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ORIGINAL ARTICLE

Perinatal outcome and cardiac dysfunction in preterm growth-restricted neonates in relation to placental impairment severity☆

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KEYWORDS
Intrauterine growth restriction;
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Abstract
Introduction: Intrauterine growth restriction (IUGR) and prematurity have been associated with increased perinatal morbidity and mortality and also with cardiovascular foetal programming. However, there are few studies on the impact of placenta-related IUGR on perinatal outcomes and cardiovascular biomarkers in pre-term infants.
Objectives: To determine differences in neonatal morbidity, mortality and cord blood biomarkers of cardiovascular dysfunction between pre-term placenta-related IUGR and non-IUGR new-borns, and to analyse their relationship with the severity of IUGR according to foetal Doppler evaluation.
Material and methods: Prospective cohort study: pre-term infants with placenta-related IUGR and matched pre-term infants without IUGR. A Doppler scan was performed, and placenta-IUGR was classified according to severity. Comparative analysis of perinatal outcomes, neonatal morbidity and mortality, and cord blood levels of biomarkers of cardiovascular dysfunction was performed.
Results: IUGR new-borns present lower weight, length, head circumference, and Apgar score at birth, as well as increased neonatal and cardiovascular dysfunction biomarker levels, compared

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with pre-term new-borns without IUGR. These differences increase with the severity of IUGR determined by prenatal umbilical artery Doppler scan.
Conclusions: Placenta-related-IUGR pre-term infants, irrespective of gestational age, present increased neonatal morbidity and mortality that is significantly proportional to the severity of IUGR. Placental impairment and severity also determine levels of cardiovascular dysfunction biomarkers at birth.

PALABRAS CLAVE
Restricción del crecimiento intrauterino;
Morbilidad neonatal;
Prematuridad;
Doppler fetal;
Biomarcadores cardiovasculares

Resultados perinatales y disfunción cardiovascular en prematuros con restricción del crecimiento intrauterino en relación con la gravedad de la insuficiencia placentaria

Resumen
Introducción: La restricción del crecimiento intrauterino (RCIU) y la prematuridad se han asociado con una mayor morbimortalidad perinatal, así como con una reprogramación fetal a nivel cardiovascular. Sin embargo, son escasos los estudios sobre el impacto de la RCIU de causa placentaria en los resultados perinatales y en biomarcadores cardiovasculares de recién nacidos prematuros.
Objetivos: Determinar las diferencias en morbimortalidad neonatal y biomarcadores de disfunción cardiovascular en sangre de cordón entre prematuros con RCIU de origen placentario y sin RCIU, así como estudiar su relación con la gravedad de la RCIU según el estudio Doppler fetal.
Material y métodos: Estudio prospectivo de cohortes: prematuros con RCIU de causa placentaria y prematuros sin RCIU adecuadamente apareados. Clasificación de la gravedad de la RCIU según el Doppler. Análisis comparativo de resultados perinatales, de morbimortalidad neonatal y de niveles en sangre de cordón de biomarcadores de disfunción cardiovascular.
Resultados: Los prematuros con RCIU presentan un menor peso, longitud, perímetro craneal y Apgar al nacimiento, así como un aumento de la morbilidad neonatal y de los niveles de biomarcadores de disfunción cardiovascular, comparado con los prematuros sin RCIU. Estas diferencias aumentan con la gravedad de la RCIU determinada por el estudio hemodinámico Doppler prenatal.
Conclusiones: Los prematuros afectados de RCIU de causa placentaria presentan un incremento de la morbimortalidad neonatal independiente de la prematuridad, que aumenta de forma estadísticamente significativa con la gravedad de la RCIU. La afectación placentaria y su gravedad también determinan la alteración de biomarcadores de disfunción cardiovascular al nacimiento.

Introduction

Prematurity and intrauterine growth restriction (IUGR), together with congenital malformations, infections and anoxia, are the most important problems in foetal medicine, and are the main causes of perinatal morbidity and mortality. Incidence of severe IUGR is estimated at 3%–5% of pregnancies.[1]

Several studies have reported increased perinatal and neonatal morbidity and mortality in newborns with IUGR or low birth weight, together with an increase in cardiovascular morbidity in adulthood, a phenomenon known as foetal programming of adult disease.[2–23] The neonatal morbidity and mortality described in these patients include complications related to prematurity (respiratory distress, bronchopulmonary dysplasia, necrotising enterocolitis, sepsis, low 5-minute Apgar test score, altered thermoregulation, retinopathy of prematurity [ROP], intraventricular haemorrhage, periventricular leukomalacia and neonatal death), and haematological and metabolic complications (thrombocytopaenia, coagulopathy, leukopaenia, initial hypoglycaemia, subsequent hyperglycaemia, altered cord blood lipids, cholestasis and jaundice).[2–23] Increased neonatal morbidity and mortality and the foetal programming phenomena may be due to the foetal hypoxia-ischaemia presented by these IUGR patients. Hypoxia-ischaemia gives rise to haemodynamic adaptation, a phenomenon in which the brain, heart and adrenals are spared in detriment to the maturity of other organs.[11,14,16,24] However, some studies seem to demonstrate that this haemodynamic redistribution does not completely spare priority organs from hypoxia-ischaemia and nutrient deficiency.[25–32] Cardiovascular abnormalities have been described in IUGR patients using both echocardiography and measurement of cord blood cardiovascular dysfunction markers, specifically, increased levels of B-type natriuretic peptide (BNP).[25–27] These alterations could be related to the mechanisms underlying foetal programming of cardiovascular disease in adulthood.