Gestational Sepsis Induces Oxidative Stress, Neurovascular Unit Modulation and Microglia Activation in the Hippocampus and Frontal Cortex of Neonatal Mice

MARCELO GOMES GRANJA[1,2], Flávia Maciel de Moraes[2,3], Letícia Pires Alves[2,3], Giulia Andrade[2], Vanessa Estato[2], Hugo Caire de Castro Faria Neto[1,2,3].

1. Programa de Pós-Graduação em Biologia Molecular e Celular, Universidade Federal do Estado do Rio de Janeiro - UNIRIO - Rio de Janeiro (RJ), Brasil.
2. Laboratório de Imunofarmacologia, Fundação Oswaldo Cruz - Fiocruz - Rio de Janeiro (RJ), Brasil.
3. Programa de Pós Graduação em Imunologia e Inflamação, Universidade Federal do Rio de Janeiro - UFRJ - Rio de Janeiro (RJ), Brasil.

Objective: Gestational sepsis can trigger a systemic inflammatory response that affects fetal brain development. Nitric oxide (NO) is a molecule that plays a crucial role in regulating the cardiovascular and immune systems, and its levels can be affected by gestational sepsis. Additionally, neurovascular unit and microglia cells are crucial for the integrity of neurodevelopment. This study aims to evaluate the effects of gestational sepsis on the frontal cortex and hippocampus of neonatal rats by assessing NO, Lactate and LDH production, neurovascular unit integrity and microglia cells profile. **Methods:** Pregnant mice on the 14th embryonic day were instilled intratracheally with 0.9% saline solution (saline) and *Klebsiella pneumoniae* ($3x10^8$) (sepsis). The animals received subcutaneous treatment with Meropenem (10 mg/kg) for the following 5, 24, 48, and 72 hours. The offspring of the animals with moderate sepsis were sacrificed on the 2nd (P2) and 8th (P8) days of life, and the frontal cortex and hippocampus of these animals were collected in both groups. We used the Griess method to evaluate NO production. Biochemical kits for LDH and lactate production, immunohistochemistry for microglia and astrocytes analyses and ANGIOTOOL for vessels identification. **Results:** The results revealed a significant increase in NO in the frontal cortex of the septic group at age P2 compared to the saline group. However, at the age of P8, the differences were reduced. In the analysis of the hippocampus, NO levels showed a small increase in the septic group at both ages, P2 and P8, relative to the control group. We found an increase in Lactate levels in the frontal cortex and hippocampus in pups at P2. In the hippocampus region, however, LDH levels are not increased only in the offspring at P2. Microglial cells were analyzed by fluorescence immunohistochemistry showing an activated profile of microglia at the sepsis group and the astrocyte/vessels overlay was evaluated demonstrating a reduction of interaction between these neovascular unit components in the frontal cortex of P8. **Conclusion:** These data suggest that maternal sepsis may be causatively related to the development of cerebral inflammation, and neurovascular dysregulation and induces oxidative stress in neonatal life.

Keywords: Gestational sepsis, nitric oxide, neuronal nitric oxide, oxidative stress.

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