Journal of Blood Medicine

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ORIGINAL RESEARCH

Efficacy and Safety of Ferric Carboxymaltose in the Management of Iron Deficiency Anemia: A Multi-Center Real-World Study from India

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Video abstract

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Background: Parenteral iron preparations, like ferric carboxymaltose (FCM), are commonly used to manage moderate-to-severe iron deficiency anemia (IDA). Real-world data on efficacy and safety of FCM is limited in India.

Methods: A retrospective, observational and real-world study was conducted to assess the efficacy and safety of FCM in adolescents and adults with IDA across 269 centers in India. Data was retrieved from medical records of patients who received FCM for management of IDA. Physicians' clinical assessment of efficacy and safety of FCM was also assessed. Data were analyzed for hematological parameters at baseline and at 4 ± 1 week for study population, and for severity of anemia.

Results: In 1800 patients with IDA, intravenous FCM resulted in a significant increase in hemoglobin (Hb) of 2.76 g/dL, serum ferritin of 35.85 µg/L, red blood cell (RBC) count, hematocrit, mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH) ($P < 0.001$ for all) at 4 ± 1 week as compared to baseline. In subjects with severe IDA, an increase in Hb was of 3.31 g/dL, serum ferritin increased of 35.84 µg/L, RBC count, hematocrit and MCH improved significantly ($P < 0.001$ for all). In subjects with moderate IDA, Hb (increase of 2.63 g/dL), serum ferritin (increase of 35.92 µg/L), RBC count, hematocrit, MCV, and MCH improved significantly ($P < 0.001$ for all). In subjects with mild IDA, only the mean Hb values at 4 weeks were significantly higher ($P < 0.001$; increased by 1.89 g/dL). Physicians rated efficacy of FCM as very good to good in 97.5% of patients. Similarly, safety of FCM was rated very good to good in 97.2% subjects.

Conclusion: FCM efficiently, safely and quickly corrects moderate-to-severe anemia in Indian patients in a short span of 4 weeks. Physicians' positive clinical impression of efficacy and safety supports clinical usage of FCM in real-world scenario.

Keywords: ferric carboxymaltose, iron deficiency anemia, pregnancy, efficacy, safety, India

Introduction

Anemia is a global public health problem affecting approximately one-third (22.8%) of the world population in 2019.[1] The 2019–2020 National Family Health Survey (NFHS-5) data shows that 57% of all Indian women and 25% of all Indian men in the age group of 15–49 years have anemia.[2] Anemia is a serious public health concern in India because of its high prevalence across all age groups.[3] Additionally, severe anemia, defined as hemoglobin

Received: 5 February 2022
Accepted: 23 May 2022
Published: 8 June 2022

(Hb) levels <7 g/dL, continues to be a substantial problem despite Indian guidelines and a focus on eradicating anemia.[3,4]

Iron deficiency anemia (IDA) is the most common cause of anemia.[5] IDA is primarily treated with iron supplementation, which can be either oral or parenteral. Oral preparations are inadequate in moderate-to-severe anemia where a faster improvement in Hb level and replenishment of iron stores is desired. Hence, parenteral iron preparations are the mainstay of treatment in moderate-to-severe anemia. However, both oral and parenteral iron preparations have side effects, which often limit their use.[6,7] Therefore, newer intravenous (IV) iron formulations with a favorable adverse events profile as compared to traditional parenteral iron products were developed.[7] Ferric carboxymaltose (FCM) is a third-generation parenteral iron formulation designed to overcome the limitations of existing parenteral iron preparations.[7] FCM is a novel non-dextran IV iron agent having a very low immunogenic potential and therefore not predisposed to a high risk of anaphylactic reactions.[8] Its properties permit the administration of large doses (maximum of 1000 mg/infusion) in a single session (15-minute infusion) without the requirement of a test dose.[8–10]

Evidence suggests that FCM is highly effective in rapidly replenishing iron stores and correcting anemia in patients with IDA associated with a broad spectrum of anemia etiologies covering pregnancy, post-partum, gynecological causes, peri- and post-surgical, etc.[8,11–16] However, real-world evidence (RWE) of the efficacy and safety of FCM is largely lacking, especially from India. RWE substantiates the evidence collected through clinical trials.[17] The present RWE study was conducted with the objective of evaluating the efficacy and safety of intravenous FCM in the management of IDA in the adolescent and adult Indian population in a real-life scenario.

Materials and Methods

Study Design

This was a multi-center, retrospective, observational, data collection study across 269 centers in India.

Patient Characteristics

Adolescents and adults aged ≥14 years with IDA (hemoglobin [Hb] level between 4.0 and <12 g/dL), who provided informed consent for future use of their medical records for research, were included in the study. For subjects <18 years of age, informed consent was taken from their parent or legal guardian. The subjects were routinely treated by their physician with FCM 500/1000 mg injection in their clinical practice between January 01, 2021 and December 31, 2021. Subjects with available data on their medical records for at least two hematological parameters at baseline and/or for a minimum of 4 ± 1 week (reported as 4 weeks for simplicity) were included in the study. Subjects with a diagnosis of anemia other than IDA, severe iron deficiency with Hb <4 g/dL, known hypersensitivity to FCM or to any of its excipients, known serious hypersensitivity to other parenteral iron products, evidence of iron overload (eg, hemochromatosis/hemosiderosis), malignancy, pregnant women in the first trimester or if participant was considered unsuitable for the study by the investigator, were excluded from the study.

Sample Size

Convenience sampling[18] was used as a practical method to obtain the patient sample by utilizing the medical charts available at our disposal from the 269 centers, within the stipulated time period, and of the patients meeting the study inclusion criteria.

Treatment Characteristics

Cumulative FCM dose for iron repletion was determined based on the patient's body weight and Hb level and is detailed in Table 1. FCM (Inj Orofer FCM 500/1K, Emcure Pharmaceuticals Ltd., Pune, India) was administered as part of standard care for the patient, as an IV infusion not exceeding 1000 mg iron per infusion.

Table 1 Cumulative FCM Dose for Iron Repletion

Body Weight	Cumulative FCM Dose	
	Hb <10 g/dL	Hb 10–14 g/dL
<35 kg	500 mg	500 mg
35 kg to <70 kg	1500 mg	1000 mg
≥70 kg	2000 mg	1500 mg

Notes: Maximum tolerated single dose: 1000 mg of iron (20 mL) per day. 1000 mg of iron (20 mL) not to be administered more than once a week.
Abbreviations: FCM, ferric carboxymaltose; g/dL, grams per deciliter; Hb, hemoglobin; mg, milligram; kg, kilograms.

Outcome Measures and Statistical Analysis

Data were retrieved from the medical records of the patients meeting the study inclusion criteria and anonymously filled out by trained technicians in the case record forms (CRF) designed for the study.

Physicians' clinical opinion of the efficacy and safety of FCM was also recorded in the CRF. The efficacy and safety were individually graded as very good, good, average, or poor. Efficacy was assessed clinically based on the symptomatic and hematological improvement recorded in the medical records and safety assessment was based on the adverse events/side effects of FCM recorded in the medical records.

Demographic details and hematological parameters captured in the CRFs were entered in a Microsoft Excel sheet and analyzed using descriptive statistical methods. Data were analyzed for the entire study population, and by the severity of anemia.

Categorical data were represented as frequencies and percentages. Quantitative data was described as mean ± standard deviation (SD). A paired *t*-test was carried out to compare the hematological parameters at baselines and four weeks after FCM infusion.

The following Hb values were considered as normal as per World Health Organization's (WHO's) Hb cut-off values for anemia:[19] Non-pregnant women (≥12 g/dL); pregnant women (≥11 g/dL); men (≥13 g/dL). Anemia was categorized as mild, moderate and severe based on the World Health Organization's Hb cut-off values:[19] severe anemia (Hb <8 g/dL for men/pregnant women and <7 g/dL for non-pregnant women); moderate anemia (Hb 8–10.9 g/dL for non-pregnant women and men and 7 to 9.9 g/dL for pregnant women); and mild anemia (Hb 11–11.9 g/dL for non-pregnant women; 10–10.9 for pregnant women; 11–12.9 g/dL for men).

Ethical Consideration

This study was approved by the Ripon Independent Ethics Committee. The study was registered with the Clinical Trial Registry of India (CTRI) with a wide registration number CTRI/2021/12/039065.

Results

Baseline Characteristics

Eighteen hundred patients were found to be eligible for the study; mean age was 32.37 years (range 14 to 92 years); 96.5% were females; with a mean Hb of 8 g/dL and mean serum ferritin at 42.06 µg/L. The following comorbid conditions were identified in the study population: hypertension (2.8%), diabetes (2.3%), hookworm infestation (0.2%) and kidney disease (0.3%). The mean FCM infusion time was 18.47 minutes (range 5 to 60 minutes). The values of various hematological parameters at baseline are shown in Table 2.

Additionally, six sub-cohorts of subjects could be identified (Table 3) and the response of FCM to IDA in these sub-cohorts was also assessed.

Table 2 Patient Characteristics at Baseline

	N	Mean±SD	Median (IQR)	Range (Min-Max)
Age	1705	32.37±8.4	30(27, 35)	14 to 92
Weight	1551	57.95±9.49	58(51, 65)	30 to 98
Sex	1726	Males: 60 (3.5%)	Females: 1666 (96.5%)	–
FCM Infusion Duration (minutes)	1613	18.47±6.19	15(15, 20)	5 to 60
Baseline Hb (g/dL)	1723	8±0.98	8(7.4, 8.7)	4 to 11.5
Baseline Serum Ferritin (µg/L)	366	42.06±43.34	32.6(8.38, 60)	0.1 to 238
Baseline RBC Count (mn/mm^3)	391	3.9±1.12	3.9(3.3, 4.2)	1.7 to 12.5
Baseline Hematocrit (%)	347	31.22±6.14	31.3(26.4, 35)	16.5 to 46
Baseline MCV (fL)	371	68.94±11.55	69(62, 75)	11.3 to 102.1
Baseline MCH (pg)	363	24.07±6.16	22.61(20, 29)	2.8 to 38.8
Baseline MCHC (g/dL)	354	29.9±3.15	30(28.4, 32)	14 to 43.1
Comorbidities at baseline				
	N (%)			
Hypertension	50 (2.8%)			
Diabetes	42 (2.3%)			
Hookwork Infestation	3 (0.2%)			
Kidney Disease	6 (0.3%)			

Note: 4 weeks is 4 ±1 week.
Abbreviations: %, percentage; µg/L, micrograms per liter; FCM, ferric carboxymaltose; fL, femtoliters; g/dL, grams per deciliter; Hb, hemoglobin; IQR, interquartile range; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; min, minutes; Min-Max, minimum-maximum; mn/mm3, million per millimeter cube; N, number of participants; pg, pictograms; RBC, red blood cell; SD, standard deviation.

Table 3 All Patients' Data Set and Six Cohorts: Improvement in Hemoglobin and Serum Ferritin

	Cohort	Total Patients (N)	Improvement in Hb (g/dL) at 4 Weeks	Improvement in Ferritin (µg/L) at 4 Weeks
	All patients data set	**1800**	2.76*	35.85*
1.	Anemia in pregnancy	1191	2.8*	30.03*
2.	Anemia in Females (All diagnoses)	1666	2.78*	35.26*
3.	Anemia (Anemia diagnosis in men and women)	555	2.71*	58.6*
4.	Anemia in Women (Abnormal uterine bleeding + Anemia (cause not specified) + Perioperative anemia; Excluding pregnancy and postpartum anemia)	442	2.77*	62.07*
5.	Complete data set for all hematological parameters	194	3.19*	23.71*
6.	Anemia in males	60	2.5*	46.76#

Notes: *P<0.001; #P=0.02. P value <0.05 – statistically significant difference observed in hematological parameter; Values are expressed as Mean.
Abbreviations: µg/L, micrograms per liter; g/dL, grams per deciliter; Hb, hemoglobin.

Efficacy Outcomes

The following hematological parameters improved significantly in the study population at 4 weeks (P < 0.001 for all): Hb increased by 2.76 g/dL; serum ferritin increased by 35.85 µg/L; similarly, there was a significant increase in red blood cell (RBC) count, hematocrit, mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH). There was a non-significant improvement in the mean corpuscular hemoglobin concentration (MCHC) at 4 weeks as compared to baseline (P = 0.103) (Table 4).

A significant improvement in Hb and ferritin was seen across the six cohorts (Table 3).

Response to FCM was also analyzed according to severity of anemia (Table 5). In subjects with severe IDA (n = 350), Hb increased significantly by 3.31g/dL and serum ferritin increased significantly by 35.84 µg/L at 4 weeks as compared to baseline (P < 0.001 for both); similarly, there was a significant increase in RBC count, hematocrit, and MCH (P < 0.001 for all). MCHC and MCV improved at 4 weeks as compared to baseline, but the difference was not statistically significant (MCHC: P = 0.305 and MCV: P = 0.534).

In subjects with moderate IDA (n = 1300), Hb increased significantly by 2.63 g/dL and serum ferritin increased significantly by 35.92 µg/L at 4 weeks as compared to baseline (P < 0.001 for both) (Table 5); similarly, there was a significant increase in RBC count, hematocrit, MCV, and MCH (P < 0.001 for all). MCHC improved at 4 weeks as compared to baseline, but the difference was not statistically significant (P = 0.17).

In subjects with mild IDA (n = 28), mean Hb values at 4 weeks were significantly higher by 1.89 g/dL as compared to baseline (P < 0.001). The following hematological parameters improved at 4 weeks as compared to baseline, but the mean difference was not statistically significant (Table 5): serum ferritin (P = 0.318), RBC count (P = 0.515), hematocrit (P = 0.229), MCV (P = 0.5), MCH (P = 0.188), and MCHC (P = 0.988).

Safety

Adverse effects (AEs) were seen in 7.6% of the subjects (137/1800). The commonly reported AEs were as follows: nausea (3.9%), headache (3.4%), constipation (0.6%), allergic reaction (0.3%), and diarrhea (0.2%). No serious adverse events (SAEs) were reported in any of the subjects.

Physician's Efficacy and Safety Assessment Based on Data Available in Medical Records

Very good (61%) to good (36.5%) efficacy of FCM was noted in 97.5% subjects. Average efficacy was noted only in 2.5% subjects and no poor response was noted in any of subjects (Figure 1). Very good (62.2%) to good (35%) safety was reported in 97.2% subjects. Average safety was noted only in 2.8% subjects, and no poor safety issues were reported by the physicians in any of subjects (Figure 1).

Table 4 Comparing Hematological Parameters Before and After Administration of Ferric Carboxymaltose in the Whole Population

Parameter	N	At Baseline (Mean ± SD)	At 4 Weeks (Mean ± SD)	Mean Improvement ± SD
Hemoglobin (g/dL)	1678	8.01±0.98	10.77±1.07	2.76±1.04*
Ferritin (µg/L)	312	40.88±44.35	76.73±65.99	35.85±51.67*
RBC (mn/mm^3)	279	4.08±1.21	4.67±1.04	0.59±1.38*
Hematocrit (%)	257	32.27±6.12	35.28±7.88	3±6.85*
MCV (fL)	313	69.84±10.77	77.33±16.41	7.49±19.21*
MCH (pg)	308	24.45±6.23	28.21±6.34	3.76±7.51*
MCHC (g/dL)	302	29.76±3.17	31.01±13.9	1.25±13.31^{NS}

Notes: *P value < 0.001, Statistically significant difference; ^{NS}P value > 0.05, Non-significant difference. 4 weeks is 4 ±1 week.
Abbreviations: %, percentage; µg/L, micrograms per liter; fL, femtoliters; g/dL, grams per deciliter; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; mn/mm3, million per millimeter cube; N, number of participants; pg, pictograms; RBC, red blood cell; SD, standard deviation.

Table 5 Comparing Hematological Parameters Before and After Administration of Ferric Carboxymaltose by the Severity of Anemia

Severity of Anemia	Parameter	N	At Baseline (Mean ± SD)	At 4 Weeks (Mean ± SD)	Mean Improvement ± SD
Severe (N = 350)	**Hemoglobin (g/dL)**	350	6.83±0.68	10.14±1.07	3.31±1.11*
	Ferritin (µg/L)	83	49.16±48.16	85±41.54	35.84±61*
	RBC (mn/mm^3)	75	3.48±0.69	4.48±0.7	1±0.98*
	Hematocrit (%)	69	29.85±7.91	34.01±11.11	4.17±10.08*
	MCV (fL)	83	72.73±12.76	74.38±20.77	1.65±24.07^{NS}
	MCH (pg)	81	24.95±6.18	28.94±7.15	3.99±8.09*
	MCHC (g/dL)	83	29.72±3.73	30.64±9.06	0.92±8.16^{NS}
Moderate (N = 1300)	**Hemoglobin (g/dL)**	1300	8.28±0.75	10.91±0.99	2.63±0.97*
	Ferritin (µg/L)	227	38.15±42.69	74.06±72.9	35.92±48.17*
	RBC (mn/mm^3)	201	4.31±1.29	4.75±1.14	0.44±1.48*
	Hematocrit (%)	185	33.14±5.08	35.74±6.32	2.59±5.2*
	MCV (fL)	228	68.75±9.74	78.35±14.49	9.6±16.74*
	MCH (pg)	224	24.24±6.27	27.9±6.01	3.66±7.34*
	MCHC (g/dL)	216	29.74±2.94	31.14±15.46	1.4±14.91^{NS}
Mild (N = 28)	**Hemoglobin (g/dL)**	28	10.25±0.38	12.14±0.75	1.89±0.88*
	Ferritin (µg/L)	2	8±9.9	37.1±32.39	29.1±22.49^{NS}
	RBC (mn/mm^3)	3	4.04±0.2	4.15±0.14	0.11±0.25^{NS}
	Hematocrit (%)	3	34.5±4.01	35.83±3.2	1.33±1.35^{NS}
	MCV (fL)	2	73.7±17.39	83.3±3.82	9.6±13.58^{NS}
	MCH (pg)	3	26.77±5.95	31.6±7.3	4.83±4.25^{NS}
	MCHC (g/dL)	3	32.07±1.97	32.1±1.82	0.03±3.45^{NS}

Notes: *P value < 0.001, Statistically significant difference; ^{NS}P value > 0.05, non-significant difference. 4 weeks is 4 ±1 week.

Abbreviations: %, percentage; µg/L, micrograms per liter; fL, femtoliters; g/dL, grams per deciliter; Hb, hemoglobin; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; mn/mm3, million per millimeter cube; N, number of participants; pg, pictograms; RBC, red blood cell; SD, standard deviation.

Discussion

An expert opinion on the use of FCM in IDA found substantial evidence of the efficacy and safety of FCM in treating IDA resulting from several acute and chronic conditions.[8]

A systematic review and network meta-analysis of 21 randomized controlled trials showed that serum ferritin levels (µg/L) improved significantly with FCM as compared to oral iron (Δ 172.8; 95% confidence interval [CI] 66.7–234.4), while Hb levels (g/dL) improved significantly with FCM as compared to intravenous ferric gluconate (Δ 0.6; 95% CI 0.2–0.9), oral iron and placebo (Δ 0.8; 95% CI 0.6–0.9 and Δ 2.1; 95% CI 1.2–3.0, respectively).[5] FCM use is also associated with fewer side effects than other parenteral therapies.[20]

Real-world studies on FCM are largely lacking, especially from India. Real-world studies from Turkey[21] (N = 103 patients with IDA; ≥18 years) and Portugal[22] (N = 459 iron deficient; 81.3% had IDA) reported a statistically significant increase in Hb, ferritin, hematocrit and transferrin saturation in patients treated with FCM (P < 0.05 for all [Turkey] and

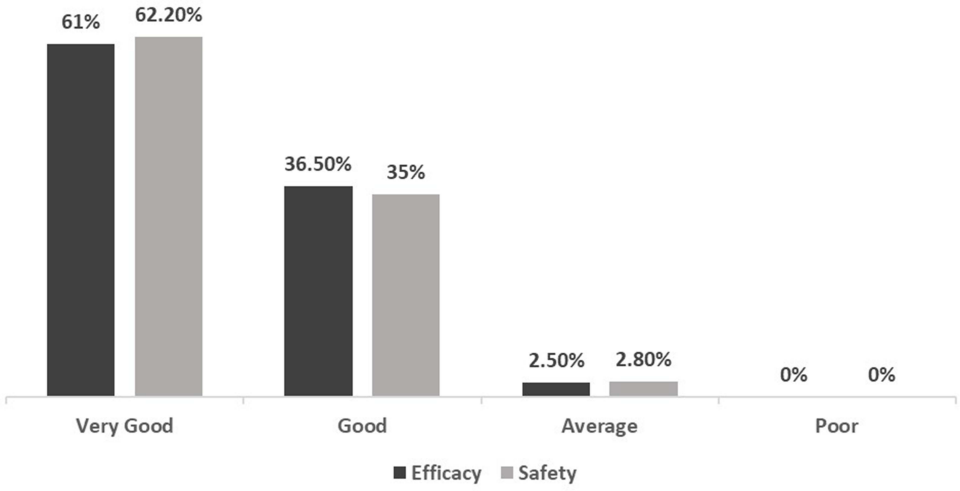

Figure 1 Physicians' assessment on efficacy and safety of ferric carboxymaltose.
Notes: Very good to good efficacy: 61 + 36.5 = 97.5%; very good to good safety: 62.2 + 35 = 97.2%.

$P < 0.001$ for all [Portugal]).[21,22] We also reported statistically significant improvement in Hb, ferritin, hematocrit, total RBC count, MCV, and MCH between baseline and 4 weeks ($P < 0.001$ for all).

It has been seen that hematological parameters in patients with moderate-to-severe IDA improve from 6 to 12 weeks after IV iron supplementation and take longer to normalize after oral iron supplementation.[9,21–25] Hb may, however, improve significantly within two to four weeks of IV FCM supplementation: an increase of ≥3 g/dL at 2 weeks[26,27] to an increase of ≥3 g/dL to 5.49 g/dL at 4 weeks.[20,28] Real-world studies have reported a significant increase in Hb levels post FCM administration; 2.6 g/dL at 4 weeks;[21] Hb increase of ≥2 g/dL and ≥3 g/dL were attained by 41% and 20% of subjects, respectively, at 6 weeks;[22] normalized Hb ≤1 year.[29] In our study, Hb improved significantly at week 4 across the study population, and irrespective of the IDA severity (increase of 1.89 g/dL in mild, 2.63 g/dL in moderate, and 3.31 g/dL in severe anemia) ($P < 0.001$ for all).

Of all the third generation intravenous iron preparations, intravenous FCM results in the highest increase in serum ferritin levels.[5,30] Significant serum ferritin increase of 30.62 µg/L has been reported after four weeks of FCM administration (from 8.32 ± 1.787 to 38.94 ± 6.095 µg/L).[20] In our study too, we reported a significant increase in ferritin at 4 weeks by 35.85 µg/L for the whole study population, by 35.84 µg/L in severe anemia, and by 35.92 µg/L in moderate anemia.

A positive response to iron therapy translating into improved hematological parameters is a true indication of IDA.[23] Hb and ferritin are the most commonly used hematological measures to assess the effect of iron supplementation. However, Hb concentration can fluctuate with posture and hydration status, while ferritin levels can change in presence of inflammatory conditions, and both the parameters can be influenced by acute exercise.[23] Therefore, assessing a battery of hematological parameters can provide a more valuable assessment of the response to therapy.

Although comprehensive laboratory tests for anemia play a crucial role in diagnosing and monitoring anemia,[31] it is practically seen that patients often do not get the advised laboratory tests done.[32] Comprehensive testing is costlier than doing only Hb.[33] This is especially true for resource-limited countries like India, where most patients bear the treatment cost out of their pockets.

Since IDA is the most common cause of anemia, and since cost is a constraint in India, many physicians in India start anemia treatment with iron supplements based on Hb values only.[34,35] This was reflected in our study as well and Hb values were available for majority of subjects (1678/1800) in our study. Since India is a resource limited country, other laboratory tests like serum ferritin, RBC count, MCV, MCH, MCHC, and hematocrit were available for few subjects in our study (Table 4).

In such a scenario, we realized, after data collection, that laboratory tests for IDA such as iron levels, iron-binding capacity and transferrin saturation were not performed in any of the centers. This could be because these investigations

are costlier than serum ferritin. It is important to note that despite its above mentioned limitations, serum ferritin is an extremely useful and commonly used test for the diagnosis and monitoring of IDA.[36–40]

In patients with hemodynamically stable IDA, FCM allows rapid administration of high iron doses with low immunogenicity.[41] Additionally, the improved Hb and ferritin levels are sustained for six months after a single IV infusion.[12] Our study too showed that FCM significantly improved Hb, serum ferritin, RBC count, hematocrit and MCH in subjects with severe IDA ($P < 0.001$ for all).

FCM can also be administered safely in emergency department in patients with hemodynamically stable IDA, with fewer follow-up visits and better improvement in Hb levels and iron stores than those not administered FCM.[41] A retrospective real-world study of 2966 adults with IDA showed that patients treated with FCM were significantly more likely to receive their full iron store repletion dose within three weeks than patients treated with ferumoxytol ($P < 0.001$) or with other parenteral iron preparations, such as iron dextran, iron sucrose, and sodium ferric gluconate in sucrose ($P < 0.001$ for all).[29] Patients on FCM were significantly more likely to have achieved the desired Hb levels within a year of index injection than those on ferumoxytol ($P < 0.001$). Patients on FCM required significantly fewer outpatient visits within that year than patients on ferumoxytol or with other parenteral iron preparations ($P \leq 0.001$ for all comparisons).[29]

FCM has a good safety profile as well, with mild-to-moderate headache, nausea, dizziness, abdominal pain, diarrhea, constipation, rash and infusion-site reactions as the most commonly reported side effects.[9,21] We too found nausea (3.9%), headache (3.4%), constipation (0.6%), allergic reaction (0.3%) and diarrhea (0.2%) as common side effects. No SAE were reported.

The study is limited by the biases associated with the retrospective study designs such as missing data, and inability to control drug dosage and frequency. Also, lack of data on transferrin saturation and serum ferritin in majority of patients is a limitation of the present study. This might be due to limited resources in the country and out-of-pocket expenses required for these particular tests. However, to the best of our knowledge, this is the largest real-world study (N = 1800), from India and globally, demonstrating the efficacy and safety of FCM in real-life scenarios of IDA, irrespective of age, sex, diagnosis and pregnancy status (for females). The study also showed that 98.3% of the subjects had moderate (77.5%) to severe (20.8%) anemia, which responded to FCM within 4 weeks. Health-related quality of life improvement has been reported after FCM administration, but literature on healthcare worker's assessment of efficacy and safety of FCM is lacking. Our study shows that the physicians assessed FCM to have very good to good efficacy and safety in 97.5% and 97.2% of the subjects, respectively.

Conclusions

IDA is very common in India. This large real-world study adds to the growing body of evidence that FCM efficiently, safely and quickly corrects moderate-to-severe anemia in Indian patients in a short span of 4 weeks, and may be useful in treating mild anemia if indicated and if patient can afford the cost. Physicians' positive clinical opinion in favor of efficacy and safety supports usage of FCM in daily clinical practice.

Drug Trial Registration

Clinical Trial Registry of India (CTRI) with a wide registration number CTRI/2021/12/039065 and available at http://ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=63378&EncHid=&userName=CTRI/2021/12/039065.

Data Transparency

All data and materials as well as software application or custom code used in the current study support the data presented and claims made in the current study and comply with the field standards of scientific writing, credibility, authenticity and personal honesty.

Data Sharing Statement

Analyzed data are available as tables and figures. Individual de-identified participant data cannot be made available. This data will be available on request if really required after contacting the corresponding author.

Ethics Approval and Informed Consent

This study was approved by the Ripon Independent Ethics Committee. This study complies with the Declaration of Helsinki. Written informed consent was obtained from all individual participants included in the study. For subjects <18 years of age, informed consent was taken from their parent or legal guardian.

Consent for Publication

No specific data or photograph of any kind of a study participant is used in this study.

Acknowledgment

The authors thank Ms. Rutuja Tope and Dr. Girish Deshmukh for data management; Dr. Srikant N for statistical analysis; Mr. Kedar Kude, Ms. Leena Darne, and Mr. Abhijeet Singh for administrative support; and Dr. Punit Srivastava and Dr. Kokil Mathur of Mediception Science Pvt. Ltd. for providing medical writing support in the preparation of this manuscript.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

Emcure Pharmaceuticals Ltd. Pune, India supported in data collection, data analysis and manuscript writing.

Disclosure

Dr. Ajinkya Rodge and Dr. Onkar C Swami are full-time employees of Emcure Pharmaceuticals Ltd., which actively markets Ferric Carboxymaltose. The authors report no other conflicts of interest in this work.

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