The Neonatal Göttingen Minipig Model for Dose Precision in Perinatal Asphyxia and Therapeutic Hypothermia

Marina-Stefania Stroe, Lieselotte Van Bockstal, Allan Valenzuela, Miriam Ayuso, Karen Leys, Pieter Annaert, Sebastien Carpentier, Anne Smits, Karel Allegaert, Adrian Zeltner, Antonius Mulder, Chris Van Ginneken, Steven Van Cruchten

1Comparative Perinatal Development, University of Antwerp, Belgium 2Drug Delivery and Disposition, KU Leuven, Belgium 3UZ Leuven, Leuven, Belgium 4Göttingen Minipigs A/S, Dalmose, Denmark 5UZ Antwerp, Antwerp, Belgium

Introduction

Perinatal asphyxia (PA) decrease body temperature (T) at 33.5°C for 72h

Therapeutic Hypothermia (TH)

Investigation of TH and systemic hypoxia (PK) in neonatal Göttingen Minipigs

Decreased body T slows metabolic rate preventing further brain damage

Methods

Control (n=6): Normothermia (38 - 39.5 °C) & Normoxia (21% Oxygen)

Therapeutic hypothermia (n=6): Cooling treatment (33.5°C) & Normoxia (21% Oxygen)

Hypoxia (n=6): Hypoxia (15% Oxygen for ~1h) & Normothermia (38 - 39.5°C)

Hypoxia + Hypothermia (n=6): (15% Oxygen for ~1h) & Cooling treatment (33.5°C)

Hypoxia was induced with a low oxygen gas mix (15% oxygen and 85% nitrogen), or by combining the gas mix with asphyxia, performing the ETT occlusion, for seven min.

Conclusions

- We showed that systemic hypoxia can be induced in the neonatal Göttingen Minipig, in a setting comparable to human NICU, and the effects of hypoxia 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 pediatric population.

Results

Study procedures were well tolerated for 24h in 24 neonatal Göttingen Minipigs of 551.12g (± 60.32g). TH 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 biochemical biomarkers in the hypoxia assessment.

Peripheral catheterization 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 catheterization via Modified Seldinger technique, showed to be the main method for vascular access, either for sampling or administration.

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