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ORIGINAL ARTICLE

Early hypophosphataemia in at risk newborns. Frequency and magnitude☆,☆☆,☆☆☆

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KEYWORDS
Hypophosphataemia;
Parenteral nutrition;
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Abstract
Objective: To determine the frequency and magnitude of neonatal hypophosphataemia (<4 mg/dL) in a neonatal Intensive Care Unit and to describe risk groups.
Patients and methods: Retrospective study of hospitalised newborns over a 44 month period (phase 1). Retrospective study of <1500 g/<32 weeks of gestation newborns over a 6 month period (phase 2). Prospective study of <1500 g or 1550–2000 g, and intrauterine growth restriction (IUGR) newborns. Measurements were made on the 1st, 3rd, 7th, and 14th days of life (phase 3).
Results: Phase 1: 34 (2.4%) of 1,394 patients had a diagnosis of hypophosphataemia, 76% of them ≤32 weeks of gestation and <1500 g, and 24% >32 weeks with weight <P10. Phase 2: 12 (16.4%) of 73 patients had a diagnosis of hypophosphataemia, with <2 mg/dL in 5 (6.8%). Eight (75%) of those with hypophosphataemia had IUGR, and 4 (25%) weighed <1000 g. Five cases had associated hypokalaemia, and three hypercalcaemia. Phase 3: 9 (45%) of 20 patients had

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☆☆ **Previous presentation:** This study has not been presented in any congresses. Álvaro Hidalgo Romero presented part of the results as part of his thesis for the Bachelor's degree in Medicine in June 2014, titled *Frecuencia del síndrome de realimentación en recién nacidos de riesgo*.

☆☆☆ Partial preliminary results presented in a clinical session held in Hospital 12 de Octubre in 2015 and in the presentation titled *Los nuevos trastornos iónicos en el prematuro extremo* included in the course *Cuidado diferencial del niño prematuro extremo en sus primeros días de vida* offered at Hospital 12 de Octubre on May 27, 2016.

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hypophosphataemia, all of them <1000 g or <1200 g and weight percentile <10. Thirty-three percent of samples on days 1, 3, and 7 showed hypophosphataemia, four of them <2 mg/dL. There was mild hypokalaemia in 5 (55%), and mild hypercalcaemia in 2 (22%) cases. Hypophosphataemia was associated with lower enteral nutrition and higher parenteral amino acid intake in the early days of life.
Conclusions: Hypophosphataemia is common, and can be severe, in the first week of life in premature infants <1000 g, and newborns <1200 g with foetal malnutrition and receiving amino acids in early parenteral nutrition.

PALABRAS CLAVE
Hipofosforemia;
Nutrición parenteral;
Prematuridad;
Hipercalcemia;
Hipopotasemia;
Recién nacido

Hipofosforemia precoz en recién nacidos de riesgo. Frecuencia y magnitud

Resumen
Objetivo: Conocer la frecuencia y la magnitud de la hipofosforemia neonatal (<4 mg/dl) en una UCIN y definir los grupos de riesgo.
Pacientes y métodos: Estudio retrospectivo en neonatos hospitalizados, en periodo de 44 meses (fase 1). Estudio retrospectivo en <1.500 g/<32 semanas de gestación en período posterior de 6 meses (fase 2). Estudio prospectivo en <1.500 g o CIR con peso 1.500-2.000 g. Determinaciones en días 1, 3, 7 y 14 de vida (fase 3).
Resultados: Fase 1: 34 de 1.394 pacientes (2,4%) fueron diagnosticados de hipofosforemia, 76% de ellos $\leq$32 semanas de gestación y <1.500 g, y 24% >32 semanas con peso <P10. Fase 2: 12 de 73 pacientes (16,4%) fueron diagnosticados de hipofosforemia, 5 (6,8%) con hipofosofremia <2 mg/dl. De ellos 8 fueron CIR y 4 <1.000 g. Cinco pacientes asociaron hipopotasemia y 3 hipercalcemia. Fase 3: 9 de 20 pacientes (45%) presentaron hipofosforemia, todos <1.000 g o con peso al nacer <1.200 g y percentil <10. El 33% de las muestras de los días 1, 3 y 7 mostraron hipofosforemia, <2 mg/dl en 4 muestras. Asociaron hipopotasemia leve 5 casos (55%) e hipercalcemia leve 2 (22%). La hipofosforemia se asoció a menor nutrición enteral y más aporte parenteral de aminoácidos en los primeros días.
Conclusiones: La hipofosforemia es frecuente y puede ser crítica en la primera semana en prematuros <1.000 g y en los nacidos con desnutrición fetal y peso <1.200 g que reciben aminoácidos en la nutrición parenteral precoz.

Introduction

Hypophosphataemia is an electrolyte disturbance that has been overlooked by neonatology reference books and protocols for the management of ill newborns until very recently.[1,2] Before year 2000, reports of hypophosphataemia were limited to cases associated with the bioavailability of the inorganic phosphates formerly used in parenteral nutrition,[3] and it was not until 2006 that cases of hypophosphataemia in newborns potentially associated with refeeding syndrome were first reported.[4]

In our unit, we started administering amino acids (Primene 10%®) parenterally to preterm newborns with birth weights of less than 1500 g from the first day of life in 2001. Around the middle of that decade, hypophosphataemia started to be detected in newborns as a chance finding in blood tests performed for unrelated reasons. In 2010, due to the frequency and severity of some of the episodes of hypophosphataemia, our hospital developed a protocol for screening at-risk newborns and for the prevention and management of hypophosphataemia. The lack of relevant research in neonatology posed a challenge in the development of this initial protocol, for which we resorted to the extrapolation of data on treatment of adults with refeeding syndrome.[5–8] The first reports of hypophosphataemia in very low birth weight preterm newborns were published in 2012, and different authors started to propose refeeding syndrome as a potential aetiology.[9–11] Subsequent publications have described its pathophysiology, an association with a high amino acid intake and a potential increase in the risk of sepsis that would compound the direct and possibly fatal effects of severe hypophosphataemia.[12–14]

The objectives of our study were to define the risk groups for hypophosphataemia in our hospital and to determine the frequency, severity and temporal distribution of early episodes of hypophosphataemia in the first 2 weeks of life.