Oral

[O25-8] O25-8: Infections in pediatrics

Chairs: Camelia Grigore, Romania / Natella Rakhmanina, USA
Mon. Sep 25, 2017 4:00 PM - 5:00 PM Room C1 (1F)

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[O25-8-2] Population Pharmacokinetics of Amoxicillin and gentamicin in term neonates undergoing moderate hypothermia

Yuma Bijleveld[1], Ron Mathot[2], Anton Van Kaam[3], Timo De Haan[4], Floris Groenendaal[5] (1.Academic Medical Center, 2.Academic Medical Center, 3.Academic Medical Center, 4.Academic Medical Center, 5.University Medical Center Utrecht)

Keywords: amoxicillin, gentamicin, neonate, population pharmacokinetics, moderate hypothermia

Background

Term neonates who experience a severe hypoxic-ischemic insult during birth and develop encephalopathy are treated with moderate hypothermia.(1,2) Amoxicillin (AMX) and gentamicin (GNT) are frequently used antibiotics in these patients.(3) Studying the potential effect of hypothermia on their pharmacokinetics (PK) is important, as this information is mostly lacking. This study prospectively evaluates and describes the population PK of these antibiotics in this specific patient population. If necessary, more rational dosing regimens will be proposed.

Methods

Data of patients included in a multicenter prospective observational cohort study conducted in ten Dutch and two Belgian NICUs between November 2010 and October 2014 (the “PharmaCool Study” (3)) were collected. Term newborns (>37 weeks gestational age (GA)) fulfilling the criteria of perinatal asphyxia were cooled <6 hours after birth to a core body temperature (TEMP) of 33.5˚C for 72 hours. Thereafter the infants were rewarmed to normothermia (36.5˚C) over 8 hours. Blood samples were drawn during the cooling-, rewarming- and normothermic phase. A non-linear mixed-effects regression analysis (NONMEM®) was performed to describe the population PK of AMX and GNT. The optimal dosing regimens were evaluated based on Monte Carlo simulations of the final PK models.

Results

Forty-seven and 125 patients received GNT and AMX, respectively. See table 1 for the demographic information. The PK of both antibiotics were best described by an allometric 2-compartment model with first order elimination with a priori 3/4 allometric scaling on birthweight. AMX clearance (Cl_{AMX}) increased with increasing postnatal age (PNA), GA, TEMP and urine volume (for all covariates $p<0.001$). GNT clearance (Cl_{GNT}) increased with increasing GA and PNA (for both covariates $p<0.001$). Furthermore, Cl_{GNT} was constant during hypothermia and rewarming, but increased with 29% after reaching normothermia (>96 hours PNA). The Cl_{AMX} and Cl_{GNT} for a patient with GA 40 weeks and BW of 3 kg are shown in figure 1.

Conclusions

We recommend an empiric dose of 50 or 75 mg/kg/24h AMX in 3 doses for patients with GA 36 or 38-42 weeks, respectively. For GNT we recommend 5 mg/kg every 36 or every 24 hours for patients with GA 36-40 weeks and GA 42 weeks, respectively.

Acknowledgements:
Funding for this study has been received by the Dutch Government (ZonMw Grant number: 40-41500-98-

9002). The authors thank Irmgard Corten of the Clinical Research Unit Academic medical Centre (CRU) for her contributions with regard to the data management.

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Tables &figures

Table 1: Demographic information of study population
Zoom image

Figure 1: Clearance of amoxicillin and gentamicin versus postnatal age (PNA) for a typical patient with gestational age 40 weeks and birth weight 3 kg.
Zoom image