P07 INTER-INDIVIDUAL VARIATION IN MORPHINE CLEARANCE IN CHILDREN

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Objectives Morphine is the drug of choice for severe pain. There is a four-fold variation in the recommended dose of intravenous morphine. We decided to determine the extent of inter-individual variation in clearance of morphine in children.

Methods A systematic literature review was performed to identify papers describing the clearance of morphine in children. The following databases were searched: Medline (1946 to May 2013), Embase (1974 to May 2013), International Pharmaceutical Abstracts (1974 to May 2013), CINAHL (1937 to May 2013) and Cochrane library. From the papers the range in plasma clearance and the coefficient of variation (CV) in plasma clearance were determined.

Results Twenty eight articles were identified. Only 12 studies gave clearance values for individual patients. The majority of the studies were in critically ill patients.

Inter-individual variability of morphine clearance was observed in all age groups.

The CV was 16–97% in preterm neonates, 24–150% in term neonates, 4.5–140% in infants, 14–55% in children and 14–74% in adolescents.

The variation ratios of clearance were 2–13 fold (185 preterm neonates), 2–23 fold (72 term neonates), 2–10 fold (120 infants) 1.3–3 fold (17 children) and 2–2.6 fold (8 adolescents).

The mean clearance was higher in children (21.5 to 80.5 ml/min/kg) than in neonates (2.2 to 20.2 ml/min/kg).

Conclusions Large inter-individual variation was seen in morphine clearance values in critically ill neonates and infants. The variation in clearance is far greater than the variation in recommended doses. The dose of morphine should be titrated according to need after adequate pain assessment.