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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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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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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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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Background Neonatal abstinence syndrome (NAS) is a complex of symptoms in newborns exposed to substances/drugs in-utero or after birth. Clonidine is a central alpha-2 agonist and recent studies have shown it can decrease NAS symptoms in opiate withdrawal.
Objective To determine the efficacy of clonidine as an adjunctive agent to phenobarbitale (PB). To elucidate demographic factors, maternal drug profile, nature of the symptoms in infants. To compare NAS profile with PB and PB+clonidine. To show associated side effects with clonidine.
Design/Methods Retrospective review of infants ≥ 35 weeks GA admitted to HSC, Winnipeg from January 2005 to July 2010. Abstinence scores 20 hours before and 40 hours after PB and PB+clonidine were measured by Finnegan scoring system and compared by ANOVA.
Results Twenty four infants (GA 39.3±1.4 wks, BW 3316±595g) were treated by PB+clonidine combination. Fifty eight percent exposed to multiple drugs. Methadone was the most common drug of exposure. Tremor, increased tone, regurgitation and poor feeding were common symptoms. When PB was used alone as initial therapy, NAS scores increased from 6.9±3.3 to 7.5±3.0 ($p>0.05$) at pre and post medication periods respectively. Clonidine was added to PB at 3.5 to 5.3 mg/kg/day and NAS scores were decreased from 8.7±3.4 to 7±3.5 ($p<0.001$). There were no recorded side effects for clonidine.
Conclusions Our study suggests that clonidine may be a useful adjunctive treatment of NAS in infants who respond incompletely to PB. Cardiovascular side effects were not common in our study.

1647 UNLICENSED AND OFF-LABEL MEDICATION USE IN THE NEONATAL INTENSIVE CARE UNIT: A PROSPECTIVE COHORT STUDY

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Background Many medications have not been extensively studied in children. Medications may be prescribed for indications for which their use has not been approved (unlicensed use); or may be given for an approved indication, but to an age group or at a dose or frequency or by a route that has not been approved (off-label use). We wished to determine the extent of unlicensed and off-label prescription in our NICU.
Methods We prospectively studied infants admitted to our tertiary level NICU over 2 months. We recorded demographic data and all medications prescribed for all infants. We compared the use of each medication to their licensed indications as contained in the Summary of Product Characteristics.
Results 110 infants were admitted. All infants received a prescribed medication. 79 different medications were prescribed to these 110 infants, a median (IQR) of 4 (3, 12) each. 41% of prescribed medications were given in an unlicensed manner and 15% in an off-label manner. 12 (11%) infants received an unlicensed medication, 5 (4%) infants received an off-label medication and 38 (35%) infants received both an unlicensed and off-label medication. Of infants < 32 weeks, 91% received unlicensed and 85% off-label medications. 100% of infants < 28 weeks received an unlicensed and an off-label medication. There were 2 adverse events related to medications.
Conclusions Most medications prescribed to newborn are unlicensed or given for off-label indications. Many infants, and the majority of preterm infants, admitted to NICU receive unlicensed and off-label prescriptions. Adverse events appear uncommon.

1648 CLINICAL COURSE AND DRUG SUSCEPTIBILITY FOR INFANTS WITH UREPALSMA INFECTION

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Objectives Ureaplasma species were associated bronchopulmonary dysplasia in preterm infants. We aim to analyze the antibiotic susceptibility of ureaplasma urealyticum and clinical manifestations in preterm infants with ureaplasma urealyticum colonization.
Methods In a retrospective study, 416 preterm infants (≤ gestation 32 wk) and their mothers admitted to Severance Children's Hospital and Gangnam Severance Hospital NICU between Jan 2008. to Jun 2011, were reviewed. Ureaplasma test was done by culture for mothers and PCR in urine and tracheal aspirates for preterm infants. Ureaplasma colonization was confirmed 7.5% of infants, and 31% of the mothers. If positive result was noted, all infants were initially treated with erythromycin empirically.
Results Thirty one infants who had positive ureaplasma PCR test (28.3±3.1wk, 1050±490g) and 385 infants with negative test (29.0±3.2 wk, 1190±550g) were recruited as controls. Infants with ureaplasma infection had longer durations of oxygen administration ($p=0.039$) and mechanical ventilation ($p=0.041$). The incidence of pathologic chorioamnionitis were significantly higher ($p<0.001$). Infants with ureaplasma infection had higher incidence of moderate/severe BPD. For antimicrobial susceptibility, 23% of erythromycin resistance, 16% of zithromycin resistance, 38% of ciprofloxacin resistance and no jasamycin resistance were shown. Among 31 infants with erythromycin treatment, 18 (58%) of susceptible, 6 (19%) of intermediate were cured after 13 days of treatment, and 4 showed poor response erythromycin treatment, 2 changed to josamycin and 2 infants to clarithromycin and all were completely treated.
Conclusion Ureaplasma colonized infants showed higher incidence of BPD. Proper antimicrobial use may reduce the morbidity associated with ureaplasma colonization.

1649 RETROSPECTIVE ANALYSIS OF DOXAPRAM FOR THE TREATMENT OF APNEA OF PREMATURITY

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Background and Aims Only one small randomized controlled study on doxapram to treat apnea of prematurity is available. Before the implementation of a local treatment protocol, we aimed to evaluate the frequency of administration of doxapram in our NICU. We asked, if frequency and severity of apneas were affected by doxapram, if intubation for apnea was avoided, and if side effects occurred.
Methods We retrospectively analysed all premature infants < 30 weeks treated with doxapram during 03/2008 to 03/2010. We registered the number of apneas, bradycardias, and desaturations, an hour before, at the start of, and during 48 hours after onset of treatment.
Results 17 of 64 (27%) infants (mean gestational age 26.1 weeks, mean birth weight 733g) were treated during two years. All of them had been treated with caffeine before doxapram was applied. 70 therapy courses of 16 infants were analyzed. In 8 of 70 (11%) therapy courses, infants were intubated because of apnea during 48 hours of doxapram treatment. The frequency of apneas (2.24 vs. 0.17), bradycardias < 80/min (0.93 vs. 0.14), and desaturations