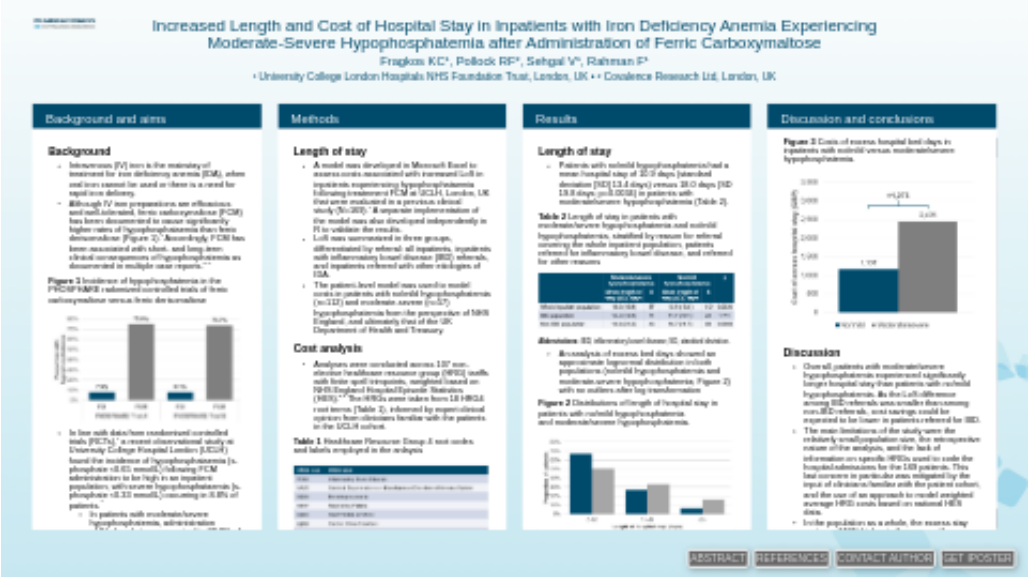
Increased Length and Cost of Hospital Stay in Inpatients with Iron Deficiency Anemia Experiencing Moderate-Severe Hypophosphatemia after Administration of Ferric Carboxymaltose



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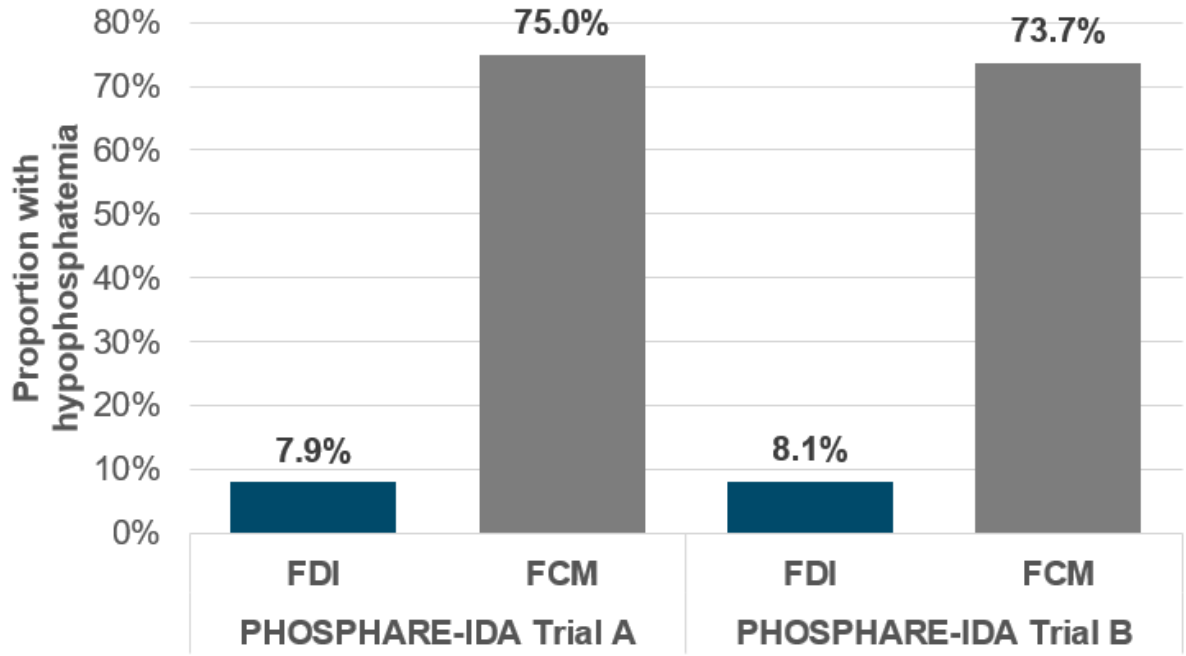
BACKGROUND AND AIMS

Background

- Intravenous (IV) iron is the mainstay of treatment for iron deficiency anemia (IDA), when oral iron cannot be used or there is a need for rapid iron delivery.
- Although high-dose IV iron preparations are efficacious and well-tolerated, ferric carboxymaltose (FCM) has been documented to cause significantly higher rates of hypophosphatemia than other IV irons such as ferric derisomaltose (FDI; Figure 1).[1-2] Accordingly, FCM has been associated with short- and long-term clinical consequences of hypophosphatemia, including fractures and osteomalacia, as documented in multiple case reports.[2–7]

Figure 1 Incidence of hypophosphatemia in the PHOSPHARE-IDA randomized controlled trials of ferric carboxymaltose versus ferric derisomaltose



- In line with data from randomized controlled trials (RCTs),[1-2] a recent observational study at University College Hospital London (UCLH) found the incidence of hypophosphatemia (s-phosphate <0.65 mmol/L) following FCM administration to be high in an inpatient population, with severe hypophosphatemia (s-phosphate <0.33 mmol/L) occurring in 8.8% of patients.[7]
  - In patients with moderate/severe hypophosphatemia, administration of IV phosphate was required in 29.8% of cases, with an average of 4.4 infusions required per patient. Mean length of hospital stay (LoS) was also significantly longer in patients with moderate/severe hypophosphatemia versus those with no/mild hypophosphatemia at 18.0 days versus 10.9 days (p=0.0035).[7]
- Independently of the direct clinical consequences, the cost associated with increased utilisation of health care resources in patients experiencing post-FCM hypophosphatemia remains unknown.

Aim

- Given the increased resource utilization amongst patients with moderate/severe hypophosphatemia observed in the above UCLH study, our objective was to compare LoS and associated costs in inpatients with no/mild versus moderate/severe hypophosphatemia after treatment of IDA with FCM.

METHODS

Length of stay

- A model was developed in Microsoft Excel to assess costs associated with increased LoS in inpatients experiencing hypophosphataemia following treatement FCM at UCLH, London, UK that were evaluated in a previous clinical study (N=169).[7] A separate implementation of the model was also developed independently in R to validate the results.
- LoS was summarized in three groups, differentiated by referral: all inpatients, inpatients with inflammatory bowel disease (IBD) referrals, and inpatients referred with other etiologies of IDA.
- The patient-level model was used to model costs in patients with no/mild hypophosphatemia (n=112) and moderate-severe (n=57) hypophosphatemia from the perspective of NHS England, and ultimately that of the UK Department of Health and Treasury.

Cost analysis

- Analyses were conducted across 107 non-elective healthcare resource group (HRG) tariffs with finite spell trimpoints, weighted based on NHS England Hospital Episode Statistics (HES).[8,9] The HRGs were taken from 18 HRG4 root terms (Table 1), informed by expert clinical opinion from clinicians familiar with the patients in the UCLH cohort.

Table 1 Healthcare Resource Group 4 root codes and labels employed in the anlaysis

HRG4 root	HRG4 label
FD02	Inflammatory Bowel Disease
AA25	Cerebral Degenerations or Miscellaneous Disorders of Nervous System
DZ23	Bronchopneumonia
DZ27	Respiratory Failure
EB03	Heart Failure or Shock
EB06	Cardiac Valve Disorders
EB08	Syncope or Collapse
EB12	Unspecified Chest Pain
EB13	Angina
EB14	Other Acquired Cardiac Conditions
FD10	Non-Malignant Gastrointestinal Tract Disorders
GC17	Non-Malignant, Hepatobiliary or Pancreatic Disorders
KC05	Fluid or Electrolyte Disorders
LA04	Kidney or Urinary Tract Infections
LA07	Acute Kidney Injury
SA04	Iron Deficiency Anaemia
WH09	Tendency to Fall, Senility or Other Conditions Affecting Cognitive Functions
WJ06	Sepsis

- Costs were weighted and averaged across all HRGs based on the patient-level LoS data and the excess stay costs for hospital stay durations longer than the HRG trimpoint.

RESULTS

Length of stay

- Patients with no/mild hypophosphatemia had a mean hospital stay of 10.9 days (standard deviation [SD] 13.4 days) versus 18.0 days (SD 19.8 days; p=0.0034) in patients with moderate/severe hypophosphatemia (Table 2).

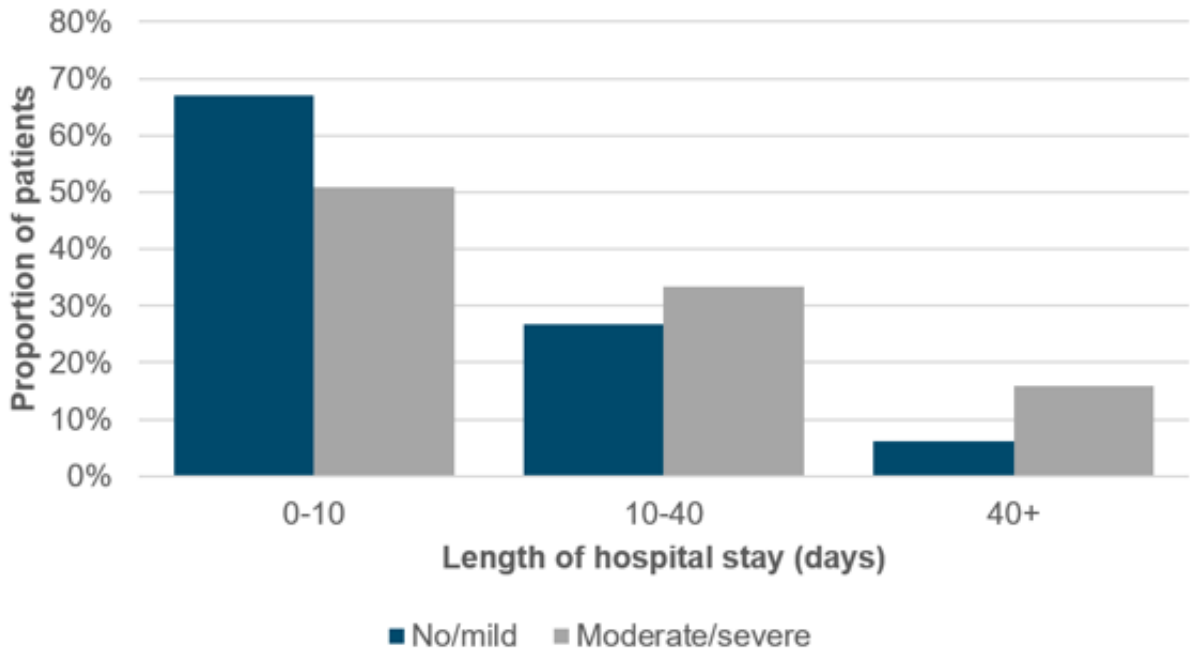
Table 2 Length of stay in patients with moderate/severe hypophosphatemia and no/mild hypophosphatemia, stratified by reason for referral covering the whole inpatient population, patients referred for inflammatory bowel disease, and referred for other reasons

	Moderate/severe hypophosphatemia		No/mild hypophosphatemia		p
	Mean length of stay (SD), days	N	Mean length of stay (SD), days	N	
Whole inpatient population	18.0 (19.8)	57	10.9 (13.4)	112	0.0034
IBD population	12.3 (13.9)	14	11.7 (19.1)	23	0.46
Non-IBD population	19.9 (21.2)	43	10.7 (11.7)	89	0.0009

Abbreviations: IBD, inflammatory bowel disease; SD, standard deviation.

- An analysis of excess bed days showed an approximate lognormal distribution in both populations (no/mild hypophosphatemia and moderate-severe hypophosphatemia; Figure 2) with no outliers after log transformation

Figure 2 Distributions of length of hospital stay in patients with no/mild hypophosphatemia and moderate/severe hypophosphatemia.

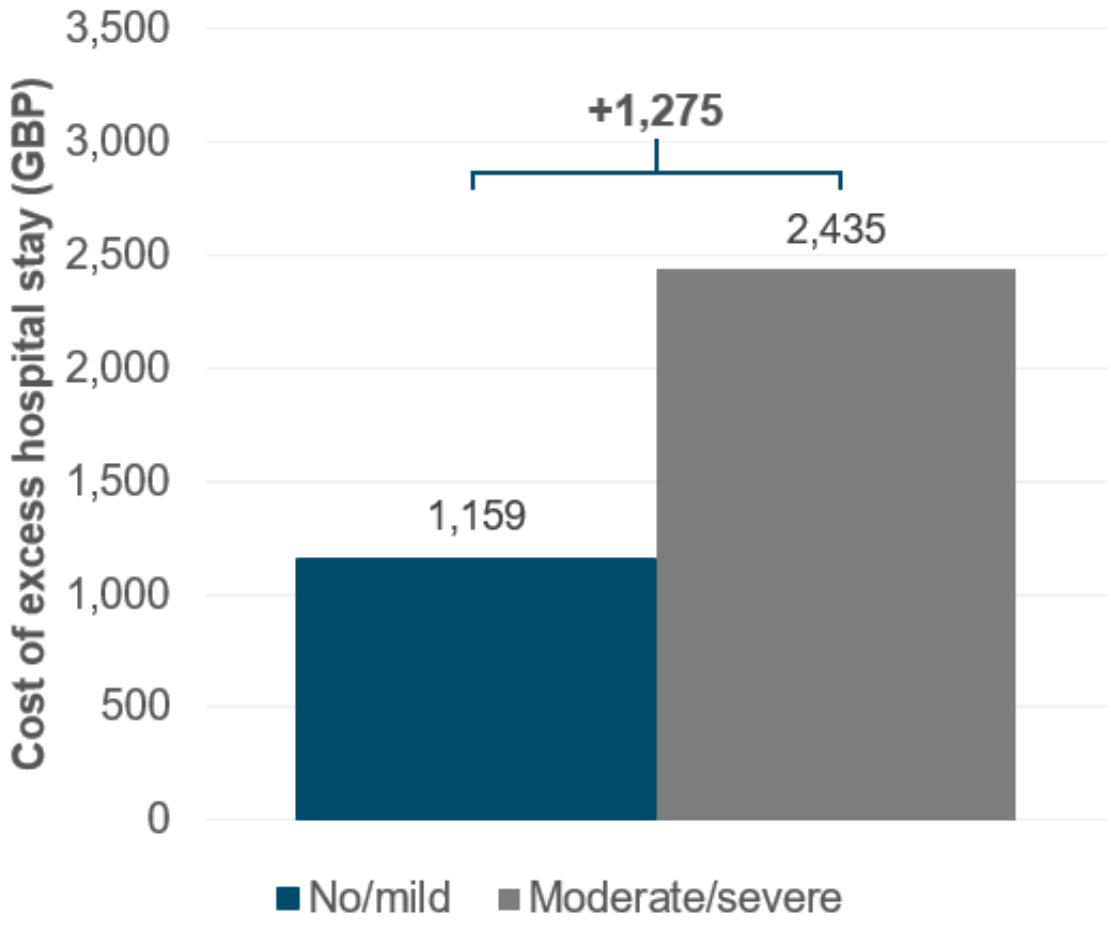


Cost analysis

- The cost analysis weighted by the 107 non-elective HRG tariffs showed an excess stay cost of GBP 1,159 in patients with no/mild hypophosphatemia versus GBP 2,435 in patients with moderate/severe hypophosphatemia, a difference of GBP 1,275 (+110%) per hospital spell (Figure 3).

DISCUSSION AND CONCLUSIONS

Figure 3 Costs of excess hospital bed days in inpatients with no/mild versus moderate/severe hypophosphatemia.



Discussion

- Overall, patients with moderate/severe hypophosphatemia experienced significantly longer hospital stay than patients with no/mild hypophosphatemia.
- The main limitations of the study were the relatively small population size, the retrospective nature of the analysis, and the lack of information on specific HRGs used to code the hospital admissions for the 169 patients. This last concern in particular was mitigated by the input of clinicians familiar with the patient cohort, and the use of an approach to model weighted average HRG costs based on national HES data.
- In the population as a whole, the excess stay cost was 110% higher in the group with moderate-severe hypophosphatemia versus no/mild hypophosphatemia (Figure 3).
- This study documents the significant cost increases associated with hypophosphatemia following FCM administration in an inpatient setting. The majority of IV iron administrations take place in an outpatient setting, where the healthcare utilization associated with hypophosphatemia is expected to be less significant. However, with at least 30% of iron infusions being administered to inpatients at UCLH, the choice of IV iron preparation could substantially affect healthcare resource utilization costs.
- **The present HRG trimpoint-based analysis showed that developing moderate-severe hypophosphatemia post-FCM has a substantial impact on utilization of healthcare resources.**

ABSTRACT

BACKGROUND AND AIMS

Intravenous (IV) iron is the mainstay of treatment for iron deficiency anemia (IDA), when oral iron cannot be used or there is a need for rapid iron delivery. Ferric carboxymaltose (FCM) is a widely used IV iron preparation known to cause moderate-severe hypophosphatemia (serum phosphate <0.65 mmol/L) in up to 75% of patients. The objective was to analyze length of hospital stay (LoS) and cost in inpatients with no/mild versus moderate-severe hypophosphatemia after treatment of IDA with FCM.

METHODS

A patient-level model was developed to evaluate LoS and cost in inpatients with IDA of various etiologies treated with FCM at University College Hospital, London, UK (N=169). LoS and costs were modeled in patients with no/mild hypophosphatemia (n=112) and moderate-severe (n=57) hypophosphatemia. Analyses were conducted across 107 non-elective healthcare resource group (HRG) tariffs with finite trimpoints weighted using NHS England Hospital Episode Statistics (HES). Costs were calculated based on excess stay costs for stays longer than the HRG trimpoint.

RESULTS

Patients with no/mild hypophosphatemia had a mean hospital stay of 10.9 days (standard deviation [SD] 13.4 days) versus 18.0 days (SD 19.8 days; p=0.0035) in patients with moderate/severe hypophosphatemia. The cost analysis weighted by the 107 non-elective HRG tariffs showed an excess stay cost of GBP 1,159 in patients with no/mild hypophosphatemia versus GBP 2,435 in patients with moderate/severe hypophosphatemia, a difference of GBP 1,275 (+110%) per hospital spell.

CONCLUSIONS

Patients with moderate-severe hypophosphatemia experienced significantly longer hospital stay than patients with no/mild hypophosphatemia. A patient-level HRG-based cost analysis weighted by HES data showed that the excess stay cost was 110% higher in the group with moderate-severe hypophosphatemia versus no/mild hypophosphatemia. In this inpatient population, hypophosphatemia may have been related to treatment with FCM and the excess cost may therefore represent an additional cost of treatment with FCM.

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