O15 LIDOCAINE PLASMA CONCENTRATIONS AND ANTI-EPILEPTIC EFFICACY IN TERM AND PRETERM NEONATES: PROSPECTIVE VALIDATION OF A NEW DOSING REGIMEN

[1]L Favié*, [1]C Rademaker, [2]M van den Broek, [1]T Egberts, [3]F van Bel, [3]F Groenendaal. [1]*Clinical Pharmacy, University Medical Center Utrecht, Utrecht*; [2]*Clinical Pharmacy, St Antonius Hospital, Nieuwegein*; [3]*Neonatology, University Medical Center Utrecht, Utrecht, The Netherlands*

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Background Lidocaine is used as an add-on anti-epileptic drug (AED) in neonates when seizures persist despite treatment with first line anticonvulsants. Although lidocaine has shown to be an effective anticonvulsant, cardiac toxicity associated with plasma concentrations >9 mg/L have limited its wide scale use.[1] Previous studies from our group have proposed a dosing regimen for effective and safe lidocaine use in term and preterm neonates with plasma concentrations not exceeding 9 mg/L.[2,3]

Aim The present study evaluated lidocaine use as anticonvulsant in neonates and prospectively validated the new dosing regimen.

Methods Data were collected at the neonatal intensive care unit of the University Medical Centre Utrecht. Neonates refractory to at least one AED received lidocaine according to clinical protocol. Lidocaine was administered as a 2 mg/kg loading dose in 10 minutes followed by a three stage maintenance phase with tapering lidocaine doses. Lidocaine plasma concentrations were measured from blood samples taken at the end of the first stage (highest lidocaine dose) and during the second or third stage (tapered lidocaine dose). Efficacy was determined as abolishment of seizures during lidocaine therapy and no recurrence within 24 h after cessation.

Results Lidocaine data were available from 75 neonates (gestational age 36.2 weeks [range 25.0–42.4, < 36.0 38.7%], birth weight 2771 g [range 675–4875], male 64.0%, mortality 45.3%). 23 patients (30.7%) received the new dosing regimen, 52 patients (60.7%) the old regimen. Highest measured plasma concentration with the new regimen was 9.15 mg/L and 16.8 mg/L with the old regimen. Efficacy with the new regimen was 56.5% and 53.8% for the old regimen. No cardiac toxicity was observed in either group.

Conclusions The new lidocaine dosing regimen leads to safe and effective lidocaine plasma concentrations and has similar efficacy compared to the previous dosing regimen.

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O16 PIGLETS AS ANIMAL MODEL TO ASSESS THE CONTRIBUTION OF FLUID THERAPY TO THE DEVELOPMENT OF AUGMENTED RENAL CLEARANCE IN CHILDREN

[1]L Dhondt*, [1]S Croubels, [2]P De Paepe, [2,3,4]P De Cock, [1]M Devreese. [1]*Department of Pharmacology, Toxicology and Biochemistry, Ghent University, Merelbeke*; [2]*Heymans Institute of Pharmacology, Ghent University*; [3]*Department of Pharmacy*; [4]*Department of Paediatric Intensive Care, Ghent University Hospital, Ghent, Belgium*

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Background The past years augmented renal clearance (ARC), observed in the critically ill paediatric population, has received an increased attention by researchers due to its major impact on drug exposure.[1] Since a recent report demonstrated that the maturation of the glomerular filtration rate (GFR) in juvenile pigs is comparable to children, pigs may be a potential animal model to investigate the impact and mechanisms of ARC on drug pharmacokinetics (PK) in children.[2]

In this pilot study, the contribution of intravenous (IV) fluid administration on the development of ARC was investigated in piglets.

Methods Eight seven-week-old pigs underwent an experiment without fluid therapy and two consecutive fluid treatments as CRI of a 0.9% NaCl solution (3 mL/kg/h and 6 mL/kg/h) over 36 hours, each time combined with IV administration of a cocktail of renal markers after 4 and 24 h of fluid administration. This cocktail consisted of iohexol (64.7 mg/kg body weight (BW), Omnipaque 300®, marker for GFR) and para-aminohippuric acid (10 mg/kg BW, marker for effective renal plasma flow). To assess the impact of ARC on the PK of antimicrobials, amikacin (7,5 mg/kg BW, Amukin®) was administered after 24 h of fluid therapy. PK modelling was performed with Phoenix® WinNonlin®.

Results Generally, an increase in GFR was observed after fluid administration when compared to the GFR values observed without fluid administration. 4 and 2 out of 7 pigs demonstrated ARC after 4 h of a CRI at 3 mL/kg/h and 6 mL/kg/h, respectively. 4 out of 7 pigs displayed ARC after 24 h of a CRI at 3 mL/kg/h and 6 mL/kg/h. Similar results were obtained for amikacin clearance.

Conclusion An important effect of fluid therapy on the development of ARC was observed in juvenile pigs. Further research is necessary to confirm this results in critically ill children.

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