ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 16, Issue 7, 2023

Online - 2455-3891
Print - 0974-2441

Research Article

TO COMPARE INTRAVENOUS FERRIC CARBOXYMALTOSE VERSUS INTRAVENOUS IRON SUCROSE IN POST-PARTUM WOMEN WITH IRON-DEFICIENCY ANEMIA

VISHAKHA KARWASARA[1]*, PARUL PRAKASH[1], SANDEEP DATIKA[2], PRIYA GOYAL[1]

[1]Department of Gynecology, Sardar Patel Medical College, Bikaner, Rajasthan, India. [2]Department of Radio-Diagnosis, RML PGIMER, New Delhi, India. Email: vishakhakarwasara312@gmail.com

Received: 04 May 2023, Revised and Accepted: 16 June 2023

ABSTRACT

Objectives: The objective of this study was to compare intravenous ferric carboxymaltose (FCM) versus intravenous iron sucrose in post-partum women with iron-deficiency anemia (IDA).

Methods: This was a hospital-based prospective randomized controlled study, comprising 100 post-natal women with IDA with hemoglobin level <11 g/dL admitted in post-natal ward of the Obstetrics and Gynecology Department in SP Medical College, Bikaner, from June 2021 to May 2022.

Results: In age, residence, socioeconomic status, the incidence of IDA in both the groups were comparable and is more among rural areas, low socioeconomic status. Improvement in hemoglobin, serum ferritin, and blood indices in both the iron sucrose and FCM groups, but it was faster and greater with ferric carboxymaltose when compared with iron sucrose. Other advantages are large dose administration at 1 time, therefore, lesser total number of doses required in the FCM group as compared to the IS group.

Conclusion: FCM is well tolerated, safer, and effective than iron sucrose in treatment of post-natal IDA.

Keywords: Iron-deficiency anemia, Ferric carboxymaltose, Iron sucrose.

 DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i7.48520. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Iron-deficiency anemia (IDA) is the most common and major hematological, nutritional deficiency but manageable health problem encountered among pregnant women globally but more common in developing countries, especially in tropics like India, especially in underprivileged population. According to the World Health Organization, about 591,000 perinatal deaths and 115,000 maternal deaths globally are due to IDA directly or indirectly [1]. India alone contributes to about 80% of the maternal deaths due to anemia in South Asia. The prevalence of anemia in pregnant women in India is 50% in the National Family Health Survey-4 [2]. The Indian Council of Medical Research has categorized anemia during pregnancy as - mild anemia - Hb - 10–10.9 g%, moderate anemia - Hb - 7–9.9 g%, severe anemia - Hb - 4–6.9 g%, and very severe anemia - Hb - <4 g% [1]. Iron deficiency in post-partum women reflects IDA that existed in women during their pregnancy. Building up iron stores and correcting IDA in post-partum period will improve health of mother and will also decrease the complication in subsequent pregnancy. Iron supplementation in post-partum period will improve the prognosis in the subsequent pregnancies and decrease the incidence of anemia pre-term deliveries, morbidity, and mortality [3].

A single IV iron infusion is an effective and safe option for treatment of post-partum IDA. Iron sucrose and ferric carboxymaltose (FCM) are dextran-free iron preparation for parenteral therapy. Iron sucrose in November 2000 got FDA-approved forming iron hydroxide-sucrose complex in water with 34,000–60,000 Dalton molecular weight [4]. It is administered as infusion in 200 mL normal saline over 15–20 min and maximum daily dosage of 200 mg, not more than thrice a week [5].

Recently, a new parenteral iron preparation, FCM, was developed to facilitate the effective treatment of IDA. FCM is novel non-dextran which is administered in dose of 15 mg/kg as intravenous infusion [6]. Maximum dose per sitting should not exceed 1000 mg. While IV iron in pregnancy improves hematological parameters, there is an absence of evidence for improvements in important maternal or perinatal outcomes. The current IV iron preparation of choice is largely determined by cost and convenience of administration. This study was designed to test the efficacy of FCM versus iron in treating post-partum anemia.

Aim

The aim of this study was to compare the efficacy, compliance, and safety of the administered intravenous FCM versus intravenous iron sucrose in post-partum women with IDA.

METHODS

This was a hospital-based prospective randomized controlled study, comprises of 100 post-natal women with IDA with hemoglobin level <11 g/dL were enrolled after full filing selection criteria and giving valid consent admitted to post-natal ward of obstetrics and gynecology department in SP Medical College, Bikaner, from June 2021 to May 2022. Iron deficit is calculated using "Ganzoni formula" with the aim of target hemoglobin 11 g. Patients were explained about the risk and benefits of both drugs and consent was taken for infusion therapy. After randomization, 50 post-natal women received iron sucrose and 50 women received FCM. For iron sucrose, only 200 mg was administered at 1 time, whereas in the FCM group, 1000 mg can be administered as a single dose. The outcomes are compared and analyzed using unpaired t-test and by Chi-square test. The investigations used are hemoglobin, serum ferritin, and blood indices before and after treatment.

Women with intolerance to oral iron therapy and likely to come for follow-up were enrolled in the study. Women with a history of parenteral iron intolerance, thalassemia or sickle cell disease, non-iron-deficiency anemia, chronic bleeding or renal failure, presence of chronic infections such as hepatitis and HIV, and a history of blood transfusion within 48–72 h were excluded.

Ganzoni formula

Total iron deficit (mg) = Body weight (kg) × (target Hb-actual Hb) × 2.4 + depot iron (mg)

Depot iron = 500 mg if body weight >35 kg,
15 mg/kg if body weight <35 kg
Target Hb level was taken as 11 g/dL.

The patient was randomly divided into two groups; in the iron sucrose group (Group A), the dose of iron sucrose was 200 mg intravenously in 200 mL 0.9% normal saline over a period of 30 min on alternate days until the total dose was administered, not to exceed 600 mg/week. In the FCM group (Group B), intravenous infusion was given in 200 mL 0.9% normal saline immediately after dilution over 15 min. Maximum dose of FCM per sitting was 1000 mg or 15 mg/kg. Subsequent doses if needed were planned at 1-week intervals (on the 7th and 14th days).

Dilution should not be lower than 2 mg/mL to ensure stability. The general condition of patients, blood pressure, and pulse rate were noted before and after infusion. Any minor and major adverse effects such as rash, vomiting, headache, or any other anaphylactic reaction was noted.

Patients were followed up at 3 and 6 weeks of parenteral therapy, with CBC and serum ferritin levels. Pre-treatment and 3rd-week and 6-week post-partum investigations were done for both the groups, and the results were compared on the basis of hemoglobin, mean corpuscular volume (MCV), and serum ferritin.

The investigation was started after receiving ethical approval from the institute. Written informed consent was obtained from all the study subjects.

Statistical analysis

Data were recorded as per pro forma. The data analysis was computer based; SPSS-22 was used for analysis. Serum ferritin values were obtained from Unicel DXL 800 access immunoassay system. For category variables, Chi-square test was used. For continuous variables, independent sample's unpaired t-test was used. $p<0.05$ was considered significant.

RESULTS

Maximum number of patients 23 (46%) and 31 (62%) were in the age group of 21–25 years in Group A and Group B, respectively. Thirty-one (62%) in Group A and 33 (66%) in Group B belonged to rural area and in lower socioeconomic status.

Maximum women 21 (42%) belonged to P2 (Para 2) in Group A whereas maximum 22 (44%) belonged to p1in Group B ($p<0.05$) (Table 1). Thirty-nine (78%) were lower segment cesarean section (LSCS) operated in Group A (FCM) whereas 35 (70%) were LSCS operated in Group B (IS).

According to mode of delivery, 11 (22%) patients were normal vaginally delivered and 39 (78%) were LSCS operated in Group A (FCM). Fifteen (30%) patients were normal vaginally delivered and 35 (70%) were LSCS operated in Group B (IS) ($p>0.05$).

Improvement of Hb in the FCM group was from pre-treatment mean Hb 8.66 g/dL to 10.25 g/dL at 3 weeks and 11.56 g/dL at 6 weeks while improvement of Hb in the IS group from pre-treatment mean Hb 8.58 g/dL to 9.36 g/dL at 3 weeks and 10.60 g/dL at 6 weeks (Fig. 1). Improvement of MCV in the FCM group was from pre-treatment mean MCV 77.18 fl to 82.16 fl at 3 weeks and 88.24 fl at 6 weeks while improvement of MCV in the IS group was from pre-treatment mean MCV

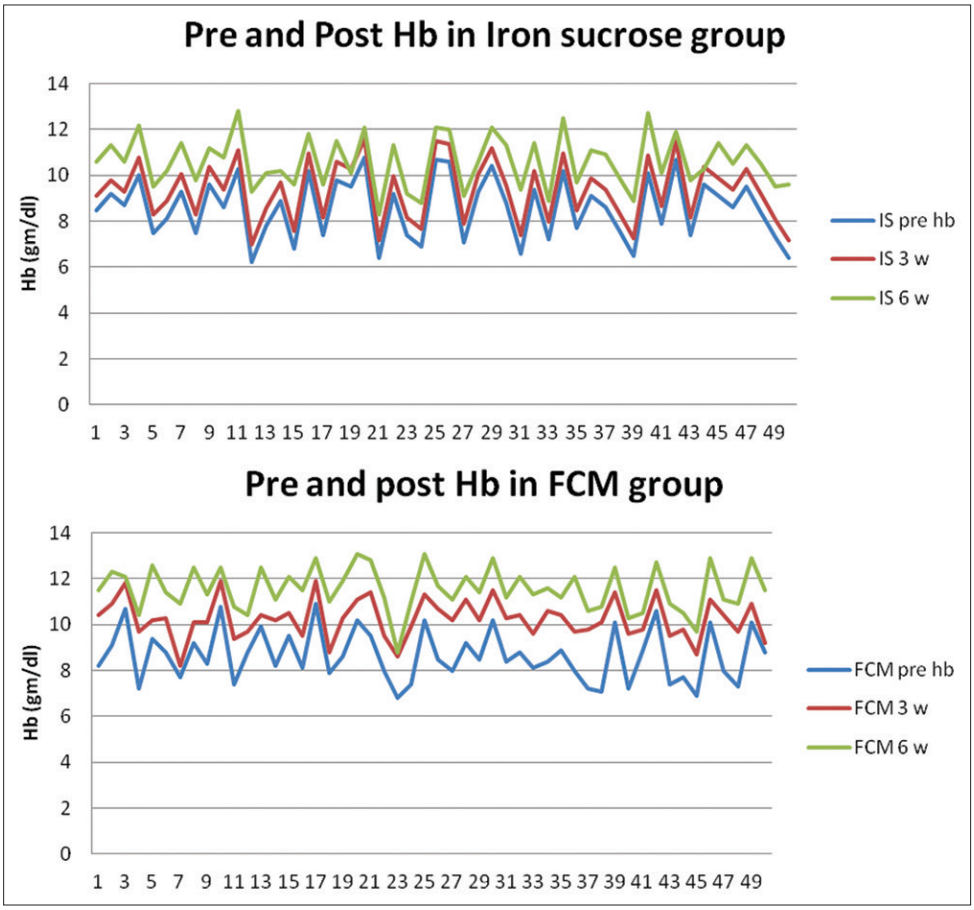

Fig. 1: According to pre and after Hb level

Table 1: Age distribution of patients

Age distribution (years)	Group A (FCM)	Group B (IS)	p-value
≤20	2	2	0.456
21–25	23	31	
26–30	22	11	
>30	3	5	
Mean	25.72±2.93	25.22±3.70	
Residence			
Rural	31	33	0.835
Urban	19	17	
Socioeconomic status			
Class I (upper class)	0	0	0.988
Class II (upper middle)	1	0	
Class III (lower middle)	4	5	
Class IV (upper lower)	12	14	
Class V (lower)	33	31	
Parity			
P1	11	22	0.002*
P2	21	18	
P3	17	4	
P4	1	6	

FCM: Ferric carboxymaltose

Table 2: Evaluation of efficacy of FCM and IS

Increased Hb Level (mean)	Group A (FCM) mean	Group B (IS) mean	p-value
At 3 week	1.59	0.78	0.001
At 6 week	2.9	2.02	0.006
Increased MCV			
At 3 week	4.98	2.24	0.0001
At 6 week	11.6	7	0.0001
Serum ferritin			
At 3 week	179.84	109.52	0.0001
At 6 week	143.06	87.71	0.0001

FCM: Ferric carboxymaltose

Table 3: Distribution of patients according to adverse reactions

Adverse reactions	Group A (FCM)	Group B (IS)
Nausea vomiting	1	2
Pain at injection site	0	1
Tingling sensation	0	0
Itching	0	0
Headache	0	0
Fever	0	1
Severe anaphylactic reaction	0	0

FCM: Ferric carboxymaltose

76.04 fl to 78.28 fl at 3 weeks and 83.04 fl at 6 weeks. Serum ferritin in the FCM group from pre-treatment mean serum ferritin 37.73 ng/dl to 217.57 ng/dL at 3 weeks and 180.79 ng/dL at 6 weeks while changes in Serum ferritin in the IS group from pre-treatment mean serum ferritin 42.47 ng/dL to 151.99 ng/dL at 3 weeks and 130.18 ng/dL at 6 weeks. The difference between the two groups was comparable at baseline and on follow-up improvement in Hb level, MCV and ferritin was faster and greater in the FCM group as compared to the IS group and was found to be statistically significant at 3 and 6 weeks (Table 2).

In the iron sucrose group, total 4 patients complained of minor reactions: 2 patients (nausea vomiting), 1 patient (pain at injection site), and 1 patient (fever) (Table 3). Apart from few minor reactions, no major adverse reactions were seen in both the groups.

DISCUSSION

In our study, the mean age was 25.72 years in the FCM group and 25.255 years in the IS group and maximum number of patients 31 (62%) belonged to rural area. Other studies like Wajid *et al.* [7] also show a mean age group comparable to our study that was 26.16 years in the IS group and 26.86 years in the FCM group.

In our study, the distribution of patients according to parity was as follows: 11 (22%) belonged to p1, 21 (42%) belonged to p2, 17 (34%) belonged to p3, and 1 (2%) belonged to p4 in Group A (FCM). Twenty-two (44%) patients belonged to p1, 18 (36%) belonged to p2, 4 (8%) belonged to p3, and 6 (12%) belonged to p4 in Group B (IS) which were in contrast to the study findings reported by Wajid *et al.* [7], in which out of 80 patients, 61 (76.2%) were para <3 in the IS group and 55 (68.8%) in the FCM group. 3 or more para in 19 (23.8%) in the IS group and 44 (27.5%) in the FCM group.

In our study improvement of Hb in the FCM group from pre-treatment mean Hb 8.66 g/dL to 10.25 g/dL at 3 weeks and 11.56 g/dL at 6 weeks while improvement of Hb in the iron sucrose group from pre-treatment mean Hb 8.58 g/dL to 9.36 g/dL at 3 weeks and 10.60 g/dL at 6 weeks. It shows that in the FCM group, the average increase is about 1.59 g/dL at 3 weeks and 2.9 g/dL at 6 weeks, while in the iron sucrose group, the average increase is about 0.78 g/dL at 3 weeks and 2.02 g/dL at 6 weeks.

Similar findings were evident in an earlier study in India conducted by Kumari *et al.* [8], in which patients when received iron sucrose hemoglobin increased from 8.27 g% to 9.17 g% and 10.48 g% post-therapy at 2 weeks and 4 weeks, respectively, while in the FCM group, Hb increased from 8.3 g% to 10.177 g and 11.83 g% at 2 weeks and 4 weeks, respectively, post-infusion therapy. It shows that in the FCM group, the average increase is about 1.87 g/dL at 2 weeks and 3.53 g/dL at 4 weeks, while in the iron sucrose group, the average increase is about 1.44 g/dL at 2 weeks and 3.53 g/dL at 6 weeks. Results were further supported by a study conducted by Rathod *et al.* [9], in which Hb improved from baseline 7.71 g/dL to 10.87 g/dL at 2 weeks and 12.11 g/dL at 6 weeks after FCM infusion; similarly, Hb improved from baseline 8.05 g/dL to 10.41 g/dL at 2 weeks and 11.40 g/dL at 6 weeks after iron sucrose therapy. Similarly higher efficacy of FCM was reported in studies done by Smita *et al.* [8], Lunagariya *et al.* [10], and Sharma *et al.* [11]. Our study results were also comparable with a study of Modi *et al.* [12] who found that the average baseline Hb was 7.82±0.84 g/dL which was significantly increased up to 12.4±1.33 g/dL at 6 weeks ($p<0.05$). In a study of Sumathy and Arulmozhi [13] among the iron sucrose group, an increase in level of Hb was observed by 1.65 g/dL and 2.35 g/dL after 2 and 4 weeks of treatment. Similarly, in case of the FCM group, they observed an increase in 2.04 g/dL and 2.83 g/dL at 2 and 4 weeks of treatment.

In our study, serum ferritin which indicates iron status of body increased more significantly in the FCM group from pre-treatment mean serum ferritin 37.73 ng/dL to 217.57 ng/dL at 3 weeks and 180.79 ng/dL at 6 weeks while changes in serum ferritin in the iron sucrose group from pre-treatment mean serum ferritin 42.47 ng/dL to 151.99 ng/dL at 3 weeks and 130.18 ng/dL at 6 weeks. In the FCM group, the average increase is about 179.84 ng/dL at 3 weeks and 143.06 ng/dL at 6 weeks, while in the iron sucrose group, the average increase is about 109.52 ng/dL at 3 weeks and 87.71 ng/dL at 6 weeks.

In a similar study, Smita *et al.* [8] reported that serum ferritin increased from 77.91 ng/dL to 182.86 ng/dL in the iron sucrose group and from 78.05 ng/dL to 195.39 ng/dL in FCM patients after 4 weeks.

The current study is in concurrence with other reported literature - Setu *et al.* [9], Sharma *et al.* [11], and Modi *et al.* [12].

We analyzed in our study that improvement of MCV in the FCM group was from pre-treatment mean MCV 77.18 fl to 82.16 fl at 3 weeks and 88.24 fl g at 6 weeks. Improvement of MCV in the IS group from pre-treatment mean MCV 76.04 fl to 78.28 fl g at 3 weeks and 83.04 fl at 6 weeks. In the FCM group, the average increase is about 4.98 fl at

3 weeks and 11.6 fl at 6 weeks. In the iron sucrose group, the average increase is about 2.24 fl at 3 weeks and 7 fl at 6 weeks. Similar result were found in Smita *et al.* [8] who reported an increase in MCV from 71.55 fl to 74.05 fl in iron sucrose and from 71.62 fl to 77.57 fl in the FCM group after 4 weeks. Wajid *et al.* [7] also reported more improvement of MCV in the FCM group as compared to the iron sucrose group as MCV level increase from 66.82 fl to 80.38 fl in iron sucrose and 64.08 fl to 81.33fl in the FCM group at 3 weeks. Furthermore, our study results were also similar to that of other studies like Lunagariya *et al.* [10] and Sumathy and Arulmozhi [13].

We also compared the safety of both intravenous drugs and found that the FCM group reported with less side effect, as in our study, only one patient in the FCM group complained of nausea vomiting, while in the iron sucrose group, total 4 patients complained of minor reactions: 2 - nausea and vomiting, 1 patient - pain at injection site, and 1 patient - fever. Apart from few minor reactions, no major adverse reactions were seen in both the groups.

Likewise in case of a study of Lunagariya *et al.* [10], 16 patients in the iron sucrose group showed minor adverse reaction: 6 - pain at injection site, 3 - itching and rash, 3 - headache, 2 - abdominal pain, and 2 - nausea and vomiting. While, in the FCM group, 12 patients showed adverse effect: 5 - pain at injection site, 2 - itching and rash, 3 - headache, 2 - abdominal pain, and 2 - nausea and vomiting, and it was 32% and 24% with both the IS and FCM groups, respectively.

CONCLUSION

This study compared the efficacy of FCM versus iron sucrose in the management of post-natal iron-deficiency anemia. Although our results showed improvement in hemoglobin, serum ferritin, and blood indices in both the iron sucrose and FCM groups, it was faster and greater with ferric carboxymaltose when compared with iron sucrose. Other advantages are large dose administration at 1 time therefore lesser total number of doses required in the FCM group as compared to the IS group. This not only saves hospital resources but also improves patient satisfaction. Adverse reactions were also low in the FCM group as compared to iron sucrose; therefore, FCM is well tolerated, safer, and effective than iron sucrose in treatment of post-natal IDA.

ACKNOWLEDGMENT

We owe a debt of gratitude to the Sardar Patel Medical College, Bikaner, for assistance during the course of the research.

AUTHORS' CONTRIBUTION

All the authors have contributed equally.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR'S FUNDING

The authors hereby state that they did not get any financial assistance for their research, writing, or publication of this paper.

REFERENCES

1. FOGSI General Clinical Practice Recommendations. Management of Iron Deficiency Anaemia in Pregnancy; 2016. Available from: https://www.fogsi.org/wpcontent/uploads/2016/05/the-evidence-based_IDA pregnancy. [Last accessed on 2018 Dec 28].
2. Misra R. Ian Donald's Practical Obstetrics Problems. 9th ed. Netherlands: Wolters Kluwer India Pvt Ltd. Available from: https://books.google.co.in/books?id=hEbrDwAAQBAJ.2020
3. Milman N. Postpartum anemia I: Definition, prevalence, causes, and consequences. Ann Hematol 2011;90:1247-53. doi: 10.1007/s00277-011-1279-z, PMID 21710167
4. Singh S, Dhama V, Chaudhary R, Singh P. Comparing the safety and efficacy of intravenous iron sucrose and intravenous ferric carboxymaltose in treating postpartum anemia. Int J Reprod Contracept Obstet Gynecol 2016;5:1451-6. doi: 10.18203/2320-1770.ijrcog20161303
5. Indian Council of Medical Research. Evaluation of Nutritional Anaemia Prophylaxis Program Task Force Study New Delhi; 1989. Available from: https://www.icmr.nic.in/sites/default/files/icmr_bulletins/bufeb00.pdf [Last accessed on 2018 Dec 25].
6. Joshi SD, Chikkagowdra S, Cm VC. Comparative study of efficacy and safety of intravenous ferric carboxy maltose versus iron sucrose in treatment of postpartum iron deficiency anemia. Int J Reprod Contracept Obstet Gynecol 2016;5:2566-70. doi: 10.18203/2320-1770.ijrcog20162199
7. Wajid RA, Gondal ME, Tahira T, Maqbool SA, Kausar R, Khalil NA. Comparison of efficacy and safety of ferric carboxymaltose injection with IV iron sucrose complex for correction of postpartum iron deficiency anemia. Pak J Med Health Sci 2021;15:826-9.
8. Kumari S, Singh SH. Iron sucrose or ferric carboxy maltose: Comparative study for treatment of post-partum iron deficiency anemia. Int J Res Prof 2019;5:157-62.
9. Rathod S, Samal SK, Mahapatra PC, Samal S. Ferric carboxymaltose: A revolution in the treatment of postpartum anemia in Indian women. Int J Appl Basic Med Res 2015;5:25-30. doi: 10.4103/2229-516X.149230, PMID 25664264
10. Lunagariya M, Nakum KD, Vithal A, Patel J, Patel M. Option in Cases of Postpartum iron Deficiency Anemia. Available from: https://www.ijcmr.com/uploads/7/7/4/6/77464738/ijcmr_1852_v1.pdf [Last accessed on 2023 Feb 20].
11. Sharma N, Thiek JL, Natung T, Ahanthem SS. Comparative study of efficacy and safety of ferric carboxymaltose versus iron sucrose in post-partum anaemia. J Obstet Gynaecol India 2017;67:253-7. doi: 10.1007/s13224-017-0971-x, PMID 28706363
12. Modi R, Modi A, Bhimani N, Patel P. Efficacy and safety of intravenous ferric carboxymaltose in moderate to severe postpartum iron deficiency anemia. Natl J Physiol Pharm Pharmacol 2022;12:225-8. doi: 10.5455/njppp.2022.12.12456202130122021
13. Sumathy C, Arulmozhi V. Comparative study of intravenous ferric carboxymaltose and iron sucrose in the management of iron deficiency anemia. Paripex Indian J Res 2017;6:91-4.