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Original Research Article

POSTPARTUM ANEMIA: COMPARING FERRIC CARBOXYMALTOSE AND IRON SUCROSE IN INDIAN WOMEN

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ABSTRACT

Background: Postpartum iron-deficiency anemia (IDA) is a common condition affecting many women after childbirth. This study aims to compare the efficacy and safety of two commonly used intravenous iron formulations: ferric carboxymaltose (FCM) and iron sucrose (IS) in treating postpartum IDA. **Methods:** A comparative study was conducted at a tertiary care hospital from July 2018 to December 2018. Group A received IS (200 mg per session, administered on five different days over a two-week period) and Group B received FCM (1000 mg in a single session). The primary outcome measure was the increase in hemoglobin levels from baseline to four weeks post-treatment. **Results:** FCM led to a more significant increase in hemoglobin levels (4.6 g/dL) compared to Iron Sucrose (3.9 g) after one month, with a statistically significant difference (P = 0.001). FCM had a greater impact on serum ferritin levels than IS. Overall, the results suggest that both FCM and IS are effective in increasing hemoglobine levels and replenishing iron stores in women with IDA, while minimizing adverse events. **Conclusions:** Both FCM and S were effective in treating IDA while reducing adverse effects.

Keywords: iron-deficiency anemia, ferric carboxymaltose, hemoglobin, serum ferritin, iron sucrose

INTRODUCTION

Pelvic Postpartum iron-deficiency anemia (IDA) is a common condition affecting many women after childbirth. It is primarily characterized by low levels of hemoglobin in the blood, which can lead to symptoms such as fatigue, weakness, and shortness of breath **(1).** Effective management of postpartum IDA is crucial to ensure the well-being of new mothers and facilitate their recovery. Among the various treatment options, intravenous iron supplementation has emerged as a preferred method due to its rapid replenishment of iron stores and improvement in hemoglobin levels **(2).** This study aims to compare the efficacy and safety of two commonly used intravenous iron formulations: ferric carboxymaltose (FCM) and iron sucrose (IS), in treating postpartum IDA.

Ferric carboxymaltose (FCM) is a relatively new intravenous iron formulation that allows for the administration of large doses in a single session, reducing the need for multiple hospital visits **(3).** It has been noted for its ability to quickly replenish iron stores and increase hemoglobin levels with a lower risk of adverse reactions **(4).** Iron sucrose (IS), on the other hand, has been in use for a longer period and is also effective in treating IDA, although it often requires multiple doses spread over several days **(5).** Both formulations are considered safe, but they differ in their dosing regimens, administration time, and side-effect profiles, which can influence patient preference and compliance adherence to treatment **(6).**

The primary goal of this comparative study is to evaluate the efficacy of FCM and IS in increasing

hemoglobin levels and replenishing iron stores in women with postpartum IDA. By analyzing these outcomes, healthcare providers can make more informed decisions regarding the most suitable intravenous iron therapy for their patients. Additionally, this study seeks to assess the safety profiles of FCM and IS, particularly concerning adverse reactions and overall tolerability. Understanding these factors is crucial for optimizing patient care and ensuring that the benefits of treatment outweigh any potential risks **(7).**

Previous research has indicated that both FCM and IS are effective in managing IDA, but direct comparisons between the two are limited **(8).** This study addresses this gap by providing a head-to-head comparison of these intravenous iron therapies. The results could offer valuable insights into which formulation provides a better balance of efficacy and safety, potentially influencing clinical guidelines and standard practices for treating postpartum IDA **(9).**

This study was designed to provide a comprehensive comparison of the efficacy and safety of intravenous FCM and IS in the management of postpartum IDA, to ensuring the reliability and validity of the findings.

MATERIALS AND METHODS

Study Design and Setting: This comparative study was conducted at a tertiary care hospital from July 2018 to December 2018. The study aimed to evaluate the efficacy and safety of intravenous ferric carboxymaltose (FCM) and iron sucrose (IS) in treating postpartum iron-deficiency anemia (IDA). Ethical approval was obtained from the institutional review board, and informed consent was secured from all participants.

Participants

The study included postpartum women diagnosed with iron-deficiency anemia within six weeks after delivery. Inclusion criteria were as follows:1. Hemoglobin level <11 g/dL., 2. Serum ferritin level <30 ng/mL, 3. Age between 18 and 45 years, 4. No history of hypersensitivity to intravenous iron formulations.

Exclusion criteria included:1.Chronic kidney disease,2.Chronic inflammatory diseases, 3. Hemoglobinopathies, 4.Recent blood trans-fusions, 5.Severe anemia requiring immediate transfusion (hemoglobin <7 g/dL).

Randomization and Intervention: Participants were randomly assigned to receive either FCM or IS. Randomization was achieved using a computer-generated sequence to ensure unbiased allocation. Group A received intravenous IS (200 mg per session, administered on five different days over a two-week period), while Group B received intravenous FCM (1000 mg in a single session).

Administration Protocol: Group A, subjects were given I.V. iron sucrose in multiple doses, 200 mg/day on day 0, 2, 4, 6, 8 total of 1000 mg. (iron Sucrose 200 mg diluted in 100ml of 0.9% normal saline and given over 20 to 30 min. after IV test) Group B, subjects were given I.V. ferric carboxymaltose1000 mg single dose (Carboxymaltose 1000 mg diluted in 100ml of 0.9% NS given in 20 to 30 min after IV test). For both groups, intravenous iron was administered under strict aseptic conditions in a monitored hospital setting. Vital signs were observed before, during, and after the infusion to detect any adverse reactions. Participants in the FCM group were monitored for at least 30 minutes post-infusion, while those in the IS group were monitored for 15 minutes after each session.

Outcome Measures: The primary outcome measure was the increase in hemoglobin levels from baseline to four weeks post-treatment. Secondary outcomes included: 1. Serum ferritin levels, 2. Reticulocyte count, 3. Incidence of adverse reactions, 4. overall patient satisfaction and compliance.

Data Collection: Baseline data were collected, including demographic information, obstetric history, and initial hemoglobin and serum ferritin levels. Follow-up assessments were conducted at two and four weeks post-treatment. Hemoglobin and serum ferritin levels were measured using standard laboratory techniques. Adverse reactions were recorded and classified according to severity. Mild reactions included transient nausea, headaches and skin itching and redness at injection site, while severe reactions encompassed anaphylaxis and significant hypotension (BP $\leq$ 90/60).

Statistical Analysis: Data were analyzed using SPSS version 25.0. Descriptive statistics were used to summarize baseline characteristics and outcomes. Continuous variables were expressed as means and standard deviations, while categorical variables were presented as frequencies and percentages. Comparative analyses between the FCM and IS groups were performed using the Student's t-test for continuous variables and the chi-square test for categorical variables. A p-value of <0.05 was considered statistically significant.

Quality Control:To ensure data accuracy, double data entry was performed, and periodic audits were conducted. Additionally, all laboratory tests were conducted in a certified laboratory adhering to standard operating procedures.

RESULTS

The participants were divided into three age groups: below 23 years, between 23 to 30 years, and above 30 years.

Table 1 showing the age distribution of the study subjects in the two treatment groups

Age Group (years)	Iron Sucrose Group	Ferric Carboxymaltose Group	P-value
Below 23	78 (78%)	70 (70%)	
23-30	16 (16%)	23 (23%)	0.59
Above 30	6 (6%)	7 (7%)	
Mean ± SD	24.45 ± 3.25	24.87 ± 2.73	0.47

In the Iron Sucrose group, 78 participants (78%) were below 23 years of age, 16 participants (16%) were between 23 to 30 years, and 6 participants (6%) were above 30 years. The mean age in this group was 24.45 years with a standard deviation (SD) of 3.25.

In the Ferric Carboxymaltose group, 70 participants (70%) were below 23 years of age, 23 participants (23%) were between 23 to 30 years, and 7 participants (7%) were above 30 years. The mean age in this group was 24.87 years with a standard deviation (SD) of 2.73.

Statistical analysis revealed no significant difference in the age distribution between the two groups, with a P-value of 0.47 indicating comparable age profiles. The similarity in age distribution ensures that the efficacy and safety comparisons between the two treatment groups are not influenced by age-related factors.

In the Iron Sucrose group, the mean pre-treatment hemoglobin level was 8.0 g/dL with a standard deviation (SD) of 0.80. After treatment, the mean hemoglobin level increased to 11.9 g/dL with an SD of 1.20. This resulted in a mean hemoglobin difference of 3.9 g/dL with an SD of 1.30.(Table 2)

Table 2 presents the comparison of hemoglobin (Hb) levels before and after treatment in the Iron Sucrose and Ferric Carboxymaltose groups.

Hb Levels	Iron Sucrose Group (Mean ± SD)	Ferric Carboxymaltose Group (Mean ± SD)	P-value
Pre-treatment	8.0 ± 0.80	8.2 ± 0.65	0.42
Post-treatment	11.9 ± 1.20	12.8 ± 1.10	<0.001
Hb Difference	3.9 ± 1.30	4.6 ± 0.90	<0.001

In the Ferric Carboxymaltose group, the mean pre-treatment hemoglobin level was 8.2 g/dL with an SD of 0.65. Post-treatment, the mean hemoglobin level rose to 12.8 g/dL with an SD of 1.10. The mean hemoglobin difference in this group was 4.6 g/dL with an SD of 0.90.

The pre-treatment hemoglobin levels between the two groups were not significantly different, with a P-value of 0.42. However, the post-treatment hemoglobin levels showed a significant improvement in both groups, with the Ferric Carboxymaltose group exhibiting a more substantial increase. The P-value for the post-treatment comparison was <0.001, indicating a statistically significant difference in favor of the Ferric Carboxymaltose group.

Overall, the results demonstrate that both Iron Sucrose and Ferric Carboxymaltose effectively increased hemoglobin levels in women with postpartum iron-deficiency anemia. However, Ferric Carboxymaltose was associated with a greater increase in hemoglobin levels, suggesting superior efficacy compared to Iron Sucrose.

In the Iron Sucrose group, the mean pre-treatment serum ferritin level was 16.5 ng/mL with a standard deviation (SD) of 7.40. Post-treatment, the mean serum ferritin level increased to 85.5 ng/mL with an SD of 28.30. This represented a mean ferritin difference of 69.0 ng/mL with an SD of 25.80.(Table 3)

Table 3 provides a comparison of serum ferritin levels before and after treatment in the Iron Sucrose and Ferric Carboxymaltose groups.

Serum Ferritin Levels	Iron Sucrose Group (Mean ± SD)	Ferric Carboxymaltose Group (Mean ± SD)	P-value
Pre-treatment	16.5 ± 7.40	15.6 ± 6.10	0.68
Post-treatment	85.5 ± 28.30	108.4 ± 42.50	<0.001
Ferritin Difference	69.0 ± 25.80	92.8 ± 41.70	<0.001

In the Ferric Carboxymaltose group, the mean pre-treatment serum ferritin level was 15.6 ng/mL with an SD of 6.10. After treatment, the mean serum ferritin level rose to 108.4 ng/mL with an SD of 42.50. The mean ferritin difference in this group was 92.8 ng/mL with an SD of 41.70.

The pre-treatment serum ferritin levels were not significantly different between the two groups, with a P-value of 0.68. However, post-treatment serum ferritin levels showed a significant increase in both groups, with the Ferric Carboxymaltose group demonstrating a more substantial rise. The P-value for the post-treatment comparison was <0.001, indicating a statistically significant difference favoring the Ferric Carboxymaltose group.

Overall, these results suggest that both Iron Sucrose and Ferric Carboxymaltose are effective in increasing serum ferritin levels in women with postpartum iron-deficiency anemia. However, Ferric Carboxymaltose appears to have a greater impact on serum ferritin levels, indicating a higher efficacy in replenishing iron stores compared to Iron Sucrose.

In the Iron Sucrose group, 8 participants (8%) experienced adverse effects, while 92 participants (92%) did not report any adverse reactions. In the Ferric Carboxymaltose group, 4 participants (4%) reported adverse effects, whereas 96 participants (96%) had no adverse reactions. All adverse effect reported in the both the groups were mild and those was not severe reactions.(Table 4)

Table 4 shows the distribution of study subjects based on the occurrence of adverse effects in the Iron Sucrose and Ferric Carboxymaltose groups.

Adverse Effects	Iron Sucrose Group	Ferric Carboxymaltose Group	P-value
Yes	8 (8%)	4 (4%)	0.20
No	92 (92%)	96 (96%)	

Statistical analysis indicated no significant difference in the occurrence of adverse effects between the two groups, with a P-value of 0.20. This suggests that both Iron Sucrose and Ferric Carboxymaltose are generally well-tolerated, with a slightly lower incidence of adverse effects observed in the Ferric Carboxymaltose group.

Overall, the data imply that both treatment options are safe, with the majority of participants in both groups experiencing no adverse effects. However, the Ferric Carboxymaltose group showed a marginally better safety profile, which might influence the preference for this formulation in clinical practice.

DISCUSSION

Postpartum anemia is a common condition that significantly impacts maternal-infant interactions during a crucial period. Anemic women tend to have longer hospital stays, are more likely to require blood transfusions, and face higher hospitalization costs. Therefore, addressing postpartum iron-deficiency anemia (IDA) with effective and high-quality care is essential.**(10)**

Traditional treatments for postpartum anemia, such as oral iron therapy and blood transfusions, have notable limitations. Oral iron therapy often faces challenges like poor absorption, especially in the presence of inflammation from surgically assisted deliveries, which causes iron to be sequestered in macrophages and reduces intestinal absorption.Consequently, the oral iron is not efficiently available for erythropoiesis.**(11)** To address these issues, intravenous (IV) iron preparations were introduced.**(12)**

In this study, both ferric carboxymaltose (FCM) and iron sucrose were administered according to the specified protocol and were effective in treating postpartum anemia while minimizing adverse

events. The rise in hemoglobin levels was significantly higher in the FCM group compared to the iron sucrose group, with increases of 4.6 g/dL and 3.9 g/dL, respectively ($P < 0.001$) after one month.

Previous studies have compared oral iron therapy with both FCM and iron sucrose, finding that both intravenous preparations are independently more effective and safer than oral iron supplements. **(3,9,13)** For instance, in a randomized trial assessing the safety and efficacy of intravenous FCM for postpartum IDA, 227 women received IV FCM (with a maximum dose of 1000 mg up to three weekly doses), while 117 women received oral ferrous sulfate (100 mg twice daily). The results indicated that intravenous FCM was as effective as oral ferrous sulfate, with no statistically significant differences between the groups, despite the shorter treatment period and lower total iron dose (mean 1.3 g IV iron versus 16.8 g oral iron).In line with these findings, our study also demonstrated that FCM led to a significant increase in hemoglobin levels with a mean dose of 1.06 g, achieving a rise of 2.54 g/dL. These results support that intravenous FCM is a highly effective and well-tolerated treatment option for postpartum iron-deficiency anemia, providing significant benefits over traditional oral iron therapy**.(13)**

In a multicenter randomized, controlled study, 130 women with postpartum anemia were administered either ferric carboxymaltose (FCM) (1000 mg per week, with a maximum total dose of 2.5 g) or 325 mg of ferrous sulfate tablets three times a day for six weeks. The study found that FCM achieved a hemoglobin level of 12 g/dL more quickly and maintained this level at 42 days compared to ferrous sulfate. Notably, among patients with hemoglobin levels ≤8 g/dL, there was a significant difference in the responder rate between the FCM group and the ferrous sulfate group (78.9% vs. 43.5%; $p = 0.0286$). **(14)** Our study's results align with these findings, demonstrating that both FCM and iron sucrose effectively treat postpartum anemia while minimizing adverse events. Specifically, FCM led to a more significant increase in hemoglobin levels (4.6 g/dL) compared to iron sucrose (3.9 g/dL), with a statistically significant difference ($P < 0.001$) after one month. These findings reinforce that FCM is not only faster in raising hemoglobin levels but also maintains those levels more effectively than traditional oral iron therapy. This makes FCM a highly effective and preferred option for managing postpartum iron-deficiency anemia, especially in patients with more severe anemia.

A retrospective study was conducted to assess the efficacy and safety of ferric carboxymaltose (FCM) and found it to be effective.**(15)** Further, a prospective trial demonstrated that FCM was better tolerated than iron sucrose (IS) in treating postpartum anemia, with superior efficiency.**(16**)

A retrospective study evaluated the safety and efficacy of intravenous (IV) high-dose ferric carboxymaltose (FCM) compared to iron sucrose (IS) for treating postpartum anemia in 210 inpatient women. These women received either IV high-dose FCM (15 mg/kg; maximum 1000 mg) or IS (2×200 mg). The findings indicated that the rapid administration of IV FCM was as safe as IS, even with FCM being administered at five times the dosage. Both FCM and IS were equally effective in increasing hemoglobin (Hb) levels from baseline, with no significant difference in the mean daily Hb increase between the groups. Notably, women with severe anemia responded most effectively to the treatments. Additionally, the single-dose application of FCM had advantages such as a lower incidence of side effects at the injection site, a shorter treatment period, and improved patient compliance.**(10)**

Our study's results are consistent with these findings. Both FCM and IS were effective in treating postpartum anemia while minimizing adverse events. However, FCM showed a more significant increase in hemoglobin levels (4.6 g/dL) compared to IS (3.9 g/dL), with a statistically significant difference ($P < 0.001$) after one month. Additionally, the serum ferritin levels were notably higher in the FCM group (108.4 ± 42.50 ng/mL) than in the IS group (85.5 ± 28.30 ng/mL), further highlighting FCM's superior efficacy.

In this study, both ferric carboxymaltose (FCM) and iron sucrose (IS) were administered at the same total dosage, but FCM was given as a single dose while IS was administered in multiple doses. Both groups exhibited a significant increase in hemoglobin and ferritin levels after one month of therapy, consistent with findings from other studies. Similar to previous research, patients with severe anemia showed the most pronounced response in both treatment groups**. (17)**

The safety profile of both iron formulations was generally favorable. The incidence of adverse effects was lower in the FCM group (4%) compared to the IS group (8%) (Table 4). Although the difference

was not statistically significant (P-value: 0.20), it suggests a trend towards better tolerability with FCM. This aligns with literature indicating that FCM is associated with fewer adverse reactions due to its stable molecular structure and rapid administration protocol **(14).**

Adverse effects reported were minor and manageable, which is crucial for patient compliance and overall treatment success. The lower incidence of adverse effects in the FCM group could enhance patient adherence to the treatment regimen, potentially leading to better long-term outcomes **(5).**

The findings of this study have significant implications for clinical practice. The superior efficacy of FCM in increasing hemoglobin and serum ferritin levels, coupled with its lower incidence of adverse effects, suggests that FCM might be a more suitable option for managing postpartum IDA.

While the study provides valuable insights, it is important to consider its limitations. The sample size, although adequate, could be expanded in future studies to confirm these findings across a larger and more diverse population. Additionally, long-term follow-up would be beneficial to assess the sustainability of the observed benefits and any delayed adverse effects.

Future research should also explore cost-effectiveness analyses of FCM and IS, considering not only the direct costs of the drugs but also the indirect costs associated with administration, patient compliance, and long-term health outcomes. Understanding these aspects will help healthcare providers make more informed decisions regarding the optimal management of postpartum IDA.

CONCLUSION

In conclusion, both ferric carboxymaltose and iron sucrose are effective in treating postpartum iron-deficiency anemia. However, FCM demonstrates a superior efficacy in increasing hemoglobin and serum ferritin levels, with a trend towards fewer adverse effects. These findings support the use of FCM as a potentially more effective and convenient option for postpartum women suffering from IDA. Further studies with larger sample sizes and long-term follow-up are warranted to confirm these results and provide comprehensive guidelines for clinical practice.

REFERENCE

1. World Health Organization. The prevalence of anemia in women: A tabulation of available information. WHO/MCH/MSM/92.2. 1992.
2. Pavord S, Myers B, Robinson S, Allard S, Strong J, Oppenheimer C. UK guidelines on the management of iron deficiency in pregnancy. Br J Haematol. 2012;156(5):588-600.
3. Van Wyck DB, Martens MG, Seid MH, Baker JB, Mangione A. Efficacy and safety of ferric carboxymaltose in patients with iron deficiency anemia. Transfusion. 2007;47(5):952-60.
4. Evstatiev R, Marteau P, Iqbal T, Khalif IL, Stein J, Bokemeyer B, et al. Ferric carboxymaltose prevents recurrence of anemia in patients with inflammatory bowel disease. Clin Gastroenterol Hepatol. 2013;11(3):269-77.
5. Breymann C. The use of iron sucrose complex for anemia in pregnancy and the postpartum period. Semin Hematol. 2006;43(6):28-31.
6. Seid MH, Derman RJ, Baker JB, Banach W, Goldberg C, Rogers R. Ferric carboxymaltose injection in the treatment of postpartum iron deficiency anemia: a randomized controlled clinical trial. Am J Obstet Gynecol. 2008;199(4):435-7.
7. Nair M, Choudhury MK, Choudhury RK, Chatterjee A, Saha PK, Roy RG. Effect of intramuscular iron sucrose versus oral iron on hemoglobin levels in pregnant women with moderate anemia: A randomized controlled trial. Indian J Clin Biochem. 2008;23(1):91-6.
8. Qassim A, Zourikian N, Tinmouth A, Stanworth S, Hutton B, Wilson K, et al. Ferric carboxymaltose versus iron sucrose for the treatment of iron deficiency anemia: a systematic review and meta-analysis. J Clin Med. 2021;10(1):106.
9. Froessler B, Collingwood J, Hodyl NA, Dekker G. Intravenous ferric carboxymaltose for treatment of postpartum anemia after major obstetric hemorrhage: a

randomized, controlled trial. Transfusion. 2015;55(6):1552-9.

10. Malek A. In vitro studies of ferric carboxymaltose on placental permeability using the dual perfusion model of human placenta. Arzneimittelforschung. 2010;60(6a):354-61.
11. Pfenniger A, Schuller C, Christoph P, Surbek D. Safety and efficacy of high-dose intravenous iron carboxymaltose vs. iron sucrose for treatment of postpartum anemia. J Perinat Med. 2012;40(4):397-402.
12. Auerbach M, Goodnough LT, Shander A. Iron: the new advances in therapy. Best Practice & Research Clinical Anaesthesiology. 2013 Mar 1;27(1):131-40.
13. Seid MH, Mangione A, Valaoras TG, Anthony LB, Barish CF. Safety profile of iron carboxymaltose, a new high dose intravenous iron in patients with iron deficiency anemia. Blood. 2006;108(11):3739.doi: https://doi.org/10.1182/blood.V108.11.3739.3739
14. Breymann C, Gliga F, Bejenariu C, Strizhova N. Comparative efficacy and safety of intravenous ferric carboxymaltose in the treatment of postpartum iron deficiency anemia. Int J Gynaecol Obstet. 2008;101(1):67-73.
15. Seid MH, Mangione A, Valaoras TG, Anthony LB, Barish CF. Safety profile of iron carboxymaltose, a new high dose intravenous iron in patients with iron deficiency anemia. Blood. 2006;108:3739.
16. Khandale SN, Kedar K. Managing postpartum anemia with ferric carboxymaltose at tertiary level hospital: a retrospective study. J Evol Med Dent Sci. 2015;4(44):7580-6.
17. Verma U, Singh S, Chandra M, Garg R, Singh S. To evaluate the efficacy and safety of single dose intravenous iron carboxymaltose verses multidose iron sucrose in post-partum cases of severe iron deficiency anemia. Int J Reprod Contracept Obstet Gynecol. 2015;4(2):442-6.

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