O3-6

Propofol administration to the fetal-maternal unit reduced myocardial injury in late-preterm lambs subjected to severe prenatal asphyxia and cardiac arrest

Seehase M. (1,2), Houthuizen P. (3), Jellema R.K. (2), Collins J.J.P. (2), Bekers O. (4), Breuer J. (1), Kramer B.W. (2)
Department of Pediatric Cardiology, University of Bonn, Bonn, Germany (1);

Dept. of Paediatrics, Maastricht University Medical Center, Maastricht, The Netherlands (2);

Department of Physiology, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Center, Maastricht, The Netherlands (3);

Department of Clinical Chemistry, Maastricht University Medical Center, Maastricht, The Netherlands (4)

Introduction: Cardiac dysfunction is reported in the majority of cases after severe perinatal asphyxia. We hypothesized that the maternal anaesthesia during an emergency caesarean section offers a therapeutic window and that propofol administration to the maternal-fetal-unit can diminish cardiac injury and dysfunction in preterm fetuses exposed to global severe asphyxia in utero. We proposed that propofol would interfere with the fetal mitochondrial apoptosis pathway by activating anti-apoptotic cellular mediators, such as the kinase family AKT and the signal transducer and activator of transcription-3 (STAT-3) with its effector molecule B-cell lymphoma-extra large (Bcl-xL). Bcl-xl can reduce the cytochrome c release from mitochondria which results in less activation of apoptosis initiating and effector caspases, such as caspase-3 and -9.

Methods: 36 late-preterm lambs (133d gestational age (GA), term 150d) underwent standardized total umbilical cord occlusion (UCO) or sham-treatment in utero. Eight animals served as GA controls. UCO resulted in global asphyxia and cardiac arrest. Mothers were randomized to either propofol or isoflurane anaesthesia. After emergency Caesarean section, the fetuses were resuscitated and subsequently anaesthetized the same way as their mothers. Cardiac function and injury was assessed by determination of left ventricular ejection fraction (LVEF) and troponin T release into the plasma.

Results: Propofol treatment resulted in higher median LVEF of 84% in comparison to isoflurane treatment (LVEF=74%) after cardiac arrest, resuscitation and 8h of intensive care. Cardiac troponin T increased after asphyxia only in isoflurane treated lambs. Fetal propofol treatment before and after UCO resulted in reduced activation of caspase-3, caspase-9, and cytochrome c release when compared to asphyctic isoflurane animals. On the other hand, Bcl-xL increased to 269%, its transcription factor pSTAT-3 to 655% and the AKT kinase family by nearly 5-fold if compared to isoflurane animals suffering from asphyxia.

Conclusions: Early propofol administration to the maternal-fetal unit preserved cardiac function of late-preterm lambs after cardiac arrest and resuscitation better than isoflurane. The underlying mechanism is probably an activation of anti-apoptotic STAT-3 and AKT pathway.