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ORIGINAL ARTICLE

Neonatal sepsis as a risk factor for neurodevelopmental changes in preterm infants with very low birth weight☆,☆☆

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KEYWORDS
Psychomotor performance;
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Abstract
Objective: to evaluate neonatal sepsis as a risk factor for abnormal neuromotor and cognitive development in very low birth weight preterm infants at 12 months of corrected age.
Methods: this was a prospective cohort study that followed the neuromotor and cognitive development of 194 very low birth weight preterm infants discharged from a public neonatal intensive care unit. The Bayley Scale of Infant Development (second edition) at 12 months of corrected age was used. The outcomes were the results of the clinical/neurological evaluation and the scores of the psychomotor development index (PDI) and mental development index (MDI) of the Bayley Scale of Infant Development II. The association between neonatal sepsis and neuromotor development and between neonatal sepsis and cognitive development was verified by logistic regression analysis.
Results: mean birth weight was 1,119 g (SD: 247) and mean gestational age was 29 weeks and 6 days (SD: 2). Approximately 44.3%(n = 86) of the infants had neonatal sepsis and 40.7% (n = 79) had abnormal neuromotor development and/or abnormal psychomotor development index (PDI < 85) at 12 months of corrected age. On the mental scale, 76 (39.1%) children presented abnormal cognitive development (MDI < 85). Children with neonatal sepsis were 2.5 times more likely to develop changes in neuromotor development (OR: 2.50; CI: 1.23-5.10). There was no association between neonatal sepsis and cognitive development impairment.
Conclusion: neonatal sepsis was an independent risk factor for neuromotor development impairment at 12 months of corrected age, but not for mental development impairment.

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PALAVRAS-CHAVE
Desempenho psicomotor;
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Lactente;
Seguimento

A sepse neonatal como fator de risco para alteração no neurodesenvolvimento em prematuros de muito baixo peso ao nascer

Resumo
Objetivo: avaliar a sepse neonatal como fator de risco para alterações no desenvolvimento neuromotor e mental de prematuros de muito baixo peso aos 12 meses de idade corrigida.
Métodos: estudo de coorte prospectivo que acompanhou o desenvolvimento neuromotor e mental de 194 prematuros de muito baixo peso oriundos de uma UTI neonatal pública no Rio de Janeiro. Utilizou-se a Escala Bayley de Desenvolvimento Infantil (segunda edição) aos 12 meses de idade corrigida. Os desfechos foram o resultado da avaliação clínica/ neurológica e os resultados da área motora da Escala Bayley e os resultados da área mental (cognitiva) da mesma escala. A associação entre sepse e o desenvolvimento neuromotor e entre sepse e o desenvolvimento mental foi verificada através de regressão logística.
Resultados: a média do peso ao nascer foi 1119 g (DP 247) e da idade gestacional 29 semanas e 6 dias (DP 2). Cerca de 44,3% (n = 86) das crianças apresentaram sepse neonatal e 40,7% (n = 79) apresentaram alteração neuromotora e/ou no índice do desenvolvimento psicomotor (PDI<85) aos 12 meses de idade corrigida. Na escala mental, 76 (39,1%) crianças apresentaram alteração (MDI < 85). As crianças que apresentaram sepse neonatal tiveram 2,5 vezes mais chances de desenvolver alteração do desenvolvimento neuromotor do que as crianças que não apresentaram sepse (OR: 2,50; IC 1,23-5,10). Porém, não houve associação entre sepse neonatal e alteração cognitiva.
Conclusão: a sepse neonatal foi um fator de risco independente para alteração do desenvolvimento neuromotor, mas não para alteração do desenvolvimento mental.

Introduction

Sepsis is characterized by systemic manifestations resulting from bacterial invasion and multiplication in the bloodstream, and can lead to high neonatal mortality and morbidity.[1] Preterm newborns are at increased risk of developing sepsis. There is evidence that perinatal and neonatal infections are associated with neurodevelopmental impairment in preterm infants.[2–6]

Some studies indicate sepsis as one of the major risk factors for developmental delay and cerebral palsy, as well as neonatal mortality.[7–11] However, there are few studies that assess the age range studied (12 months of corrected age) and, to date, only one Brazilian publication that investigated the association between sepsis and neurodevelopment was retrieved.[12] Furthermore, it is necessary to use an appropriate methodology for the control of several confounding factors already established in the literature, such as low gestational age, male gender, bronchopulmonary dysplasia (BPD), and brain injuries that can influence neurodevelopment in this population.

The aim of this study was to evaluate neonatal sepsis as a risk factor for neurodevelopment impairment in preterm infants with very low birth weight at 12 months of corrected age.

Methods

This prospective cohort study was performed in a tertiary hospital, at a referral unit for high-risk newborns. Preterm infants (gestational age < 37 weeks) with birth weight less than 1,500 g who were born from 2004 to 2010 were included in the cohort. Gestational age was estimated based on the date of the last menstrual period; when that date was uncertain, by early ultrasound and by the New Ballard Score.[13] When birth weight was below the 10th percentile for gestational age,[14] the infant was classified as small for gestational age. The exclusion criteria were: infants with infection, congenital malformations, genetic syndromes, or those born in other hospitals; neonatal and post-neonatal deaths were excluded. Children not assessed by the Bayley scale were excluded from the analysis and considered as study loss.

Neonatal sepsis was considered in the presence of a positive blood culture and/or clinical and laboratory signs suggestive of infection.[11] Clinical signs included worsening of respiratory distress: tachypnea, sternal and/or subcostal retraction, groaning and cyanosis, apnea, body temperature instability, hyper- or hypoglycemia, poor peripheral perfusion, food intolerance, arterial hypotension, and underactive infants.[11]

Laboratory parameters included: complete blood count with three or more altered parameters according to Rodwell et al.[15] and/or C-reactive protein > 0.5 mg/dL; negative or not performed blood culture; no evidence of infection at another site; and established and maintained antimicrobial therapy. Rodwell et al.[15] considered the following hematological parameters: leukocytosis (white blood cells [WBC] $\geq$ 25,000 at birth, or $\geq$ 30,000 between 12 to 24 hours, or > 21,000 at over 48 hours of life), leukopenia (WBC $\leq$ 5,000); neutrophilia or neutropenia; increased number of immature neutrophils; increased neutrophilic index; ratio of immature over segmented neutrophils $\geq$ 0.3; neutrophils with toxic granulation and vacuolization; and thrombocytopenia