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Use and Effectiveness of Carboximaltose Iron in Preoperative Anemia Treatment: A Multicenter and Retrospective Study

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Aim: Anemia, primarily due to iron deficiency, is a key risk factor in both elective and emergency surgeries. Immediate preoperative treatment with ferric carboxymaltose (FCM) in anemic patients can reduce the need for transfusions and the length of hospital stay, thereby optimizing surgical outcomes. The objective of this study was to assess the effectiveness and describe the use of administering intravenous FCM prior to elective scheduled surgery for patients diagnosed with anemia.

Methods: Multicenter, retrospective cohort study that encompassed patients aged 18 years and older who underwent surgery between January 2017 and December 2018. Demographic variables, dose scheme, baseline and perioperative haemoglobin (Hb), transfusion requirements, and admission days were collected. The primary endpoints were the response rate and effectiveness of FCM, defined as the proportion of patients with Hb preoperative levels of ≥13 g/dL. A patient response was deemed to occur when Hb level increased by 1 g/dL or more. The secondary endpoints were the appropriateness of FCM dose, transfusion requirement rate, and length of hospital stay.

Results: 446 patients (55.2% women, median age 69 IQR:52–78 years) were included. The median total dose of FCM administered was 1000 mg over a span of 5 day (IQR: 0–16) days before surgery. 62.8% of patients received lower doses, 24.9% had an INCREASE of Hb ≥ 1 g/dL, 11.6% had Hb ≥ 13 g/dL and 21.3% required blood transfusions, with a mean of 0.73 units transfused. The length of the hospital stay was 12 days (IQR:6–23).

Conclusion: Low percentage of patients achieved a hemoglobin level of 13 g/dL or experienced an increase in hemoglobin of 1 g/dL or more following the administration of FCM, indicating the low effectiveness of FCM in treating perioperative anaemia in our surgical patients. There is underdosing of FCM and insufficient time between FCM administration and surgery in most patients. Both transfused and non-transfused patients show similar Hb increases, while those receiving a standard 1000 mg dose of FCM experience shorter hospital stays compared to those receiving 500 mg, and patients with more transfusions have longer hospital stays.

Keywords: iron intravenous administration, ferric carboxymaltose, iron deficiency anemia

Introduction

Anaemia, as defined by the World Health Organization (WHO), is characterized by a circulating hemoglobin (Hb) concentration below 130 g/L in men and 120 g/L in women. The WHO defines anaemia in children under 5 years of age and pregnant women as a haemoglobin concentration <110 g/L at sea level and anaemia in non-pregnant women as a haemoglobin concentration <120 g/L. According to the WHO, iron deficiency anemia (IDA) is defined as ferritin levels below 15 micrograms/L, with hemoglobin levels under 12 g/dL for nonpregnant females aged 12 and older and under 13 g/dL for males aged 15 and older.[1] Preoperative anaemia can contribute to complications during and after surgery. In several large studies of non-cardiac surgical patients, the prevalence of preoperative anaemia ranged from 10–70% depending on the definition of anaemia and type of intervention. This was found to be higher in oncological and

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gynaecological surgery.[1–4] Preoperative anemia stands as an autonomous risk factor for perioperative blood transfusion, morbidity, and mortality.[4,5] In surgical patients, the administration of red blood cell transfusions (RBCT) may be associated with an increased risk of infection, circulatory overload, and thromboembolic events. Additionally, it can lead to prolonged hospitalization, impaired quality of life, and should therefore be minimized or avoided whenever possible.[1,6]

Since preoperative haemoglobin concentration is a major predictor of perioperative transfusion, haemoglobin optimisation is a key aspect of patient blood management. The toxicity concerns from EPO erythropoietin (EPO) would reinforce the role of IV iron. Indeed, the majority of guidelines from professional associations and international consensus documents endorse the use of intravenous iron in the management of perioperative anemia.[5,7–15] Prior research has indicated that administering intravenous ferric carboxymaltose (FCM) treatment a minimum of 1 week prior to surgery elevates hemoglobin levels and, thereby, is expected to decrease the necessity for RBCT during the perioperative phase.[4,6,10,16–18] Various intravenous iron formulations are commercially available, and research has demonstrated the safety and efficacy of all these formulations, depending on the dose, for correcting anaemia. Intravenous FCM is the predominant treatment for iron deficiency anemia in Spain. It enables the administration of high iron doses (up to 1000 mg) through short infusions, with a low risk of severe anaphylactic reactions (incidence approximately 1 in 250,000 administrations). Iron carboxymaltose is ideal for treating perioperative anemia because it quickly replenishes iron stores, crucial for surgical patients needing rapid recovery. Its intravenous administration ensures effective absorption, bypassing gastrointestinal issues often associated with oral iron. This reduces the risk of delays or complications due to anemia. Additionally, fewer doses improve patient compliance and streamline pre-surgical preparation. Its safety profile and efficiency make it suitable for managing anemia in the perioperative setting.[5,19,20]

Iron deficiency anemia is a surprisingly common condition in various surgical and other patient populations. Even among patients whose anemia is attributed to other causes (eg, chronic kidney disease or inflammation), there may be some degree of iron deficiency. People with iron deficiency should be treated with iron rather than transfusions, unless the anemia is extremely severe and there is a risk of organ ischemia, as discussed separately. If iron is administered, sufficient time should be allowed for effective treatment of anemia before surgery (usually two to four weeks for partial correction and six to eight weeks for complete correction). In people with unexplained iron deficiency, determining the underlying cause is an essential part of treatment.

Another study concludes that intravenous iron is an effective intervention to improve Hb concentration in patients with iron deficiency anemia, despite the majority of patients not receiving the full dose based on their baseline Hb level and weight. Increasing the interval time between infusion and surgery was associated with a greater increase in Hb, with only a minimal increase observed if given less than 2 weeks prior to surgery.[21]

Oral iron replacement can be started in a patient with iron deficiency if at least four to six weeks are available before the planned surgery. Intravenous (IV) iron is an option if there are fewer than four to six weeks until the scheduled surgery and for patients who cannot tolerate oral iron or do not respond (eg, due to malabsorption). In this context, intravenous iron can replenish the body's iron stores more quickly and effectively than oral iron treatment; however, time is still needed for the iron to incorporate into developing red blood cells and for the hemoglobin level to rise, and Although it has been observed that in certain cases FCM administration was associated with a reduced need for perioperative transfusion and can safely stabilize hematological parameters,[22,23] the available trials do not have sufficient statistical power to determine if transfusion rates are indeed lower.

Given this context, the present study was formulated to evaluate the effectiveness of administering preoperative FCM in patients undergoing surgery for deficiency anaemia. The secondary endpoints included appropriateness of the doses, transfusion requirement rate, and length of hospital stay.

Materials and Methods

Ethical approval for this study was obtained from the Ethics Committee of CEIm 2019.10. EO provided by the Ethical Committee of Guadalajara University Hospital, Guadalajara, Spain, chaired by Prof. Juan Ramon Urbina Torija, on February 12, 2019 (Investigation Protocol Number: PR-FE-01). This committee reviewed the study upon which this manuscript is based and granted approval to waive the requirement for informed consent based on the principles outlined in the Declaration of Helsinki. All patient information is confidential and protected under applicable privacy laws.

Unauthorized access, use, or disclosure of patient data is strictly prohibited and may result in disciplinary action and legal consequences. We are committed to ensuring the privacy and security of all patient records.

This multicentre cohort retrospective study was conducted at three Spanish hospitals: Guadalajara University Hospital (UGH), Virgen del Rocío University Hospital (UVRH) and Vall d'Hebron Hospital (UVEH). Consecutive non-probability sampling was used. The institutional review board granted approval for this study.

The study population comprised individuals aged 18 years and older who underwent elective surgery and were treated with FCM between January 2017 and December 2018 (24 months). There were no restrictions on the surgical procedures. The study excluded patients who underwent emergency surgery and individuals with concurrent illnesses associated with anemia, such as hematological and oncological conditions or renal failure, and those lacking perioperative hemoglobin data (preoperative Hb and Hb in hospital stay). Emergency surgery was defined as a medical emergency necessitating immediate surgical intervention, where postponement was not feasible for successful resolution.

The primary endpoints were the response rate and effectiveness of FCM, defined as the percentage of patients with preoperative hemoglobin levels of 13 g/dL or higher (regardless of gender). We defined preoperative hemoglobin as the last hemoglobin measurement before the index operation. A patient's response was deemed to occur when the hemoglobin (Hb) level increased by at least 1 g/dL or if the Hb level reaches ≥13 g/dL. In this study, a hemoglobin level of 13 g/dL was considered appropriate for both sexes, supported by numerous studies. It may no longer be justifiable to use a lower hemoglobin threshold to define anemia in women, as this increases the risk of adverse outcomes and the need for costly transfusions. The definition of anemia should be standardized across sexes, especially in the perioperative setting, with a hemoglobin level below 130 g/L requiring intervention for both men and women.[2,24–28]

The secondary endpoints were the appropriateness of FCM doses, transfusion requirement rate, and length of hospital stay.

Demographic variables (sex and age), weight, surgical procedure, bleeding risk, dose scheme, baseline and perioperative hemoglobin (Hb) levels, preoperative ferritin levels, transfusion requirements, and days of hospital admission were collected from the electronic health records. We defined baseline hemoglobin as the hemoglobin value on the day of the preoperative anesthesia consultation when FCM was administrated. Analytical variables were collected before FCM administration in the perioperative period and at discharge. Iron deficiency was delineated based on the criteria set forth by the World Health Organization (WHO).[29] The risk of bleeding was classified as high, moderate, or low based on the type of intervention. (according to the Consensus Document of the Spanish Society of Cardiology, 2018: "Perioperative management and periprocedural antithrombotic treatment").[30]

The appropriateness of FCM doses was evaluated according to the Ganzoni Formula [Iron dose (mg)= [target haemoglobin (Hb) (g/dL) – actual haemoglobin (Hb) (g/dL)] x weight (Kg) x 2.4 + iron deposits (500 mg in adults); target Hb: 13 g/dL], and FCM Summary of Product Characteristics (SPC).[31] For the administration of intravenous iron in surgeries planned in less than a month, the FCM dose must be calculated using the Ganzoni Formula (FG). Patients without weight data were estimated by considering an average weight of 70 kg for men and 65 kg for women. The time between the administration of FCM and surgery is defined as the number of days between the day the dose of ferric carboxymaltose is administered (along with the corresponding lab tests) and the day the patient undergoes surgery (also with the corresponding lab tests).

It is recommended to apply "restrictive" transfusion criteria for red blood cell concentrates (RBCs) in most hospitalized patients (medical, surgical, or critical) without active bleeding and who are hemodynamically stable (including those with sepsis, upper gastrointestinal bleeding, or postpartum anemia) if they present symptoms or an Hb level <7.0 g/dL. For cardiac surgery patients, restrictive transfusion criteria are recommended at an Hb ≤7.5 g/dL. For patients with a history of cardiovascular disease undergoing orthopedic surgery or hip fracture repair, restrictive transfusion criteria are recommended at an Hb <8.0 g/dL.[32–44]

Statistical Analysis

Baseline characteristics were described using the median with interquartile range (IQR) for continuous data and percentages for categorical data. Mean and standard deviation were utilized for normally distributed continuous data. Qualitative variables were compared using the $\chi 2$ test, with Fisher's exact test applied if expected counts were below five. For quantitative variables, comparisons were conducted using either the *t*-test or ANOVA for normally distributed data,

while the Mann–Whitney *U*-test or Kruskal–Wallis test was used for non-normally distributed data. Logistic regression analysis was employed to evaluate the association between FCM administration and increased Hb levels, reported as odds ratios (OR) with 95% confidence intervals (CI). All statistical tests were two-tailed, with significance set at a p-value <0.05.

Statistical analysis was conducted utilizing the SPSS statistical software package v.15 for Windows and STATA v.16 for Mac.

Results

Baseline and Clinical Characteristics

A total of 446 of 506 patients treated with FCM were included in this study. Sixty patients did not have any perioperative Hb data and were excluded. Two hundred forty-six (55.2%) patients were female, and the median age was 69 (IQR 52–78) years. Baseline characteristics, surgical procedures, and proportion of patients with preoperative bleeding are shown in Table 1.

Table 1 Baseline Characteristics, Surgical Procedure and Bleeding Risk

	Total	UGH	UVRH	UVEH	
Demographic characteristics					
Sex	446	103	71	272	
Females (%, n)	55.2% (246)	54.4% (56)	67.6% (48)	52.2% (142)	p=0.066
Age (median; IQR)	69 (52–78)	72 (59–82)	58 (46–71)	70 (53–78.8)	p=0.052
Prevalence of anaemia					
Total	84.3% (376)	93.2% (96)	98.6% (70)	77.2% (210)	
Women (Hb<12 g/dL)	76.8% (189)	89.3% (50)	97.9% (47)	64.8% (92)	p=0.466
Men (Hb<13 g/dL)	93.5% (187)	97.9% (46)	100% (23)	90.8% (118)	p= 0.427
Prevalence of iron deficiency anaemia (IDA): Only 67.8% (255) patients had ferritin data.					
Total (ferritin<15 µgrams/L)	2.1% (8)	4.2% (4)	No data	1.9% (4)	
Surgical Procedure (SP)					
Gastrointestinal	39.7% (177)	62.1% (64)	46.5% (33)	29.4% (80)	p<0.001
Orthopaedic	17% (76)	4.9% (5)	9.9% (7)	23.5% (64)	
Cardiovascular	15.5% (69)	4.9% (5)	16.9% (12)	19.1% (52)	
Gynaecological	6.5% (29)	16.5% (17)	8.5% (6)	2.2% (6)	
Urologic	2% (9)	2.9% (3)	0.0% (0)	2.2% (6)	
Ophthalmic	0.9% (4)	3.9% (4)	0.0% (0)	0.0% (0)	
Other	18.4% (82)	4.9% (5)	18.3% (13)	23.5% (64)	
Bleeding risk					
Total (excluded=6)	98.7% (440)	99.0% (102)	97.2% (69)	98.9% (269)	
Low	9.5% (42)	17.6% (18)	10.1% (7)	6.3% (17)	p<0.001
Moderate	52.5% (231)	61.8% (63)	43.5% (30)	51.3% (138)	
High	38.0% (167)	20.6% (21)	46.4% (32)	42.4% (114)	

Abbreviations: IQR, interquartile range; UGH, Guadalajara University Hospital (Guadalajara); UVRH, Virgen del Rocío University Hospital (Seville); UVEH, Vall d'Hebron Hospital (Barcelone).

The overall prevalence of anaemia was 84.3% (n=376): 93.5% in males (Hb<13 g/dL) and 76.8% in females (Hb<12 g/dL). The UVEH group had a significantly lower number of patients with anaemia (77.2%). Prevalence of iron deficiency anaemia (IDA) was 2.1%, with ferritin data available for only 67.8% (255) of patients. Ferritin data was unavailable for the UVRH group.

The most common procedures performed in the total population were gastrointestinal surgery (39.7%), orthopedic surgery (17%), cardiovascular surgery (15.5%), and excluding gynecological surgery (6.5%). As presented in Table 1, patients treated with UGH and UVEH more commonly presented a moderate bleeding risk, whereas those treated with UVRH presented a high bleeding risk.

Primary Outcomes

At the time of data collection, the median baseline Hb (bHb) were 10.5 g/dL (IQR 9.6 11.7). The evaluation of haemoglobin levels is presented in Table 2.

Regarding the increase in Hb achieved, 11.6% of patients had preoperative Hb ≥13 g/dl, and 52.5% (21) had high-risk bleeding. Overall, the response rate, defined as bHb ≥1 g/dL, was 24.9% (excluding patients with preoperative Hb ≥13 g/dl), with the highest proportion in the UVRH group (50.7%). The mean increase in Hb levels compared to baseline was 0.28 g/dL (SD 0.09).

FCM was administered 5 (IQR, 0–16) days before surgery, and 15.3% (68) of patients had more than four weeks between FCM administration and surgery, allowing sufficient time for erythropoiesis and iron use (FCM SPC). There was large variability between hospitals. UVRH showed longer periods between administration and surgery (24 days; IQR 9.75 43.5).

Secondary Outcomes

The median FCM dose administered was 1000 mg (IQR 500–1000). There were no significant differences among the three hospitals (p>0.05). A total of 280 (62.8%) patients received lower dosages according to the FCM SPC recommendations. According to the Ganzoni Formula, 20.9% (93) of patients received higher doses than needed: between 500–1000 mg in 17.6% (78) of patients and higher than 1000 mg in 3.4% (15) of patients.

The doses received by FCM are shown in Table 3.

This table titled “Ferric carboxymaltose dosage according to Summary of Product Characteristics” presents data on the actual doses of FCM administered to patients compared with the doses recommended in the technical guidelines. The data is stratified by patients’ weight (35–70 kg and >70 kg) and hemoglobin (Hb) levels (<10 g/dL, 10 to <14 g/dL, and ≥14 g/dL).

For patients with Hb < 10 g/dL and weighing 35–70 kg, the recommended FCM dose was 1500 mg, but only 8.5% of these patients received this dose, with the majority receiving either 500 mg (38.8%) or 1000 mg (48.8%). In those weighing more than 70 kg, the recommended dose was 2000 mg, yet 72.4% received only 1000 mg. Among patients with Hb 10 to <14 g/dL, for those in the 35–70 kg group, the recommended dose was 1000 mg, but nearly half (49.8%) received 500 mg, and 45.7% received the full 1000 mg dose. In the >70 kg group, the recommended dose was 1500 mg, with 68.8% receiving 1000 mg and 29.2% receiving 1500 mg. For patients with Hb ≥ 14 g/dL in the 35–70 kg group, the recommended dose was 500 mg, which was received by the majority (52.6%), while some received higher doses of 1000 mg (36.8%) or 1500 mg (10.5%), and no patients in the >70 kg category with Hb ≥ 14 g/dL were included in this dataset.

In the analysis of transfusion requirements (Table 2), 95 patients (21.3%) required transfusion after FCM administration, and the mean number of RBC units transfused was 0.73, with less in the UVEH group (13.2% and 0.26 units). We analysed a subgroup of patients in need of transfusion according to an increase in bHb ≥1 g/dL, dosage received, and the risk of bleeding. Overall, 27.4% of patients with an increase in Hb ≥1 g/dL were transfused compared to 72.6% of patients with an Hb variation <1 g/dL (p=0.23), and 27.4% of patients who received 500 mg FCM required transfusion compared to 57.9% of patients who received 1000 mg FCM (p=0.003). Regarding the risk of bleeding, 37.9% of patients with a high bleeding risk needed transfusion compared with 61.0% of patients with a moderate bleeding risk requiring transfusion compared with 1.0% of patients with a low bleeding risk requiring transfusion (p<0.05).

The median duration of hospitalization (Table 2), calculated from the day of surgery to discharge, was recorded as 12 days (IQR: 6–23 days). A subgroup analysis showed a median of 15 days (IQR 8–31) in patients who received

Table 2 Evolution of Haemoglobin, Transfusion Requirement and Hospital Stay

	Total	UGH	UVRH	UVEH	
Evolution of haemoglobin					
bHb Median (IQR) (g/dL)	10.5 (9.6–11.8)	10.7 (9.6–11.7)	9.9 (9–10.5)	10.8 (9.8–12)	p<0.001
Hb perioperative median (IQR) (g/dL)	10.9 (9.8–12.1)	11.3 (10.1–12.3)	11 (9.8–12)	10.7 (9.7–12)	p=0.250
Hb preoperative ≥ 13 g/dL (%, n)	11.6% (52)	19.2% (10)	13.5% (7)	67.3% (35)	p=0.622
Increase bHb ≥1 g (dL) (%, n)	24.9% (111)	34.0% (35)	50.7% (36)	14.7% (40)	p<0.001
Mean increase Hb (SD)	0.28 (SD 0.09)	0.61 (SD 0.15)	1.09 (SD 0.23)	−0.06 (SD 0.11)	p=0.028
Time between FCM and surgery (median; IQR) (days)	5 (0–16)	10 (5–21)	24 (9.75–43.5)	1 (0–8)	p<0.001
Transfusion					
Need for transfusion (patients) (%, n) Mean units transfused (SD) 500 mg FCM 1000 mg FCM 1500 mg FCM 2000 mg FCM	21.3% (95) 0.73 (1.9) 27.4% (26) 57.9% (55) 8.4% (8) 6.3% (6) p=0.003 (vs Need for transfusion patients)	33.0% (34) 1.51 (2.8) 5.8% (2) 91.2% (31) – 3.0% (1)	35.2% (25) 1.51 (2.7) 0.0% (0) 56.0% (14) 24.0% (6) 20% (5)	13.2% (36) 0.26 (0.7) 66.7% (24) 27.8% (10) 5.5% (2) 0.0% (0)	p<0.001 p<0.001 p<0.001
Low risk bleeding Moderate risk bleeding High risk bleeding	1.0% (1) 61.0% (58) 37.9% (36) p<0.05	0.0% (0) 76.5% (26) 23.5% (8)	4.0% (1) 44.0% (11) 52.0% (13)	0.0% (0) 58.3% (21) 41.7% (15)	p=0.070
bHb≥1 mg/dL bHb<1 mg/dL	27.4% (26) 72.6% (69) p=0.23 (vs Need for transfusion patients)	72.6% (11) 27.4% (23)	28.0% (7) 72.0% (18)	22.2% (8) 77.8% (28)	p=0.479
Hospital stay					
Median Time (days, IQR)	12 (6–23)	8 (5–14)	5 (3–11)	16 (8–31.8)	p<0.001
Patients with transfusion (days, IQR) Patients without transfusion (days, IQR)	15 (8–31) 10 (6–20)	12.5 (8–19.5) 6 (4.7–9.25)	10 (6.50–20.00) 4 (2–7)	28.50 (14.25–53.00) 15 (8–27.75)	–
500 mg FCM (days, IQR) 1000 mg FCM (days, IQR) 1500 mg FCM (days, IQR)	16 (8–32) 9 (5–19) 8 (4–18)	9.50 (4.50–43.75) 8 (5–14) –	– 5 (2.25–9) 5 (4–10)	16 (8–32) 16 (8–31) 25.5 (12–54.75)	–
Low risk bleeding (days, IQR) Moderate risk bleeding (days, IQR) High risk bleeding (days, IQR)	13 (6.75–34.25) 11 (6–21) 12 (6–25)	8.50 (5.75–25.00) 8 (5–13) 8 (4–18)	5 (4–7) 6.50 (3–13.50) 4.50 (2–10.75)	21 (12.50–38.00) 14.50 (8–30) 16 (8–32.25)	–

Abbreviations: FCM, ferric carboxymaltose; IQR, interquartile range; UGH, Guadalajara University Hospital; UVRH, Virgen del Rocío University Hospital; UVEH, Vall d'Hebron Hospital; Hb, haemoglobin; bHb, Hb before FCM administration.

a transfusion versus 10 days (IQR 6–20) in those who did not (p<0.05). The length of hospital stay was similar according to the risk of bleeding (13 days with low risk, 11 days with moderate risk, and 12 days with high risk). The median hospitalisation time was 16 days among patients who received 500 mg FCM and 9 days among patients who received 1000 mg FCM (p<0.05).

Table 3 Ferric Carboxymaltose Dosage According to Summary of Product Characteristics

Weight (*)	35–70 Kg Weight		>70 Kg Weight	
Hb (g/dL) (n)	**FCM SPC Dose**	**Received Dose (n, % Patients)**	**FCM Dose (SPC)**	**Received Dose (n, % Patients)**
<10	1500 mg	500 mg (50, 38.8%) 1000 mg (63, 48.8%) **1500 mg (11, 8.5%)** 2000 mg (4 3.1%) 3000 mg (1, 0.8%)	2000 mg	1000 mg (21, 72.4%) 1500 mg (3, 10.3%) **2000 mg (5, 17.2%)**
10 a <14	1000 mg	500 mg (110, 49.8%) **1000 mg (101, 45.7%)** 1500 mg (3, 1.4%) 2000 mg (7, 3.2%)	1500 mg	1000 mg (33, 68.8%) **1500 mg (14, 29.2%)** 2000 mg (1, 2.1%)
≥14	500 mg	**500 mg (10, 52.6%)** 1000 mg (7, 36.8%) 1500 mg (2, 10.5%)	500 mg	No patients

Notes: (*) No patients with weight <35 Kg. Bold text included is recommended dose.
Abbreviations: FCM, ferric carboxymaltose; SPC, Summary of Product Characteristics; Hb, haemoglobin.

Discussion

We found that anaemia, as defined by the WHO Health Organization criteria, was highly prevalent in patients preoperatively. From this perspective, we aimed to determine whether preoperative FCM administered before surgery would correct the underlying iron deficits. We also aimed to understand the use of FCM and its impact of FCM administration in clinical outcomes.

In the effectiveness analysis, almost 25% of the patients had an increase in Hb levels in the preoperative period compared with bHb ≥1 g/dL after the administration of FCM. In comparison to standard care, intravenous iron resulted in a notable increase in hemoglobin levels by 0.8 g/dL, contrasting with the 0.1 g/dL improvement observed with conventional treatment, as demonstrated by a randomized controlled trial encompassing 72 patients undergoing major abdominal surgery (p=0.01) upon admission.[6] One systematic review discovered that among a subgroup of anemic patients undergoing colorectal surgery, there was a slightly greater increase in hemoglobin at the conclusion of preoperative treatment with intravenous iron compared to placebo. However, this difference was not statistically significant nor clinically relevant.[13]

It is important to note that 11.7% of the patients were treated with FCM and had no anaemia (preoperative Hb level ≥13 g/dl). They were excluded from the effectiveness analysis; however, more than half of these patients had a high risk of bleeding.

The prevalence of iron deficiency anaemia (IDA) observed in this study was relatively low at 2.1%, which could be interpreted in several ways. First, it may suggest effective iron management within the patient population. However, the limited availability of ferritin data (only 67.8% of patients) raises concerns about potential underdiagnosis. Ferritin is a key marker for diagnosing IDA, and the absence of this data in over 30% of patients suggests that the true prevalence could be higher than reported.

Based on our findings, approximately 90% of the patients treated with FCM had a high or moderate risk of bleeding. The median dose received was 1000 mg, and almost a quarter of the patients received higher doses than needed, according to the Ganzoni Formula, and approximately 70% of the patients received an inadequate dosage according to the FMC SPC recommendations. In the preoperative period following FCM administration, a quarter of the patients experienced a rise in Hb level of at least 1 g/dL. Almost a quarter of the patients required transfusion.

While ideally, the intravenous iron dosage should be calculated based on the total body iron deficit using the Ganzoni formula, in clinical practice, this calculation is of limited relevance due to the maximum allowable iron dose being restricted to 1000 mg. In our study, almost a quarter of the patients received a dose higher than the ideal dose according

to the Ganzoni formula. UVEH did not collect patient weight data, and considered an average weight of 70 kg for men and 65 kg for women to calculate the FCM dose using the Ganzoni Formula. This may have influenced the mean dose used by patients in this study.

In relation to Table 3, which analyzes the discrepancies between recommended and administered doses of Ferric Carboxymaltose (FCM) in patients based on their hemoglobin levels and body weight. The data reveal a significant discrepancy between the recommended doses of FCM according to technical guidelines and the actual doses administered to patients. For patients with Hb < 10 g/dL, the recommended doses were often not met, particularly in the higher weight category where a substantial number of patients received only half of the recommended dose. This trend is consistent across all Hb levels, where lower than recommended doses were frequently administered. The variation in dosing, particularly the administration of doses lower than those recommended, could be due to a variety of factors including clinical judgment, concerns about side effects, or limitations in resource availability. However, this discrepancy raises concerns about the potential for under-treatment, especially in patients with severe anemia, which could impact their recovery and overall outcomes.

The international statement on the perioperative management of anaemia[14] suggests oral iron administration when there is a suitable interval before surgery, typically ranging from 6–8 weeks, and when there are no contraindications present. In our study, we did not record whether the patients had taken oral iron prior to intravenous iron administration, but the average time between FCM administration and surgery was not sufficient to obtain an adequate Hb increase. The average time spent in the three hospitals was 5 days. Prior research has demonstrated that the administration of intravenous iron at least one week prior to surgery elevates hemoglobin levels, thereby potentially decreasing the requirement for RBCT units during the perioperative period.[10,17,45]

In relation to RBCT, both the percentage of patients and the quantity of units transfused were notably higher compared to those reported in other studies. In Calleja et al[16] out of the subgroup of patients with colon cancer who received preoperative FCM, only 9.9% were transfused and 0.2 units transfused. In Bisbe et al's controlled trial, Just 7% of patients in the FCM group necessitated RBCT transfusion.[45] In our study, patients who received transfusions spent more days in the hospital compared to those that did not, with statistically significant result (p=0.003). Likewise, increased length of hospital stay in patients who received transfusions has been reported in other studies.[7,46] Despite this, the Hb increase in transfused patients was similar to that in non-transfused patients.

This study had several limitations that warrant acknowledgement. First, it had a retrospective and non-comparative design with a surgical population that did not receive FCM. It is not possible to determine with certainty whether the improvement in perioperative outcomes was due to FCM. Additionally, nearly 20% of patients lacked hemoglobin data during the perioperative period. This may have led to potential bias in the interpretation of the results.

Our study, however, has several strengths, particularly the large sample size of patients considered for the analysis, the participation of three large Spanish hospitals, and the representation of "real-life" clinical practice.

Conclusions

In conclusion, there was a low proportion of patients achieving a hemoglobin level of 13 g/dL or experiencing an increase in hemoglobin of 1 g/dL or more following the administration of FCM, which indicates the low effectiveness of FCM in treating preoperative anaemia in our surgical patients. Future randomised controlled trials focused on evaluating the effectiveness of FCM treatment for preoperative anaemia may support our findings.

Patients are regularly underdosed with FCM and the time between FCM administration and the date of surgery is insufficient for most patients. It is necessary to develop a protocol for the management of FCM to ensure adequate prescription and include any iron study as a factor in determining who to administer IV iron. The findings suggest that the administration of FCM in clinical practice often falls short of the recommended guidelines, particularly in patients with more severe anemia. This under-dosing could have significant implications for patient outcomes, indicating a need for further investigation into the reasons for these discrepancies and potentially a reassessment of clinical practices to ensure that patients receive the appropriate dosage of FCM as per the guidelines.

The lack of comprehensive ferritin data may have led to an underestimation of IDA prevalence, as patients without this data might still have had undetected iron deficiency. Therefore, the reported 2.1% prevalence should be considered with caution, and future studies should aim for more complete data collection to ensure accurate prevalence estimates.

Additionally, this finding highlights the importance of improving data completeness in clinical practice to enhance the reliability of study outcomes. Information about inflammation and other iron data status would be useful to gauge response to iron therapy. Lack of this information is a limitation.

The observation that the increase in Hb in transfused patients was similar to that in non-transfused patients reflects that the effectiveness in terms of Hb level increase does not differ significantly between the two groups.

Patients who receive a higher number of transfusions experience longer hospital stays. Patients who receive a standard dose of 1000 mg of FCM have shorter hospital stays compared to those who receive 500 mg.

Disclosure

The authors report no conflicts of interest in this work.

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