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 excipients 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