PHARMACOKINETICS OF DRUGS IN NEONATES: PATTERN RECOGNITION BEYOND COMPOUND SPECIFIC OBSERVATIONS

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Although the principles of disposition and elimination of exogenous compounds also apply in neonates, their specific characteristics warrant a focussed assessment. Children display maturation in drug disposition, but this is most prominent in the first year of life. Elimination clearance is mainly through either renal or metabolic elimination clearance.Renal elimination clearance in early life is low and almost completely depends on glomerular filtration. Despite this overall low clearance, interindividual variability is already extensive and can be predicted by covariates like postmenstrual age, postnatal age, co-administration of a non-selective cyclo-oxygenase inhibitor, growth restriction or peripartal asphyxia. These findings are illustrated by observations on amikacin, vancomycin and cefazolin disposition in perinatal life. Variation in phenotypic metabolic clearance is based on constitutional, environmental and genetic characteristics. In early life, it mainly reflects ontogeny, but other covariates may also become relevant. Almost all phase I and phase II metabolic processes display ontogeny in a iso-enzyme specific pattern. The impact of various covariates like postmenstrual age, postnatal age, disease state characteristics and polymorphisms are illustrated based or 'probe' drugs (paracetamol, tramadol, propofol) administered as part of their medical treatment in critically ill neonates.The description of a compound specific pattern is beyond compound specific relevance. The patterns described and the extent of the impact of covariates can subsequently be applied to predict in vivo time-concentration profiles for compounds that undergo similar routes of elimination. Through improved predictability, such maturational models can serve to improve both the clinical care and clinical studies in neonates.