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Original Research Article

OUTCOME OF ANTEPARTUM INTRAVENOUS FERRIC CARBOXYMALTOSE IN ANEMIC PATIENTS

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Abstract: *Iron deficiency anaemia (IDA) is a prevalent condition among pregnant women, leading to increased maternal and fetal complications. Intravenous (IV) iron therapy, particularly ferric carboxymaltose (FCM), has been proposed as an effective treatment for rapid haemoglobin (Hb) improvement. Evaluating the effectiveness of FCM in achieving target Hb levels in a short duration is essential for optimising maternal health outcomes.* ***Objective:*** *To determine the efficacy of ferric carboxymaltose (FCM) in increasing haemoglobin levels for the treatment of iron deficiency anaemia (IDA) in pregnant women at a tertiary care hospital in Islamabad.* ***Methods:*** *A descriptive case series was conducted at a tertiary care hospital in Islamabad. The study included 110 pregnant women diagnosed with IDA. All participants received 5 mg of folic acid daily and were administered IV-FCM. Patients were monitored for three hours post-infusion for any adverse reactions and attended weekly follow-ups. Hemoglobin levels and iron profile were reassessed after three weeks to evaluate treatment efficacy. Data analysis was performed using SPSS version 20, with results presented as mean ± standard deviation (SD) and frequencies.* ***Results:*** *The mean age of participants was 25.67 ± 5.47 years (range 18–40 years). The effectiveness of IV-FCM in increasing haemoglobin levels within three weeks was observed in 80 (72.73%) of patients, indicating a high success rate.* ***Conclusion:*** *Ferric carboxymaltose (FCM) is effective in achieving target haemoglobin levels (≥11 g/dL) within three weeks in pregnant women with IDA, with minimal side effects. These findings support using IV-FCM as a safe and efficient treatment for iron deficiency anaemia during pregnancy.*

Keywords: Efficacy, Ferric carboxymaltose, Hemoglobin, Nervous System

Introduction

Iron deficiency anaemia (IDA) is very prevalent in countries with low socioeconomic status, especially among women of childbearing age. Its prevalence has been reported as 30.2% globally (1). Anaemia is highly prevalent during pregnancy and in the post-partum period, with iron deficiency anaemia accounting for >72% of anaemia in pregnancy and 20-37% in the post-partum period (2). Iron deficiency anaemia has been reported in around 41.7% to 77% of women of reproductive age in Pakistan (3). Anaemia causes fatigue, dizziness, and a weakened immune response, making you more susceptible to infections. Anaemia is the cause of around 29% of maternal mortalities (4). During pregnancy, the demand for iron rises two to thrice, not only for haemoglobin synthesis but also for the production of specific enzymes and to support fetoplacental development and maternal adaption to pregnancy, which can lead to iron insufficiency (5). Iron deficiency anaemia can result in premature birth, low birth weight, pre-eclampsia, placental abruption, increased peripartum blood loss, heart failure, and maternal death (6). Oral and intravenous iron therapies have been proven to minimise the deterioration of maternal anaemia, hence improving maternal outcomes (7). Intravenous iron preparations such as ferric carboxymaltose (FCM), which is a dextran-free type-I iron complex, are proven to be more efficient as they can saturate the body's iron stores after one or two infusions as compared to oral iron therapy, which requires long-term compliance for treating IDA during pregnancy (8). FCM is a stable complex with the advantage of having a very low immunogenic potential and not predisposed to a high risk of anaphylactic reactions. Mishra V and colleagues assessed the use of intravenous FCM in the correction of IDA in pregnant women and also determined the adverse effects associated with the use of FCM. They found that Hemoglobin levels (Hb) improved to 11.17±2.34gm/dl from 9.07±1.15 gm/dl (p-value <0.05), and the value of serum Ferritin raised to 190.45±115.43 ng/ml from 22.73±29.55 ng/ml (p-value <0.05). They found adverse reactions in 7.4% of participants (9). Breymann C et al. found that 84% of pregnant females with IDA achieved Hb levels > 11 g/dL after three weeks of treatment with IV FCM (10).

Methodology

The descriptive case series study was commenced from May 21, 2024, to Nov 20, 2024, following the approval and permission from the Research Ethics Committee of the Hospital at Obstetrics and Gynecology UNIT-I, Federal Government Services Hospital, Islamabad, over 110 women. The sample size was calculated using WHO sample size calculated using the confidence level of 95%, Absolute precision required of 7%, and anticipated population proportion:84% (11).

All the pregnant females who fulfilled the study's inclusion criteria were enrolled in the obstetrics and gynaecology unit-I of FGPC, Islamabad. Before confirming the survey, we obtained informed written consent from all the enrolled patients. Postgraduate trainees recorded clinical details by checking the history and performing the physical examination of all the selected candidates. A complete blood picture and iron profile were examined at our hospital's pathology laboratory. The iron replenishment dosage was calculated by using Ganzoni's Formula,

Total iron dose = ((Body weight in kg) × (Target Hemoglobin (11g/dL) - Actual Hemoglobin) [g/dL)) × 0.24* + Iron stores (1000mg)

After calculating the required iron dose, all the enrolled patients received intravenous ferric carboxymaltose as per the above formula (with a maximum of 1000 mg/week) diluted in 200 ml 0.9% normal saline and administered as an IV infusion over 45 min. Test doses were given to all patients before infusion to assess any possible reaction. Treatment was given under the supervision of a consultant obstetrician with teaching experience of at least three years. All the studied women were instructed to take 5 mg of Folic acid once daily. Patients were monitored for three hours following IV-FCM administration. Patients were asked for routine clinical visits every week after therapy. Iron profile and blood CP were repeated after 3 weeks and 6 weeks. Changes in Hb were determined after 3 weeks of IV-FCM therapy by subtracting the - Baseline (before treatment) Hb from Hb after 3 weeks of therapy in all the pregnant anaemic patients. Efficacy in achieving the target level of greater than 11g/dl was considered practical. Side effects like administration site level reaction, GIT, and nervous system disorders were recorded during the therapy.

Inclusion Criteria: All pregnant females with a gestational age of more than 20 weeks and diagnosed with iron deficiency anaemia age 18-40 years with a singleton pregnancy.

Exclusion Criteria: Females who have been taking IV/oral iron therapy for the last 2 weeks, have chronic systemic disease like renal failure or liver failure, hypersensitivity to ferric carboxymaltose, and have a history of blood transfusion within the previous 4 months were excluded.

SPSS version 209 was used for analysis and entry of the data. P-value ≤0.05 was considered significant.

Results

One hundred ten pregnant females with iron deficiency anaemia (IDA) having singleton pregnancies aged 18-40 years were included in this study.

The average age of the patients was 25.67 years+5.47SD, ranging from 18-40 years. The most common age group for pregnant women suffering from IDA was 21-30 years. There were 11(10%) patients were less than 20 years old. Seventy-six (69.1%) patients were in the age range of 31-30 years, and 23(20.9%) presented at more than 30 years of age.

The average gestational age was 25.98weeks+4.94SD, while the average BMI of the patients in our study sample was 27.31/m2+3.98SD. The pregnant patients with IDA presented with an average baseline Haemoglobin (Hb) level of 8.84g/dl+0.74SD. The patients were given intravenous ferric carboxymaltose and monitored in 3rd week after treatment. The average Hb level in 3rd week was 10.99g/dl+0.82SD. The average increase in Hb level in 3rd week was 2.15g/dl + 0.49SD compared to baseline Hb, which was statistically significant by applying a paired sample t-test with p-value=0.000. Table 1

The effectiveness of ferric carboxymaltose (FCM) in terms of patients achieving the target haemoglobin level (i.e.,≥11 g/dL) in 3 weeks was observed in 80(72.73%), while in 30(27.3%) patients showed no effectiveness. This was because the patients had very low Hb at the time of presentation, which also reached the level in later stages. The safety of FCM was observed regarding adverse administration site reactions, which occurred in 5(4.5%) patients; GIT disturbance and nervous system disorder were noted in 8(7.3%) patients each. (Figure 1)

The age-wise distribution shows that the effectiveness of FCM in younger age was as high as that of old age, and it was statistically significant with a p-value of 0.041. The patients aged less than or equal to 20 years have an effectiveness of 72.7%, those aged 21-30 years contain 78.9% effectiveness, and patients more than 30 years of age have 52.2% effectiveness in pregnant women presenting with IDA. The Baseline Hb level also plays a vital role in achieving the efficacy of FCM. The patients with Hb with more than 9g/dl at baseline have a significantly higher effectiveness rate than those with Hb less than 9g/dl with p-value=0.000. Gestational age also shows significantly high efficacy results in patients with less than 30 weeks of gestation compared to pregnant women with more than 30 weeks of gestation with p-value=0.013. At the same time, the BMI shows no significant role in the effectiveness of FCM. (Table 2).

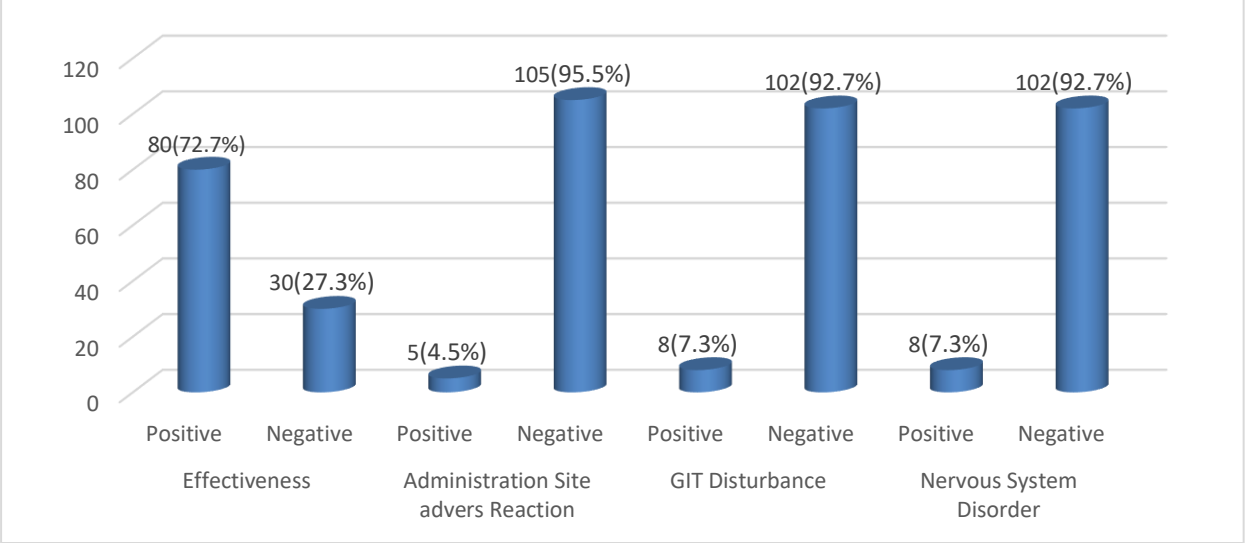

Fig 1 effectiveness and safety

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Table 1: DESCRIPTIVE STATISTICS (n=110)

	N	Mean	Std. Deviation
Gestational Age (in years)	110	25.98	4.938
BMI(Kg/m)	110	27.3141	3.98150
Age	110	25.6727	5.47406
Baseline Hb	110	8.8382	.74019
Hb at 3 week	110	10.9900	.82684
Increase in Hb	110	2.1518	.48966

Table 2: STRATIFICATION OF EFFECTIVENESS OVER AGE, GESTATIONAL AGE, AND BASELINE Hb LEVEL (n=110)

Variables	Constructs	Effectiveness				p-value
		Positive		Negative		
		Count	Row N %	Count	Row N %	
Age (in years)	<= 20.00	8	72.7%	3	27.3%	0.041
	21.00 - 30.00	60	78.9%	16	21.1%	
	31.00+	12	52.2%	11	47.8%	
Baseline Hb (g/dl)	<= 9.00	33	53.2%	29	46.8%	0.000
	9.01+	47	97.9%	1	2.1%	
Gestational Age (in weeks)	<= 30	68	78.2%	19	21.8%	0.013
	31+	12	52.2%	11	47.8%	
BMI(Kg/m)	<= 26.00	31	72.1%	12	27.9%	0.905
	26.01+	49	73.1%	18	26.9%	

Discussion

Nutritional iron deficiency anaemia (IDA) is recognised as the most common nutritional deficiency disorder in both the developed and developing world, affecting more than two billion people. A 2008 World Health Organization (WHO) report, concentrating on pre-school children and women, estimated that IDA affected worldwide one in four people, with pregnant women (11).

Also, according to the World Health Organization (WHO), the prevalence of anaemia in developed and developing countries in pregnant women is 14% and 51%, respectively. About half of the global maternal mortality due to anaemia occurs in South Asian countries (12).

The primary goal of treating IDA should involve diagnosing the underlying aetiology of the anaemia and treating this underlying disease. Otherwise, treating only the ID may lead to recurrence, especially if the underlying disease or disorder is chronic. However, while undergoing diagnostic evaluation or treatment of the underlying aetiology is underway, patients can benefit from iron replacement to immediately help counteract their symptoms of IDA (13).

Our results concur with other studies showing the safe and efficient use of FCM in pregnancy. A retrospective case-controlled study to assess the safety and efficiency of IV FCM in 128 pregnant women with IDA versus the control group (nonanemic or low-grade anaemia) showed that IV FCM was a safe and effective treatment (14)

Our study's results agree with the outcomes of several randomised controlled IV FCM trials. In a study that assessed the efficacy and safety of IV FCM versus oral ferrous sulfate (FS), FCM achieved a Hb increase of >2 g/dL in 7 days and >3 g/dL in 2 to 4 weeks (15)

A randomised controlled multicenter trial comparing the efficacy and safety of FCM with iron sucrose in patients with IBD and IDA found that more patients receiving FCM had a better response, with a haemoglobin rise of at least 2 g/dl in 65.8% of the FCM group versus 53.6% of the iron sucrose group (p =0.004). The drug-related adverse events were comparable between the two groups. Thus, in this study, FCM was a better intravenous iron formulation with greater efficacy and a good safety profile (16).

Our study shows that the majority (72.7%) of the pregnant women with IDA who received a dose of ferric carboxymaltose (FCM) remained non-anaemic (haemoglobin>11 g/dL) 3 weeks later. Among the anaemic women (n = 30), 75% had mild anaemia. Many studies have attested to a quick (within 6 weeks) and significant increase in haemoglobin concentration following the administration of FCM to anaemic antenatal and postpartum women. These findings have important clinical implications, particularly in those countries where anaemia is a public health problem (17).

A study conducted at a tertiary hospital in New Delhi, India, from January 2016 to August 2017 showed a rise in Hb from baseline at the end of 12 weeks. The mean increase in Hb at 12 weeks was significantly higher in the FCM group than in the ISC group (29 g/L vs. 22 g/L; p-value < 0.001. also, this study proves that rising at a higher rate at 3-week intervals persisted till the end of the study at 12 weeks. The baseline serum ferritin in FCM and ISC groups was 7.9 (0.4–22.3) µg/L and 9 (0.94–23) µg/L respectively. Serum ferritin level was significantly higher in the FCM group compared to ISC at 3 weeks (18). The results of FCM were consistent with our results.

One another study compared FCM with IV iron sucrose in pregnant women. It concluded that the mean increase in Hb levels was numerically more significant with FCM (1.54 g/dL) than with iron sucrose (1.17 g/dL), although this difference was not statistically significant (19). What was markedly different was the mean follow-up between the two groups (28.4 vs 41.2 days, respectively; P □□0.01), indicating that restoration of normal Hb levels was achieved much more quickly with FCM (20).

Similar to our results, many studies report fewer adverse side effects when FCM is given to patients. Another study reported that despite a five times higher dose, the safety and efficacy of FCM are equal to oral iron therapy or IV iron.

FCM can rapidly replace Hb in pregnant women. Patient satisfaction, fewer side effects, and short hospital stays are also advantages of FCM. Joshi et al. have also published that FCM has only a few side effects and can be considered as standard treatment for IDA in pregnant women (21, 22).
FCM also has a good safety profile, with mild-to-moderate headache, nausea, dizziness, abdominal pain, diarrhoea, constipation, rash, and infusion-site reactions as the most commonly reported side effects (23, 24).
This study shows the efficacy and safety of FCM in real-life scenarios of IDA, irrespective of age, diagnosis, and pregnancy status (for females). Health-related quality of life improvement has been reported after FCM administration, but literature on healthcare workers' assessment of the efficacy and safety of FCM is lacking. Our study shows that the physicians assessed FCM to have good efficacy and safety.

Conclusion

Iron supplements are an inexpensive and effective way of treating IDA patients, and their administration, in the absence of inflammation or significant ongoing blood loss, can correct anaemia, provided significant doses of iron can be tolerated. Our study demonstrates that IV FCM is effective and well tolerated in pregnant women with IDA during late-stage pregnancy and that women using this treatment give birth to healthy newborns. The increases in Hb levels were comparable between treatment arms in this study population. This treatment did improve Hb levels to a target level at three weeks. Furthermore, we demonstrated that FCM more rapidly and effectively established normalised Hb levels (Hb >11.0 g/dL) and was more effective at replenishing iron stores. Further randomised clinical trials are recommended to check its competency with other oral and intravenous drugs, which will help make some standard guidelines while treating such patients. Also, subgroup studies are needed to determine the optimal dose, the relationship between the number of doses, the increase in ferritin levels, and the various modifiers of this relationship.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-TVJSD-0832/23)
Consent for publication
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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

ANAM FAIZ (Postgraduate Resident)
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, and final approval.
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LUBNA SALEEM (Senior Registrar)
Conception of Study, Final approval of manuscript.
SHAZIA BATOOL (Associate Surgeon)
Manuscript revisions, critical input.
NAUSHIN FAROOQ (Consultant Surgeon)
Data entry and data analysis, as well as drafting the article.

References

1. Cappellini MD, Santini V, Braxs C, Shander A. Iron metabolism and iron deficiency anaemia in women. Fertil Steril. 2022;118(4):607-14.
2. Davidson EM, Scoullar MJL, Peach E, Morgan CJ, Melepia P, Opi DH, et al. Quantifying differences in iron deficiency-attributable anaemia during pregnancy and postpartum. Cell Rep Med. 2023;4(7):101097.
3. Ali SA, Abbasi Z, Shahid B, Moin G, Hambidge KM, Krebs NF, et al. Prevalence and determinants of anaemia among women of reproductive age in Thatta Pakistan: Findings from a cross-sectional study. PLoS One. 2020;15(9):e0239320.
4. Najam A, Akhtar S, Khan A, Fatima U, Fakeer Muhammad S. Prevalence of Severe Anemia among Pregnant Females and Factors Associated With Anemia in Pregnancy. Pak J Med & Health Sci. 2022;16(6).
5. Shi H, Chen L, Wang Y. Severity of Anemia During Pregnancy and Adverse Maternal and Fetal Outcomes. JAMA Netw Open. 2022;5(2):e2147046.
6. Edelson PK, Cao D, James KE, Ngonzi J, Roberts DJ, Bebell LM,et al. Maternal anaemia is associated with adverse maternal and neonatal outcomes in Mbarara, Uganda. J Matern Fetal Neonat Med. 2023;36(1):2190834.
7. Benson AE, Shatzel JJ, Ryan KS, Hedges MA, Martens K, Aslan JE et al. The incidence, complications, and treatment of iron deficiency in pregnancy. Eur J Haematol. 2022;109(6):633-642
8. Vanobberghen F, Lweno O, Kuemmerle A, Mwebi KD, Asilia P, Issa A, et al. Efficacy and safety of intravenous ferric carboxymaltose compared with oral iron for treating iron deficiency anaemia in women after childbirth in Tanzania: a parallel-group, open-label, randomised controlled phase 3 trial. Lancet Glob Health. 2021;9(2):e189-e198
9. Mishra V, Gandhi K, Roy P, Hokabaj S, Shah KN. Role of Intravenous Ferric Carboxy-maltose in Pregnant Women with Iron Deficiency Anaemia. J Nepal Health Res Counc. 2017;15(36):96-9.
10. Breymann C, Milman N, Mezzacasa A, Bernard R, Dudenhausen J. Ferric carboxymaltose vs oral iron in the treatment of pregnant women with iron deficiency anaemia: an international, open-label, randomized controlled trial (FER-ASAP). J Perinat Med. 2017;45(4):443–53
11. Friedrisch JR, Canc¸ado RD. Intravenous ferric carboxymaltose for the treatment of iron deficiency anaemia. Rev Bras Hematol Hemoter. 2015;37(6):400–405
12. Ghosh SK, Mondal R, Mandal S, Arindam De. A comparative study of ferric carboxymaltose and iron

sucrose as a parenteral iron treatment in iron deficiency anemia during pregnancy in a tertiary care hospital. Asian J Med Sci. 2024 Apr;15(4):91-8
13. Koduru P, Abraham BP. The role of ferric carboxymaltose in treating iron deficiency anemia in patients with gastrointestinal disease. Ther Adv Gastroenterol 2016;9(1):76–85
14. Pels A, Ganzevoort W. Safety and efficacy of ferric carboxymaltose in anemic pregnant women: a retrospective case-control study. Obstet Gynecol Int.2015;7.
15. Van Wyck DB, Martens MG, Seid MH, Baker JB, Mangione A. Intravenous ferric carboxymaltose compared with oral iron in treating postpartum anemia. Obstet Gynecol. 2007;110(2)Part1:267–78.
16. Evstatiev R, Alexeeva O, Bokemeyer B, Chopey I, Felder M, Gudehus M. et al. Ferriccarboxymaltose prevents the recurrence of anemia in patients with inflammatory bowel disease. Clin Gastroenterol Hepatol. 2013;11:269–77.
17. Kaur R, Kant S, Haldar P, Ahamed F, Singh A, Dwarakanathan V, et al. Single Dose of Intravenous Ferric Carboxymaltose Prevents Anemia for 6 Months among Moderately or Severely Anemic Postpartum Women: A Case Study from India. Current Devel Nutrit. 2021;1-4
18. Jose A, Mahey R, Sharma JB, Bhatla N, Saxena R, Kalaivani M, et al. Comparison of ferric carboxymaltose and iron sucrose complex for treatment of iron deficiency anemia in pregnancy randomised controlled trial. BMC Pregnancy Childbirth. 2019;19:54
19. Breymann C, Milman N, Mezzacasa A, Bernard R, Dudenhausen J. Ferric carboxymaltose vs. oral iron in the treatment of pregnant women with iron deficiency anemia: an international, open-label, randomized controlled trial (FER-ASAP). J Perinat Med. 2017;45(4):443–53
20. Christoph P, Schuller C, Studer H, Irion O, De Tejada BM, Surbek D. Intravenous iron treatment in pregnancy: comparison of high-dose ferric carboxymaltose vs. iron sucrose. J Perinat Med. 2012;40:469–74.
21. Joshi SD, Chikkagowdra S, Kumar V. Comparative study of efficacy and safety of intravenous ferric carboxymaltose versus iron sucrose complex in treating postpartum iron deficiency anemia. Int J Reprod Contracept Obstet Gynecol 2017;5(8):2566-70
22. Singh A, Yerragudi R. Comparative study of safety and efficacy of intravenous Iron sucrose Complex and ferric carboxymaltose in treating postpartum iron deficiency anemia. Int J Reprod Contracept Obstet Gynecol 2016; 5(4):1130-3.
23. Lyseng-Williamson KA, Keating GM. Ferric carboxymaltose: a review of its use in iron-deficiency anemia. Drugs. 2009;69(6):739–56.
24. Sharma N, Thiek JL, Natung T, Ahanthem SS. Comparative study of efficacy and safety of ferric carboxymaltose versus iron sucrose in post-partum anemia. J Obstet Gynaecol India. 2017;67(4):253–7.