Poster

[P26-2] P26-2: Central nervous system drugs (1)

Chair: Atsushi Yonezawa, Japan

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[P26-2-2] Lidocaine pharmacokinetics during therapeutic hypothermia after perinatal asphyxia: evaluation of an existing model

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Background

Pharmacokinetics of drugs may be affected by therapeutic hypothermia in full term neonates with perinatal asphyxia. Little information is available on the pharmacokinetics of drugs frequently administered during therapeutic hypothermia and evidence based dosing guidelines are needed.

Objective:

In the prospective, nationwide PharmaCool study (NTR2529) pharmacokinetics of lidocaine, a second line anti-epileptic drug, were studied. Aim of this study was to evaluate pharmacokinetics of lidocaine under therapeutic hypothermia as published previously (*Arch Dis Child Fetal Neonatal Ed 2013; 98 F341-F345*).

Methods

Term neonates who received lidocaine while treated with therapeutic hypothermia following perinatal asphyxia were eligible. Lidocaine was administered according to local or national protocols. A maximum of four plasma samples were obtained during the first 120 hours after birth during both hypothermia and normothermia. Plasma concentrations for lidocaine and its active metabolite monoethylglycylxylidine (MEGX) were analyzed using a validated LC-MS/MS method. Pharmacokinetic analyses were performed using NONMEM (version 7.3).

Results

For twenty patients (GA 39.9 wks [range 36.0-42.0]; BW 3458 g [range 2090-5000] data was available for analysis. All patients received a loading dose of 2 mg/kg lidocaine in 10 minutes. In 85% of the patients, this was followed by 4 mg/kg for 6h and 2 mg/kg for 12h while 15% received a different dosing regimen. Forty plasma samples were obtained; twenty during hypothermia and twenty during normothermia. Lidocaine plasma levels ranged from 0.1 to 5.5 mg/L (figure 1). Population parameters for lidocaine scaled to 3.0 kg were 1.96 L/h for clearance (Cl) and 13.2 L for volume of distribution (Vd). Clearance of lidocaine and MEGX was reduced under therapeutic hypothermia by 23% and 19%, but this effect was not statistically significant.

Conclusions

Population parameters for Cl and Vd were similar to previous findings. Although the effect of therapeutic hypothermia on the pharmacokinetics of lidocaine and MEGX was not statistically significant in this study, it is in line with the previously identified magnitude of the effect.

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Figure 1: Observed lidocaine plasma levels. Plasma concentrations above the dotted line (9 mg/L) are considered toxic and should be avoided

Zoom image