Results The development of HIE stage 3 was significantly lower in Anapexia group (8%) than in the Normothermia group (28%) (p=0.052; [RR]=0.285). Fifteen neonates in the anapexia group had normal outcome versus only 9 in the normothermia group (p=0.049; [RR]=0.5). The incidence of mortality (12% vs 16%, p=0.264, [RR]=0.75) complications and baseline characteristics were comparable.

Conclusions Anapexia if allowed to persist for 72 hours after birth, alleviates the ill effects of hypoxic ischemic insult and results in improved outcome in the neonates particularly the neurodevelopmental outcome at 6 months of age.

Background and Aims Therapeutic moderate hypothermia for neuroprotection in asphyxiated newborns can influence pharmacokinetics and pharmacodynamics. Lidocaine is administered if seizures persist despite initial therapy. Because cardiotoxicity is a potential risk of lidocaine, dose adjustment under hypothermia might be necessary to prevent toxicity. The aim was to evaluate the effect of hypothermia on lidocaine pharmacokinetics and to evaluate the efficacy and safety under hypothermia.

Methods Hypothermic data were obtained from the SHIVER-study. Term born newborns with perinatal asphyxia and encephalopathy with lidocaine therapy were included. Therapeutic hypothermia (35.5°C, for 72 hours) was applied within 6 hours after birth. Lidocaine dosing under hypothermia was reduced; initial dose 2 mg/kg in 10 minutes, followed by an infusion of 4 mg/kg/h during 6 hours. Subsequently the infusion was reduced to 2 mg/kg/h during 12 hours, and then stopped.

Data from normothermic newborns were obtained from a previously published study (van den Broek et al., 2011). Pharmacokinetic modelling was performed using NONMEM.

Results 22 hypothermic newborns were included and were compared with 26 normothermic newborns. Based on a one-compartmental model with allometric relationships, lidocaine clearance was decreased by 24% under hypothermia, while relative metabolite formation was unchanged. During hypothermia no effect of lidocaine on heart frequency could be observed and the observed efficacy, i.e. decrease of seizure activity, was 78%.

Conclusion Hypothermia has a clinically relevant effect on lidocaine clearance. The dosing regimen needs to be adjusted under hypothermia in order to maintain efficacy and to prevent adverse events. This model is currently validated.

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