IS-79 The immunosuppressant drug FK506 ameliorates neonatal cerebral mitochondrial dysfunction and energy failure after transient intrauterine ischemia in rats

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[Objective] Mitochondrial respiratory activities and energy metabolism were measured in neonatal rat brains to evaluate the influence of transient intrauterine ischemia on the near-term fetus and to assess the effect of the immunosuppressant drug FK506 treatment. [Methods] Ischemia was induced by 30 min of the right uterine artery occlusion at 17 days of gestation in Wistar rats (n = 18 pregnant rats). The vehicle or 1.0 mg/kg of FK506 was administered after 1 h of recirculation. The pups were delivered by cesarean section at 21 days of gestation and samples of cerebral tissue were obtained from pups at 1 h after birth. The mitochondrial respiration was measured polarographically in homogenates. For the analysis of ATP, ADP, and AMP, fluorometric enzymatic techniques were used. [Results] In the neonatal cortical tissue exposed to ischemia, mitochondrial activities and ATP concentrations decreased significantly to 59% and 67% of those in normoxic controls, respectively. The deterioration of both mitochondrial activities and high-energy phosphates was prevented by FK506 (p < 0.05). [Conclusion] The present results indicate that the transient intrauterine ischemia is accompanied by mitochondrial dysfunction and cellular bioenergetic failure in the neonatal rat brain and suggest that treatment with FK506 prevents the deterioration, even when administered after the ischemic periods.

IS-80 Effects of extracorporeal membrane oxygenation on hypoxemic ovine fetuses

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[Objective] The purpose was to determine the applicability of using extracorporeal membrane oxygenation (ECMO) techniques to support fetal oxygenation under hypoxic conditions. [Methods] The ECMO system was applied to three instrumented fetal sheep with the placental circulation intact. Blood, maintaining the ECMO, was obtained through a double lumen catheter (D-cath) inserted into the right atrium. After oxygenation the blood was returned to the carotid artery through a single lumen catheter (VA ECMO) or to the right atrium through the D-cath (VV ECMO). During continuous infusion of nitrogen into the maternal trachea, initially the VA ECMO was started to maintain fetal oxygenation and thereafter it changed to VV ECMO. Blood samples were drawn at control and initial hypoxemia (H) period and during hypoxemia with both types of ECMO to measure the cranial carotid arterial pO2 (Cup pO2), fetal plasma catecholamines, arginine vasopressin (AVP) and atrial natriuretic peptide (ANP). [Results] Mean values of Cup pO2 were 21, 13, 25.0 and 19.0 mmHg during control, H, VA ECMO and VV ECMO, respectively. Catecholamines and AVP increased during the experiments. ANP increased during control through the VA ECMO, however decreased during the VV ECMO. [Conclusion] The ECMO system could effectively maintain fetal oxygenation during hypoxemia, however it might be a stressful method in fetal circulation.

IS-81 Lipopolysaccharide Administration Worsen Hypoxic-ischemic Damage in Newborn Rats

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[Objective] Intrauterine infection is associated with fetal and neonatal brain damage. In this report we examined dose-response of lipopolysaccharide (LPS) administration on hypoxic-ischemic (HI) insult in the neonatal rats. [Methods] Seven-day-old Wistar rats were separated into three groups: 1) preinjection of LPS (i.p. 10 mg/kg, n = 8), 2) preinjection of saline, and 3) administration of LPS without ligation or hypoxia (n = 9). At 4 hours after preinjection, groups 1) and 2) were exposed to unilateral carotid artery-ligation followed by 1 hour of hypoxia (8% oxygen/92% nitrogen) at 33°C. All rats were sacrificed 7 days after the insult and the brains were removed for histological study. Neuronal damage was categorized as mild, < 25%; moderate, 25 - 50% ; and severe, > 50%. [Results] We found that the cerebral cortex was mainly damaged, however the hippocampal region was almost unaffected. 99% of saline group showed no neuronal death, while group 1) revealed dose-dependent increase in neuronal death, from 56% at 5 mg/kg LPS group to 70% at 10 mg/kg LPS group. No histological changes were observed either 1 mg/kg LPS or LPS alone. [Conclusion] Our results showed that LPS works additively on HI insult in a dose-response fashion to cause brain damage.