PROPYLENE GLYCOL PHARMACOKINETICS AND RENAL ELIMINATION CAPACITY: PRELIMINARY OBSERVATIONS

A. Kulo^{1,2}, V. Cossey³, J.N. de Hoon¹, R. Verbesselt¹, **K. Allegaert**³

¹*Center for Clinical Pharmacology, University Hospitals Leuven, Leuven, Belgium,* ²*Institute of Pharmacology, Clinical Pharmacology and Toxicology, University of Sarajevo, Sarajevo, Bosnia-Herzegovina,* ³*Paediatrics, University Hospitals Leuven, Leuven, Belgium*

Introduction: Unintended propylene glycol (PG) administration (34 mg/kg/24h) did not affect postnatal adaptations [1]. Subsequently, we aim to document PG disposition in neonates.

Methods: Blood and urine samples were collected in neonates to whom PG was co-administered (Paracetamol Synthetica®, Mendrisio, Italy). Plasma and urine samples were collected in the first six hours after the first drug administration (loading dose, 20 mg.kg⁻¹ paracetamol, equal to 16 mg PG kg⁻¹). An earlier described reversed phase liquid chromatographic (LC) method with ultraviolet detection was optimized for chromatographic separation.

Results: Chromatographic separation resulted in cleaner chromatograms without interfering compounds. Linearity, variations in the intra-and inter-assay precision and accuracy and stability at different temperature conditions were satisfactory. The lower limit of quantification (0.25 mg.L⁻¹) was twenty times lower than in earlier described methods. The method was suitable for quantification of PG concentrations in low volume plasma (15-46 mg.L⁻¹) and urine samples (20-175 mg.L⁻¹), strongly indicating difference between neonates and adults in the relative contribution of the renal (7.02%) compared to the metabolic route for PG elimination. Assuming a one-compartment model, peak concentrations were around 40 mg.L⁻¹, suggesting a distribution volume of 0.5 L.kg⁻¹ while the elimination half life was estimated to be 6-12 h.

Conclusion: An accurate and sensitive LC method was developed, and applied to determine PG in low volume neonate plasma and urine samples, enabling us to estimate the renal versus non-renal contribution of PG clearance in neonates.

[1] Allegaert K et al. Arch Dis Child 2010;95:1054-1058