Results: A total of 65 newborns, 55 preterm and 10 full-terms were admitted to the neonatal ward and received 265 prescriptions. Fifty four percent (143/265) of prescribed drugs were licensed, 16.6% (44/265) were off-label for paediatric use, 21% (56/265) for age, 2.4% (6/265) for dosage and 6% (16/265) for route of administration. Unlicensed drug utilisation has not been detected. Seventy one percent (46/65) of infants received at least one off-label prescription.

Conclusion: Prescriptions of off-label drugs in neonatal unit is common. Clinical trials assessing the benefit and harms of off-label or unlicensed drugs frequently prescribed should improve the lack of trial-based data for children.

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PROSPECTIVE EVALUATION OF PROPYLENE GLYCOL TOLERANCE IN (PRE)TERM NEONATES: AN ACTIVE COMPARATOR APPROACH

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Introduction: Propylene glycol (PG) is a commonly used excipiens although accumulation can result in hyperosmolarity, renal toxicity and lactic acidosis. This is of concern in neonates given their limited metabolic capacity [1]. We therefore evaluated renal, metabolic and hepatic tolerance during PG exposure in neonates.

Methods: (pre)term neonates included in the PARANEO study (NCT00969176) received iv paracetamol PG (0.8 mg PG/mg paracetamol) for up to 48 h. Data on renal (diuresis, creatinaemia), metabolic (lactate, Anion Gap[AG]) and hepatic tolerance (AST, ALT, direct bilirubinaemia) were collected from 48 h before until 48 h after iv administration and compared with earlier reported observations on renal and hepatic tolerance during iv paracetamol (Perfalgan) exposure in neonates [2,3].

Results: Based on observations available in 40 neonates (median GA 36 wk, PNA 6 days, weight 2.5 kg) and following median PG exposure of 59 (15-238) mg/kg, progressive postnatal normalization of creatinaemia and diuresis, lactate, BE, AG and liver enzymes was observed while sodium remained stable.

Conclusions: Median PG exposure of 59 mg/kg over 48 h did not affect postnatal adaptation and renal and hepatic observations were similar to earlier observations on iv paracetamol tolerance in neonates. We therefore conclude that this level of PG exposure seems to be well tolerated, but further studies on PG disposition and clearance are needed.

[1] Wittaker et al. Arch Dis Child 2009;94:F236-40, [2] Allegaert et al. Acta Paediatr 2005;94:1273-9, [3] Allegaert et al. Paediatr Anaesth 2008;18:388-92.

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HYPOGLYCEMIC AGENTS SULFONYLUREAS CONSTRICT THE FETAL DUCTUS ARTERIOSUS IN THE RAT

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Background: Sulfonylureas (tolbutamide = Rastinon, glibenclamide = glyburide, glimepiride = Amaryl) inhibit K_{ATP} channels and induce release of insulin. In in-vitro studies, glibenclamide constricts the ductus arteriosus. Placental transport of sulfonylureas is variable; high with tolbutamide, and low with glibenclamide, respectively.

Purpose: To clarify the *in-vivo* ductus constrictive effects of various sulfonylureas.

Methods: Sulfonylureas were administered orogastrically to pregnant near-term (21FD) or pre-term (19FD) Wistar rats. Fetal ductus arteriosus was studied 2, 4, 8 and 24 hours later, with a rapid whole-body freezing method and measurement of the inner diameter of the ductus.

Results: Tolbutamide constricted the fetal ductus dose-dependently. With clinical dose (10 and 30 mg/kg), the near-term fetal ductus constricted moderately, and the ductal diameter decreased to 0.8 and 0.5 compared to the control four hours later. With a large dose (100 mg/kg), the fetal ductus constricted severely, and the diameter decreased to 0.2 compared to the control four hours later. Tolbutamide constricted the pre-term ductus comparatively less. Glimepiride with a large dose of 10 mg/kg constricted the near-term fetal ductus

only mildly. With a large dose of glibenclamide (10 mg/kg), it did not constrict the near-term or the preterm ductus arteriosus, reflecting poor placental transport.

Conclusion: Clinical doses of tolbutamide constrict the fetal ductus moderately. With a 10 times larger dose, the ductus closes completely. Experimental comparison suggests tolbutamide is more potent constrictor of the fetal ductus than indomethacin, and can be used to close a premature PDA in the rat model.

FD = Fetal Days

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ALLERGY TO ORAL MACROLIDES ANTIBIOTICS IN CHILDREN

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Background: Allergic or pseudo-allergic reactions to macrolides antibiotics are relatively uncommon (0.4-3% of treatments). The allergological work-up for the diagnosis of macrolides hypersensitivity is undefined.

Methods: In our study we analyzed 95 children with history of macrolides reactions. Skin tests were performed according to EAACI guidelines by prick tests (PT) followed by intradermal test (ID) with the culprit drug. Oral Double Blind Provocation Tests (ODBPT) were performed in order to exclude or confirm a real state of drug hypersensitivity and to check the cross-reactivity.

Results: 46 females and 49 males (mean age 6.2 years) described a total of 102 reactions to macrolides (28 immediate and 70 late). The most frequently involved drug was clarithromycin (69.6%). It mainly provoked mucocutaneous eruptions. All the children with suspected clarithromycin allergy underwent the ODBPT, but the diagnosis was confirmed in the 6.25% of cases and they all tolerated an alternative macrolidic drug. Azythromycin resulted less frequently involved (19,6%) but it caused the more severe reactions. The two patients (50% of those with history of immediate reactions) with anaphylaxis to azythromycin had positive skin tests with the culprit drug, however they both tolerated clarithromycin.

Conclusion: Clarithromycin even being the most common cause of allergic reactions, it usually provokes mild cutaneous flares and a real state of hypersensitivity is rarely proven. On the contrary, azythromycin rarely resulted as cause of drug reactions but when it occurs these are severe. At last even in case of anaphylaxis allergy to macrolides seems not to be a class allergy.

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COMPARING BERACTANT AND PORACTANT ALFA FOR TREATMENT OF RESPIRATORY DISTRESS IN PREMATURE NEONATES

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Background: Respiratory distress syndrome (RDS) is a major cause of mortality and morbidity in preterm infants. The aim of this study was to compare the complications of prematurity among preterm infants treated with two different natural surfactants.

Materials and methods: In a randomized clinical trial 150 preterm infants with RDS treated with exogenous surfactant were enrolled in the study. Group A consist of 79 neonates that received poractant (curosurf). Seventy one newborn infants in group B were treated with beractant (Survanta).

Results: The mean gestational age for group A and B were 29.40±2.90 wk and 29.50±2.73 wk (P=0.82). The demographic and clinical variables were similar in both groups. The mean duration of intubation was significantly shorter in infants treated with poractant (3.13±1.80 vs. 4.06±2.7 days p=0.02). The mean duration of need for oxygen and hospitalization of patients in group A and B were 17.73±22.25 vs.19.14±17.85days (p=0.67) and 24.89±26.41 vs. 29.14±23.54 days (p= 0.32) respectively. There was no significant difference between groups with respect to mortality and morbidity including pulmonary hemorrhage, intraventricular hemorrhage (IVH), patent ductus arteriosus, sepsis, and bronchopulmonary dysplasia.

Conclusions: In this study infants had received poractant had shorter duration of intubation than infants treated with beractant without difference in the duration of oxygen therapy or admission. There was no significant superiority of poractant over beractant.