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Brief report

Intravenous ferric carboxymaltose-associated hypophosphatemia in patients with iron deficiency anemia. A common side effect☆

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ABSTRACT

Objectives: To determine the frequency, severity, time of onset and factors associated with the development of hypophosphatemia (HF) in patients with iron deficiency anemia treated with intravenous ferric carboxymatose (ivFCM).
Material and methods: Retrospective cohort study in patients iron deficiency anemia who received ivFCM and had an a prior and subsequent determination of serum phosphate. We carried out a comparative analysis between baseline and post-ivFCM levels of serum phosphate. In order to identify variables independently associated with HF a logistic regression analysis was also performed.
Results: One hundred twenty-five patients were included. HF frequency was 58%. The median time to onset of HF was 18 days. Age, baseline ferritin levels and baseline phosphate levels were independently associated with the development of HF. The risk of HF in patients with baseline phosphate levels ≤3.1 mg/dl was 67% higher than patients with ≥3.7 mg/dl.
Conclusions: ivFCM-associated HF is a frequent, early and, sometimes, prolonged effect in patients with iron deficiency anemia. Serum phosphate levels should be monitored after ivFCM administration, especially in older patients and in those with lower baseline phosphate or ferritin levels.

Hipofosfatemia asociada a la administración intravenosa de hierro carboximaltosa en pacientes con anemia ferropénica. Un efecto secundario frecuente

Palabras clave:
Anemia ferropénica
Hierro carboximaltosa
Hipofosfatemia

RESUMEN

Objetivos: Determinar la frecuencia, gravedad, momento de aparición y variables asociadas al desarrollo de hipofosfatemia (HF) en pacientes con anemia ferropénica tratados con hierro carboximaltosa por vía intravenosa (HCMiv).
Material y método: Estudio de cohortes retrospectivo en pacientes que contaran con determinaciones de fosfato previa (normal) y posterior a la administración de HCMiv. Se compara la concentración de fosfato basal y posterior a la administración de HCMiv, y mediante regresión logística binaria se determinan las variables asociadas con la HF.
Resultados: Se incluyeron 125 pacientes. La frecuencia de HF fue del 58%. El tiempo medio hasta la aparición de HF fue de 18 d. La edad, las concentraciones basales de ferritina y de fosfato se relacionaron con el desarrollo de HF. El riesgo de HF de los pacientes con fosfato basal ≤3,1 mg/dl fue un 67% mayor que en pacientes con fosfato basal ≥3,7 mg/dl.

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Conclusiones: La HF asociada a HCMiv en pacientes con anemia ferropénica es un efecto frecuente, precoz y en ocasiones prolongado. En pacientes mayores, con fosfato y ferritina más bajas, se debe vigilar el fosfato tras la administración de HCMiv.

Introduction

Ferric carboxymaltose by the intravenous route (IV FCM) supplies high doses of elemental iron in a single administration, in a short space of time, with demonstrated efficacy and safety.[1] The side effects related to IV FCM administration that have been reported include a decrease in serum phosphate levels, which, while it is not an effect exclusive to IV FCM, is exceptional among iron formulations for intravenous administration.[2–4] The information available to date on onset and severity of hypophosphataemia (HP) and time to normalisation of phosphate levels is limited.[2,4–6] The objectives of this study were to report the frequency, severity and time to HP onset and to assess which variables are associated with HP onset in patients with iron deficiency anemia (IDA) treated with IV FCM.

Materials and methods

A retrospective study of patients with a diagnosis of IDA, followed up in our unit between 2008 and 2012, who had a normal baseline phosphate (BP) determination (in the previous 15 days) and a phosphate determination subsequent to an episode of IV FCM infusion (up to 180 days). Epidemiological, clinical, IDA-related and IV FCM administration-related variables were recorded.

Table 1
Characteristics at baseline and in accordance with hypophosphataemia onset following administration of ferric carboxymaltose by the intravenous route in the patients enrolled in the study.

	All	Hypophosphataemia		*p*
	(No. = 125)	No (No. = 52)	Yes (No. = 73)	
Age (years)	76 (15)	74 (17)	77 (13)	0.09
Male	51 (40.8)	15 (28.8)	36 (49.3)	0.02
Prior history				
Anemia of any type	20 (16)	8 (15.4)	12 (16.4)	0.87
Iron-deficiency anemia	30 (24)	8 (15.4)	22 (30.1)	0.06
Diabetes mellitus	39 (31.2)	12 (23.1)	27 (37)	0.10
Chronic kidney failure	17 (13.6)	10 (19.2)	7 (9.6)	0.12
Heart failure	22 (17.6)	9 (17.3)	13 (17.8)	0.94
Chronic lung disease	14 (11.2)	6 (11.5)	8 (11)	0.92
Gastrointestinal disease	16 (12.8)	5 (9.6)	11 (15.1)	0.37
Active neoplasm	18 (14.4)	9 (17.3)	9 (12.3)	0.44
Cognitive decline/dementia	10 (8)	6 (11.5)	4 (5.5)	0.32
Osteoporosis/osteopenia	7 (5.6)	4 (7.7)	3 (4.1)	0.45
Hyperparathyroidism	1 (0.8)	1 (1.9)	0 (0)	0.42
Previous treatment				
Oral iron	44 (35.2)	17 (32.7)	27 (37)	0.62
Transfusion (15 days)	55 (44)	26 (50)	29 (39.7)	0.25
Oral anticoagulants	36 (28.8)	13 (25)	23 (31.5)	0.43
Anti-platelet agents	34 (27.2)	10 (19.2)	24 (32.9)	0.09
Bisphosphonates	5 (4)	4 (7.7)	1 (1.4)	0.16
Mechanism of anemia onset[a]				
Gastrointestinal bleeding	104 (83.2)	41 (78.8)	63 (86.3)	0.27
Gynaecological bleeding	10 (8)	5 (9.6)	5 (6.8)	0.74
Malabsorption	2 (1.6)	2 (3.8)	0 (0)	0.17
Other	4 (3.2)	1 (1.9)	3 (4.2)	> 0.99
Unknown or not studied	8 (6.4)	3 (5.8)	5 (6.8)	> 0.99
Indication for IV FCM[a]				
Need for rapid replacement	45 (36)	20 (38.5)	25 (34.2)	0.63
Lack of response to oral iron	42 (33.6)	14 (26.9)	28 (38.4)	0.18
Social cause	13 (10.4)	7 (13.5)	6 (8.2)	0.34
Malabsorption	2 (1.6)	2 (3.8)	0 (0)	0.17
Intolerance to oral iron	1 (0.8)	1 (1.9)	0 (0)	0.42
Unknown or not recorded	31 (24.8)	11 (21.2)	20 (27.4)	0.43
Haemoglobin (g/dl)	9.1 (1.8)	9.1 (1.7)	9.1 (1.8)	0.76
Ferritin (ng/ml)	12.2 (22.5)	18.6 (49.3)	10.5 (16.2)	0.02
Baseline serum phosphate (mg/dl)	3.3 (0.6)	3.5 (0.7)	3.2 (0.6)	0.02
Total dose of iron received during the risk period assessed (1–35 days)[b]		1000 (100)	1000 (400)	0.18

The data indicate frequency (percentage) for the categorical variables and median (interquartile range) for the quantitative variables. Pearson's chi-squared test or Fisher's exact test was used to compare variables between groups for categorical variables, and Student's *t* test was used to compare means for quantitative variables.
IV FCM: ferric carboxymaltose by the intravenous route.

[a] Each patient could be included in more than one category of the variable.

[b] In the group with hypophosphataemia, the dose of iron received until hypophosphataemia was assessed. In the group without hypophosphataemia, total dose up to 35 days was assessed.