ORIGINAL ARTICLE

Iron-deficiency Anemia Treatment with Ferric Carboxymaltose: A Real-world Quasi-experimental Study from Bangladesh

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Abstract

Gastrointestinal bleeding is the most common cause of iron deficiency in adult men and menstrual blood loss is the leading cause of iron insufficiency in women, anemia due to iron deficiency is mostly caused by blood loss. Ferric carboxymaltose (FCM) is a contemporary parenteral iron formulation that may be used therapeutically to treat anemia caused by an iron deficiency [iron-deficiency anemia (IDA)]. The main goal of the trial was to evaluate FCM's safety and efficacy in treating IDA. The Department of Hematology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh participated in this quasi-experimental research, which comprised adult patients with IDA. Participants were given an intravenous (IV) infusion of 500 mg of FCM, diluted in 100 mL of 0.9% normal saline, throughout a 30-minute period after their participation. The second dosage of FCM was administered after a 7-day period of the first dose. The comparison of the outcomes [hemoglobin (Hb) level, serum ferritin level, and other hematological parameters] between the baseline and day 14 postintervention was done using a paired *t*-test. Compared to baseline, patients' Hb levels rose considerably ($p = 0.001$) after FCM. Aside from serum ferritin level, additional hematological parameters that sharply increased were red blood cells (RBCs) count, mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width – coefficient of variation (RDW-CV), and iron indicators. The experiment recorded mild adverse effects such as fever, headaches, and gastrointestinal issues including vomiting, diarrhea, and constipation, but no significant adverse events. In summary, IDA may be effectively treated with FCM, a safe and secure IV medication that has no major negative effects.

Keywords: Efficacy and safety, Ferric carboxymaltose, Ferritin, Hemoglobin, Iron-deficiency anemia.

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Introduction

A worldwide public health problem, anemia affects almost two billion people, particularly in low- and middle-income nations.[1,2] South Asian developing country Bangladesh is still grappling with a relatively high anemia burden even with notable improvements in many health metrics. About 51% of children under 5 years of age and approximately 42% of women who are not pregnant are affected by anemia in this country, according to recent research.[3]

Etiological causes of anemia include viral infections, chronic blood loss, and deficits in certain micronutrients. As it explains almost two-thirds of the total anemia burden, iron-deficiency anemia (IDA) remains the leading cause of anemia.[2] Iron replacement therapy is advised to be used as the first line of treatment for IDA diagnosis.[4] Treatment for IDA has always included oral iron supplementation. A prolonged oral iron treatment of 3–6 months is usually necessary to correct the iron shortage in circulating hemoglobin (Hb) and to achieve a satisfactory clinical response.[5]

Many malabsorption diseases, such as gastric bypass surgery, Whipple's disease, Small intestinal bacterial overgrowth (SIBO), celiac disease, increased hepcidin levels, and pernicious anemia, prevent patients from benefiting from oral iron supplementation.[6] Furthermore, diarrhea, constipation, cramping in the abdomen, heartburn, nausea, and other side effects are reported by some people who take oral iron.[5]

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Ferrous iron is given intravenously (IV) to individuals who cannot take oral iron due to the possibility of adverse drug reactions (ADRs) or for whom oral iron is ineffective due to low iron absorption. The advantage of IV iron over oral iron is that it supplies iron more quickly.[7,8]

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Some of the iron formulations that may be given IV include ferric gluconate, sucrose, ferumoxytol, ferric carboxymaltose (FCM), ferric derisomaltose/iron isomaltoside, and iron dextran.[8] One of the most effective IV iron therapies has been demonstrated in numerous clinical trials involving a variety of patient populations. Ferric carboxymaltose is one of these preparations; it enables the administration of a significantly higher single dosage of IV iron over a shorter period of time.[9,10] Additionally, a variety of long-term conditions, including heart failure, chronic renal disease, heavy uterine hemorrhage or postpartum IDA, and several other conditions and surgeries, have been shown to respond well to this safe and effective treatment for IDA.[11–15]

Patients in most studies received FCM until the patient's predicted total iron replacement dosage was reached.[16] Alternatively, IV iron dosages of 500–1000 mg (or 15 mg/kg for those $\leq$ 66 kg) were administered during a 15-minute duration.

In Bangladesh, FCM is not often advised, despite being a novel IV iron therapy for IDA. There is very little relevant evidence available about the side effects and clinical outcomes of FCM. Consequently, there is an urgent need to close the information gap regarding the efficacy and safety of FCM for patients from Bangladesh.

Thus, the goal of the current study is to examine the effects and clinical results of FCM in patients with IDA from Bangladesh by giving them two split doses of 500 mg IV FCM spaced 2 weeks apart.

Materials and Methods

Study Design and Participants

The current study was conducted at the hematology department of Rajshahi Medical College Hospital in Rajshahi from January to June of 2021.

The study's inclusion criteria were satisfied by male and female patients with IDA who were older than 18 years old. A blood ferritin level over 100 ng/mL and a Hb level below 10 gm/dL were considered indicators of a proven iron deficiency. The following were included as exclusion criteria: Anemia from non-IDA-related illnesses; any active infections; a history of blood transfusions during the preceding 30 days; and a history of an unfavorable response to IV iron infusion. A total of 152 people with IDA were recruited in the present research after screening and receiving signed informed permission.

Assessment of the Patients

At enrollment, a complete clinical history, a history of previous treatments, including iron therapy, and a chronic medical condition were all gathered. A thorough assessment, including anthropometry and a general physical examination, was carried out by the attending physician. The following procedures were specifically used to diagnose anemia: hemogram, reticulocyte count, peripheral blood smear, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), Hb electrophoresis, and serum ferritin levels.

Intervention

After being included, participants had a 30-minute IV infusion of 500 mg of FCM diluted in 100 cc of 0.9% normal saline. A second dosage of FCM was administered seven days after the initial therapy.

Final Destinations

The primary endpoint of the research was the variation in Hb level between the baseline and 14 days after IV FCM treatment. Secondary objectives were included, including serum ferritin level, reticulocyte count, MCV, mean corpuscular Hb, mean corpuscular Hb concentration, and RDW.

Statistical Analysis

This research specifically used an intention-to-treat analysis. Mean corpuscular volume, mean corpuscular Hb, mean corpuscular Hb concentration, Hb, ferritin, reticulocyte count, and RDW were the endpoints that were compared to their pre- and postintervention values using the paired *t*-test. For statistical significance, a *p*-value of 0.05 or less was used. We performed all statistical analyses using Stata 16.0 (StataCorp LP, College Station, Texas, USA).

Results

There were 152 patients in total in this research, with a mean (SD) age of 38.7 (14.6) years with almost 80% of them being female. Notably, 76.7% of the participants were from low- to middle-class rural backgrounds. Table 1 shows that 69% of the patients had mild-to-moderate anemia while the remaining participants had severe anemia.

The individuals' Hb levels significantly increased from the baseline after receiving ferric carboxy maltose (FCM) for 14 days (from 8 to 10.46 g/dL, $p = 0.001$). Other hematological indicators that had significantly risen were red cell distribution width – coefficient of variation (RDW-CV), MCV, MCHC, and red blood cells (RBC) count. Furthermore, the serum ferritin level increased dramatically from 13.9 to 303 ng/mL ($p < 0.001$), one of the iron markers. Following FCM therapy, there was also a noticeable increase in reticulocyte features including absolute reticulocyte count and reticulocyte Hb level, which may be used as a stand-in for serum iron level (Table 2).

Minor adverse reactions such as diarrhea, constipation, vomiting, and gastrointestinal symptoms include fever (25.6%), headache (17.7%), dyspepsia (16%), and dyspepsia. In the trial, there were no serious adverse events reported (Table 3).

Discussion

The present research offers empirical support for the safety and effectiveness of IV FCM administration in the treatment of anemia in patients from Bangladesh who have iron deficiency. Oral iron therapy has been the mainstay of long-term IDA treatment. On the contrary, because of their higher effectiveness and ease of use, IV iron preparations have become more and more popular lately. We found that IV FCM administration increases Hb levels and other hematological parameters (reticulocyte count, MCV, mean corpuscular Hb, mean corpuscular Hb concentration, MCHC, and RDW) in patients with IDA. It also increased the serum ferritin levels—a measure of iron—in these people. FCM not only showed higher effectiveness but also showed fewer adverse events, most of which were mild side effects such as headaches, fever, and gastrointestinal discomfort. Therefore, in the setting of a heterogeneous patient population, our research offered confidence about the efficacy and safety of IV FCM for the therapy of IDA. Iron sucrose has been the gold standard of care for treating iron deficient anemia among parenteral iron preparations; the results of our study support those from previous studies in which it had

Table 1: The baseline features of the IDA patients ($n = 152$)

Characteristic	*Overall, N = 152*
Age (years)	38.67 (14.57)
Age group (years)	
18–30	52 (34.21)
31–40	40 (26.32)
41–50	31 (20.39)
51–60	18 (11.84)
>60	11 (7.24)
Sex	
Female	121 (79.61)
Male	31 (20.39)
Religion	
Islam	144 (94.74)
Others	8 (5.26)
Residence	
Rural	103 (67.76)
Urban	49 (32.24)
Education	
Up to primary	68 (44.74)
Secondary/higher secondary	73 (48.03)
University graduate	11 (7.24)
Occupation	
Employed	34 (22.37)
Unemployed	118 (77.63)
Family income	
Low	69 (45.39)
Middle	59 (38.82)
High	24 (15.79)
Food habit	
Non vegetarian	150 (98.68)
Vegetarian	2 (1.32)
BMI, mean (SD)	23.16 (2.84)
BMI category	
Underweight	6 (3.95)
Normal	115 (75.66)
Overweight	31 (20.39)
Anemia category	
Mild to moderate	105 (69.08)
Severe	47 (30.92)

BMI, body mass index; SD, standard deviation

Table 2: Impact of FCM on IDA patients

Characteristic	*Before FCM*	*After FCM*	*p-value*
Hb level	8.08 (1.92)	10.46 (1.56)	<0.001
RBC	4.05 (0.82)	4.54 (0.85)	<0.001
HCT	27.26 (7.93)	32.40 (10.25)	<0.001
MCV	65.85 (13.74)	71.81 (14.35)	<0.001
MCH	21.20 (8.40)	25.25 (10.53)	<0.001
MCHC	29.13 (3.76)	32.20 (23.29)	<0.001
RDW-CV	20.25 (6.08)	20.38 (20.80)	0.3
Platelets	332.66 (128.05)	258.63 (189.60)	<0.001
Ferritin	13.94 (26.42)	303.02 (649.92)	<0.001
Reticulocyte	1.37 (1.20)	3.57 (17.26)	<0.001
Absolute reticulocyte	0.07 (0.10)	0.10 (0.11)	<0.001
LFR	84.86 (8.39)	89.46 (10.74)	<0.001
MFR	12.06 (7.86)	9.17 (8.84)	<0.001
HFR	3.16 (4.05)	2.28 (4.39)	<0.001
IRF	14.19 (8.03)	10.42 (8.64)	<0.001
RPI	1.00 (2.89)	1.25 (0.90)	<0.001
Ret-He	19.59 (5.71)	29.98 (25.53)	<0.001

HFR, high fluorescence reticulocyte; IRF, immature reticulocyte fraction; LFR, low fluorescence reticulocyte; MFR, medium fluorescence reticulocyte; Ret-He, reticulocyte-hemoglobin; RPI, reticulocyte production index

Table 3: Adverse events after administration of ferric carboxy maltose

Adverse events	*N (%)*
Headache	27 (17.76)
Hypertension	0
Hypotension	0
Constipation	8 (5.26)
Diarrhea	4 (2.63)
Vomiting	8 (5.26)
Dyspepsia	24 (15.79)
Flatulence	2 (1.32)
Hypersensitivity	0
Pruritus	0
Urticaria	0
Backpain	5 (3.29)
Arthralgia	0
Pyrexia	39 (25.66)
Chest pain	2 (1.32)
Bronchospasm	0
Anxiety	2 (1.32)
Syncope	0
Skin pigmentation	12 (7.89)
Others	9 (5.92)

been demonstrated to be both safe and effective for treating IDA in patients with pregnancy,[17] chronic diseases like inflammatory bowel disease, heavy menstrual bleeding or postpartum IDA, heart failure, chronic kidney disease, and many other diseases as well as surgeries,[11–15] The major disadvantage of iron sucrose is that it has a restricted maximum allowable dosage in a single setting, requiring numerous visits to obtain the required iron dose, even if FCM may be given in a bigger quantity at a time. Ferric carboxymaltose may be administered in amounts ranging 500–1000 mg of iron; further doses should be given every week after that.[16] This regimen was also used in our trial, and the subjects tolerated it well while showing a high degree of effectiveness.

Conclusion

It is reasonable to infer that FCM is an IV medication that safely and efficiently cures IDA based on the results of our experiment. Its benefits include various hematological and iron parameters, as well as an early rise in Hb level and a large dose administered each sitting.

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