp 3–4.06 (1.98). GA did not seem to play a significant role in pharmacokinetics.

Drug levels higher than mean were seen in babies with rash, leucopenia and elevated LFT. Levels were adequate in babies with HIE, high in babies with NEC and lower in those with RDS.

Conclusions Ciprofloxacin can be considered safe for treating neonates.

1640 EFFICACY AND SAFETY OF MELATONIN IN NEONATES

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[1]S Aversa, [1]L Marseglia, [1]A Arco, [1]G D'Angelo, [1]E Cusumano, [1]I Barberi, [2]RJ Reiter, [1]E Gitto. *[1]Neonatal Intensive Care Unit, Department of Paediatrics, University of Messina, Messina, Italy; [2]Department of Cellular and Structural Biology, The University of Texas Health Science Center, San Antonio, TX, USA*

Background and Aims Newborns are more sensitive to oxidative stress than older infants. Melatonin, based on its properties as chronobiotic, antioxidant, or analgesic, offers perspectives of beneficial effects in neonatology. Aim of this study was to retrospectively review the efficacy and safety of melatonin administered at preterm and at term newborns in NICU.

Methods A retrospective patient record review of newborns treated with Melatonin in NICU of University of Messina (Italy) was performed.

Results 85 neonates were recruited and treated with Melatonin (5–70 mg/Kg/die) in six previously published RCT. Melatonin has been given to 55 preterm infants with RDS and 30 at term newborns (10 with sepsis, 10 with perinatal asphyxia, and 10 with surgical abdominal malformations). That has always been given intravenously except for 10 septic newborns receiving oral administration. In our studies, melatonin treatment was able to reduce the level of proinflammatory cytokines, lipid peroxidation products and clinical parameters of inflammation and sepsis, and to improve the clinical outcome in terms of reduction of bronchodysplasia in preterm infants with RDS. None adverse event has been observed in our population of newborns treated with melatonin.

Conclusions To our knowledge, studies related to the toxicity of melatonin have not uncovered evidence of toxicity in humans even when given in very high doses. Our studies confirmed the potential role of melatonin as a treatment in different neonatal pathologies and the safety of its use in neonates at relatively high doses for short term and in various formulations.

1641 DIAZOXIDE OPENS THE CLOSING NEONATAL DUCTUS ARTERIOSUS

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K Momma. *Pediatric Cardiology, Tokyo Women's Medical University, Tokyo, Japan*

Background and Aims Sulfonylureas inhibit the ATP-sensitive potassium (K_{ATP}) channel, are insulinogenic, and close the fetal ductus arteriosus. Diazoxide, a K_{ATP} channel opener, is used for neonatal hyperinsulinemic hypoglycemia, and has been associated with the reopening of the ductus arteriosus. The aim of this study is to clarify ductus-opening effect of diazoxide.

Methods Neonatal rats were delivered by caesarian section near-term and incubated at 34°C. Diazoxide and pinacidil, another K_{ATP} channel opener, were injected intraperitoneally immediately, or at one hour, or at four hours postnatally, and the ductus was studied 0.5, and 1 hour later, with a rapid whole-body freezing method.

Results Diazoxide and pinacidil both induced hyperglycemia. Diazoxide and pinacidil delayed neonatal ductus closure following injection immediately after birth. At 2 hours, the control ductus was closed, whereas the ductus treated with 100 mg/kg of diazoxide at birth was widely patent with a diameter 40% of the fetal ductus. Ductus diameter at 60 minutes postnatally dilated from 10% to 40% with diazoxide. Diazoxide given to the closed ductus at 4 hours after birth did not open reopen it. The ductus was more sensitive to pinacidil than to diazoxide.

Conclusions Diazoxide and pinacidil open the closing ductus arteriosus of the neonatal rat. This study demonstrates that opening of K_{ATP} channels results in opening of the ductus arteriosus, indicating that the K_{ATP} channel is physiologically and pharmacologically important in ductus opening. The ductus should be checked in the neonate before and after treatment with diazoxide.

1642 DESCRIBING THE USE OF OFF-LABEL AND NOT APPROVED MEDICATIONS IN A NEONATAL INTENSIVE CARE UNIT IN SOUTH BRAZIL

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[1]CG Carvalho, [2]M Ribeiro, [2]M Bonilha, [2]M Fernandes Jr, [1]RS Procianoy, [1]RC Silveira. *[1]HCPA - UFRGS; [2]UFRGS, Porto Alegre, Brazil*

Background and Aims It is known that unlicensed medicines (unapproved) or used other way than directed in the label (off-label use) are widely prescribed in children. In the NICU, the severity of the patient justifies this type of prescription, evoking the risk-benefit ratio. We aimed to analyze the exposure to unapproved or off-label drugs in NICU in a tertiary university hospital in southern Brazil.

Method A descriptive cohort of drugs prescribed during hospitalization for 129 patients within 6 weeks. The drugs were classified as non-approved, and off-label for the dose, frequency, presentation, age or indication, according to FDA-approved e-lary.

Results We identified 318 items of prescriptions for 61 patients - an average of 5 items/patient, 68 patients without medication. Prevalence of 7.5% for unapproved drugs and 27.7% for off-label, and the more prevalent off-label use was regarding to age - 19.5%. It was computed 57 medications - one patient used 10 off-label drugs during hospitalization. The prevalence of off-label uses was higher in infants < 35 weeks (p=0.00). Sepsis, malformation and extreme prematurity were the main causes to prescribe an off-label medication (p=0.00).
Conclusion Neonates exposed to off-label drugs in NICU had more severe disease, and because it is known that newborns, especially premies, use many drugs, it is necessary to prioritize research in the pharmacotherapy of this population so vulnerable.

1643 EFFECT OF ANESTHETIC USED IN LABOR ON TRANSCUTANEOUS BILIRUBIN LEVEL IN THE NEWBORN IN AN UNIVERSITY HOSPITAL IN BRAZIL

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[1,2]PDJH Nader, [3,4]SS Nader, [2]H Raymundo Chinazzo, [2]DF Dolvitsch. *[1]ULBRA, RS; [2]ULBRA; [3]Pediatrics, Universidade Luterana do Brasil, Canoas; [4]HU ULBRA/Mãe de Deus, Porto Alegre, Brazil*

Background and Aims Drugs administered on the mother can cross the placental barrier. The objective of the study is to analyze the effect of anesthetics used in caesarean section in the bilirubin level in neonates.
Methods This is a cross sectional study realized between August 2011 and March 2012, in rooming-in at Universidade Luterana do Brasil Hospital. All the babies born at term, without hemolytic disease, no fetal anomalies, apgar greater than 7 in the fifth minute and breastfeeding only. The transcutaneous bilirubin levels (TBLs) were obtained by the apparatus Dräger Jaundice Meter JM-103®. The TBLs variable was stratified according to the Bhutani nomogram. Were measured TBLs between 24 and 59 hours of life. This study was approved by the Ethics in Research.
Results From a total of 670 babies, 220(32.8%) were delivered by caesarean section by epidural anaesthesia using bupivacaine (group A). In this group, 62.2% received morphine, 12.2% fentanyl and 36.8% sufentanil. The use of different opioids presented no significant association in TBLs, when compared with vaginally delivery. The TBLs in neonates of group A were lower than vaginally delivered (p=0.014). The use of bupivacaine decreased the risk of developing hyperbilirubinemia (p=0.010). The use of ephedrine, a vasoconstrictor, by 148(22%), only in group A, showed a lower risk of developing jaundice (p=0.010). The Buthani nomogram classified as low risk 530(79.1%) neonates.
Conclusions Babies born by cesarean have a higher probability to be classified as lower risk of developing hyperbilirubinemia (p=0.015). Further studies are needed for definite results.

1644 SUCCESS OF A METHADONE TREATMENT PROTOCOL IN NEONATAL DRUG WITHDRAWAL FOLLOWING IN-UTERO EXPOSURE TO SUBSTANCES OF ABUSE

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[1]R Schumacher, [2]C Ng, [1,3,4]V Bhatt-Mehta. *[1]Pediatrics, University of Michigan Health System, Ann Arbor, MI; [2]Pharmacy, Childrens Hospital of Philadelphia, Philadelphia, PA; [3]Pharmacy; [4]Center for Global Health, University of Michigan Health System, Ann Arbor, MI, USA*

Background Neonatal abstinence syndrome (NAS) is often present following in-utero exposure to addictive substances. The Lipsitz tool is used to determine the severity of NAS. Failure to lower Lipsitz scores through supportive care results in pharmacological treatment with methadone, an opioid with an ideally suited long half-life.
Objectives To evaluate the effectiveness of a methadone treatment protocol for NAS.
Methods Neonates who received methadone treatment according to a preexisting treatment protocol were evaluated for treatment success defined as adherence to the methadone regimen with no residual signs of withdrawal. Data collected included: methadone dosages, Lipsitz scores, length of methadone treatment (LOT), and total length of stay (LOS).
Results Sixty subjects were included. The mean gestational age (GA) and birth weight (BW) were 36.8±3.03 weeks and 2.79±0.63kg. All exhibited NAS within 72 hours of life. 59/60 (98.3%) initiated treatment according to protocol. There was significant deviation from the protocol at 48 and 72 hours of treatment with 33% and 12% of the patients requiring more than the prescribed amount of methadone to control NAS. The mean (SD) total methadone exposure was 1.96±1.63 mg/kg, LOT 11.66±9 days and LOS 22.4±29.3 days suggesting significant variability in response. No significant correlation was found between BW or GA and LOT.
Conclusion At diagnosis a protocol for treating NAS was closely followed. Despite a formal protocol there was substantial variability in total methadone exposure, LOT and LOS suggesting other contributory factors for the observed variability.

1645 VANCOMYCIN IN NEWBORNS: COMPARISON OF A STANDARD DOSE TO DOSING ADJUSTED FOR BIRTH GESTATION AND AGE

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D Duffy, M Gayfieva, MA Thomson. *Imperial College Healthcare NHS Trust, London, UK*

Background Vancomycin dosing regimens and individual pharmacokinetics vary in newborns. A time lag in achieving therapeutic levels often occurs with delays in treating sepsis or toxicity.
Aims To investigate initial therapeutic trough levels (10–15 mg/l) achieved by a standard dose (15mg/kg/dose 12 hourly) for all newborns compared to new dosing accounting for birth gestation and postnatal age.[1]
Methods Admissions from March 2010- January 2012 were included. Data on gestation, age, initial therapeutic level (pre 4th dose) and creatinine were analysed.
Results 111 treatment courses in 83 infants were evaluated. The new dosing increased the proportion of therapeutic levels [18/68 (26%) vs.16/43 (37%), p=0.29], greatest in infants ≥ 29 weeks at birth, ≥ 10 days old (12% vs. 66%). Toxicity decreased [21/68 (31%) vs. 9/43 (21%), p=0.28]. Sub-therapeutic levels were unchanged (40% vs. 43%). Creatinine was higher with toxic levels compared to therapeutic/low levels (p<0.0001). No infants with creatinine < 100 umol/l had toxic levels. 18/27 (66%) with toxic levels had a creatinine of > 100 umol/l.
Conclusions Dosing accounting for birth gestation and age resulted in a greater proportion of therapeutic levels and less toxicity but sub-therapeutic levels remain frequent. We recommend large scale population studies to determine the optimal dosing strategy.
Reference:

1. Wallis, Williamson. *Arch Dis Child F&N* 2011; 96.
< 29 weeks at birth: < 10 days: 20mg/kg 18 hourly; > 10 days: 15mg/kg 12 hourly.
≥ 29 weeks at birth: < 10 days: 15mg/kg 12 hourly; > 10 days: 15 mg/kg 8 hourly.

1646 USE OF ADJUNCT CLONIDINE WITH PHENOBARBITAL TREATMENT FOR NEONATAL ABSTINENCE SYNDROME

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[1,2]H Soylu, [1]A Abou Mehrem, [1]RJ Baier. *[1]Neonatology/Pediatrics; [2]Pharmacology & Therapeutics, University of Manitoba, Winnipeg, MB, Canada*