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ORIGINAL ARTICLE

Peri-intraventricular hemorrhage and oxidative and inflammatory stress markers in very-low birth weight newborns☆,☆☆

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Oxidative stress;
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Intraventricular hemorrhage;
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Abstract
Objectives: To evaluate the association between oxidative and inflammatory stress markers with peri-intraventricular hemorrhage (PIVH) in very-low birth weight newborns.
Methods: This was a prospective study conducted in a level III neonatal unit. Basal and stimulated reactive oxygen intermediates (ROIs), reduced glutathione (GSH), and interleukin-6 (IL-6) levels were measured in umbilical cord blood. Newborns underwent serial ultrasound at the bedside, at 6, 12, 24, and 72 hours of life and at seven days for the diagnosis of PIVH, classified as grades I to IV. Two groups were assessed, those with and without PIVH; maternal and neonatal control variables were used for comparison. Univariate and multiple regression analyses were applied.
Results: A total of 125 newborns were assessed. PIVH incidence rate was 12.0%. In the univariate analysis, basal ROI, the use of two or more doses of corticosteroids, birth weight < 1,000 g, ventilatory support use, and SNAPPE II value ≥ 22 were significantly associated with PIVH. However, in the multivariate analysis, only antenatal steroid use was independently associated with the disease (OR 0,194; 95% CI: 0,048 to 0,773; p=0,02).

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☆☆ Study conducted at the School of Medical Sciences, Universidade Estadual de Campinas, Centro de Investigação em Pediatria (CIPED), Universidade Estadual de Campinas, and Hospital da Mulher Prof. Dr. José Aristodemo Pinotti, Centro de Atenção Integral à Saúde da Mulher (CAISM), Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil

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Conclusion: ROI, GSH, and IL-6 levels were not associated with the occurrence of PIVH in very-low birth weight infants
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PALAVRAS-CHAVE
Estresse oxidativo;
Espécies de oxigênio reativas;
Interleucina-6;
Glutationa;
Hemorragia cerebral;
Recém-nascido

Hemorragia peri-intraventricular e marcadores de estresse oxidativo e inflamatório em RNs de muito baixo peso ao nascer

Resumo
Objetivos: avaliar a associação entre marcadores de estresse oxidativo e inflamatório com a hemorragia peri- e intraventricular (HPIV) em recém-nascidos (RN) de muito baixo peso ao nascer.
Métodos: estudo prospectivo em unidade neonatal nível III. Foi feita dosagem em sangue de cordão umbilical de intermediários reativos de oxigênio (ROI) basal e estimulado, glutationa reduzida (GR) e interleucina-6 (IL-6). Recém-nascidos foram submetidos à ultrassonografia seriada, à beira do leito, com 6, 12, 24 e 72 horas de vida e 7 dias para o diagnóstico de HPIV, classificada em graus de I a IV. Foram avaliados dois grupos: com e sem HPIV e variáveis de controle maternas e neonatais foram usadas para comparação. Análise univariada e de regressão múltipla foram aplicados.
Resultados: foram avaliados 125 recém-nascidos. A taxa de incidência de HPIV foi de 12,0%. Na análise univariada o valor basal de ROI, o uso de duas ou mais doses de corticosteroide, peso ao nascer menor que 1.000 g, o uso de assistência respiratória e valor de SNAPPE II maior ou igual a 22 foram significativamente associados à HPIV. Porém, na análise multivariada, apenas o uso antenatal de esteroides se mostrou independentemente associado à doença (OR 0,194 IC95% 0,048-0,773 p=0,02).
Conclusão: ROI, GR e Il-6 não foram associados à ocorrência de HPIV em RN de muito baixo peso ao nascer
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Introduction

Peri-intraventricular hemorrhage (PIVH) remains a high-prevalence disease in preterm newborns, especially those with birth weight < 1,500 g and gestational age < 34 weeks. The disease is associated with the development of posthemorrhagic hydrocephalus, neurodevelopmental disorders, need for specialized rehabilitation therapies, and high social costs.[1,2]

The most common site of PIVH is the germinal matrix, which is located in the periventricular subependymal region and is irrigated by fragile and immature vasculature. It is an important proliferation site of neuronal precursors before their migration to their final location in the cerebral cortex. Several factors, especially those related to cerebral hypoperfusion and reperfusion phenomena, can result in bleeding at this site.[2,3]

In addition to the mechanism of vascular rupture associated with cerebral blood flow impairment, PIVH can occur due to other mechanisms, which may be of vascular origin or not.[2]

Experimental studies and those with humans have showed an association between PIVH and oxidative stress. In experimental studies in preterm newborn dogs, Ment et al. demonstrated that blocking the production of free radicals with etamsylate and indomethacin, or the use of superoxide-dismutase, had a protective effect on PIVH occurrence after reperfusion injury due to hypovolemic hypotension.[3–5]

More recently, there has been evidence of an association between PIVH with intrauterine inflammatory-infectious processes,[6–8] as well as an association between serum interleukin-6 (IL-6) levels and vascular endothelium matrix lesions by cytokines.[9–11]

However, the specific evaluation of oxidative stress markers such as reactive oxygen species and glutathione antioxidant enzyme has not been assessed regarding the development of PIVH.

This study aimed to evaluate the association of oxidative stress markers, specifically the production of reactive oxygen intermediates (ROIs) and reduced glutathione (GSH) levels, with inflammation markers, namely serum IL-6 levels measured in umbilical cord blood, as risk factors for the development of PIVH.

Methods

This was a prospective cohort study that included all preterm newborns (< 37 weeks of gestation) with a birth weight < 1,500 g who were hospitalized at a level 3 university neonatal unit, from May 10, 2009 to October 31, 2010. Exclusion criteria were: failure to collect umbilical cord blood; maternal or guardian refusal to allow the newborn to participate in the study; severe malformation of the

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