The neonatal Göttingen Minipig as translational model for perinatal asphyxia and therapeutic hypothermia

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Introduction

Perinatal asphyxia (PA)

Therapeutic Hypothermia (TH): cooling core body temperature (T°) at 33.5°C for 72h

Decreased body T° slows metabolic rate, preventing further brain damage

Physiology-Based Pharmacokinetic (PBPK) cooling framework as integrative predictive model in neonates

Investigation of cooling and asphyxia on pharmacokinetics (PK) in neonatal Göttingen Minipigs

Add-on drug treatment: Fentanyl Midazolam Topiramate Phenobarbital

Phase I CYP enzymes

Results

Study procedures were well tolerated for 24h in 24 neonatal Göttingen Minipigs of 551.12g (± 60.32g). Cooling was easy to control and to maintain at a target rectal temperature of 33.5°C. Hypoxia could be established for 51 (±34.82) min. Increased blood lactate 9.56 (±2.27) mmol/L and decreased pH 7.00 (±0.16) were used as key parameters for PA.

- Peripheric catheterisation was easiest in the epigastric vein, whereas catheterization of the umbilical vein depended on whether the umbilical cord was still wet or not.
- Central venous catheterisation via Modified Seldinger technique, showed to be the main method for vascular access, either for sampling or administration.

Conclusions

- We showed that perinatal asphyxia (PA) can be induced in the neonatal Göttingen Minipig, in a setting comparable to human NICU, and the effect of PA and TH on drug disposition can be studied separately, for 24h.
- These data reveal the potential of the neonatal Göttingen Minipig as promising in vivo animal model in safety assessment for conditions for the human paediatric population.

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