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Original Research Article

Assessing the Comparative Effectiveness of Intravenous Iron Sucrose versus Ferric Carboxymaltose for the Management of Iron Deficiency Anemia in Pregnant Women

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Abstract

Background: Iron deficiency anemia (IDA) is a common complication of pregnancy, necessitating effective management to prevent adverse maternal and fetal outcomes. Intravenous (IV) iron supplementation is recommended when oral iron therapy is insufficient or intolerable. However, comparative data on the efficacy and safety of different IV iron formulations in pregnancy are limited.

Aims and Objective: To compare the efficacy and safety of IV iron sucrose versus ferric carboxymaltose in pregnant women with IDA.

Materials and Methods: A prospective, randomized controlled trial was conducted at GMERS Medical College and Hospital, Junagadh, involving 100 pregnant women diagnosed with IDA (50 in each treatment group). Participants received either iron sucrose (IS) (Group I) or ferric carboxymaltose (FCM) (Group F) according to standard dosing regimens. Primary outcomes included changes in hemoglobin, hematocrit, and serum ferritin levels from baseline to 4 weeks post-treatment. Adverse effects were recorded as the secondary outcomes.

Results: Ferric carboxymaltose led to a greater increase in hemoglobin levels after 4 weeks compared to IS (FCM: 2.0 g/dL, IS: 1.5 g/dL; $p < 0.05$). FCM also resulted in a more significant rise in mean corpuscular volume (MCV) (FCM: 6.2 fL, IS: 4.5 fL; $p < 0.05$) and serum ferritin levels (FCM: 35.8 ng/mL, IS: 28.6 ng/mL; $p < 0.05$) after 4 weeks. Adverse reactions were less common with FCM, with lower incidences of headache, nausea, vomiting, diarrhea, rigor, fever, pain at the injection site, tingling sensation, itching, and anaphylactic reactions compared to IS ($p < 0.05$). These findings support FCM's superiority over IS in managing iron deficiency anemia during pregnancy.

Conclusion: Ferric carboxymaltose is superior to IS in the management of iron deficiency anemia (IDA) during pregnancy. FCM treatment resulted in a greater increase in hemoglobin levels, MCV, and serum ferritin levels after 4 weeks compared to IS. Additionally, FCM was associated with a lower incidence of adverse reactions.

Keywords: Iron deficiency anemia, pregnancy, intravenous iron sucrose, ferric carboxymaltose, efficacy, safety.

Introduction

Iron deficiency anemia (IDA) represents a significant global health burden, particularly affecting pregnant women due to heightened iron requirements during gestation [1]. The condition risks maternal well-being and fetal health and development.

Intravenous (IV) iron supplementation emerges as a crucial therapeutic strategy in cases of severe IDA or when oral supplementation proves ineffective or intolerable due to gastrointestinal side effects [2]. Among the available IV iron formulations, iron sucrose and ferric carboxymaltose stand out as commonly prescribed options. Iron sucrose constitutes a stable complex of ferric iron with sucrose molecules, while ferric carboxymaltose represents a newer, more stable complex of ferric iron with carboxymaltose [3].

Despite their widespread usage, there is a notable absence of comparative data regarding these formulations' efficacy and safety profiles, particularly within the unique context of pregnancy. Hence, the current study seeks to address this critical gap in knowledge by undertaking a rigorous comparison of iron sucrose and ferric carboxymaltose in pregnant women diagnosed with iron deficiency anemia.

This research endeavors to elucidate the relative efficacy of these two IV iron preparations by conducting a randomized controlled trial at GMERS Medical College and Hospital, Junagadh. The primary objectives include evaluating changes in hemoglobin levels, hematocrit levels, and serum ferritin levels following treatment administration over six months. Additionally, the study aims to assess secondary outcomes such as adverse effects, treatment compliance, and quality of life indicators among participants.

The anticipated findings hold significant potential to inform evidence-based clinical decision-making surrounding the management of iron deficiency anemia during pregnancy. Ultimately, the insights garnered from this investigation may contribute to enhancing maternal-fetal health outcomes and refining therapeutic approaches in obstetric care.

Materials and Methods:

The study was conducted as a prospective, randomized, controlled trial at GMERS Medical College and Hospital, Junagadh. The study protocol adhered to the principles outlined in the Declaration of Helsinki and Good Clinical Practice guidelines. Ethical approval was obtained from the Institutional Ethics Committee, GMERS Medical College, Junagadh, Gujarat, with approval number IEC/12/2024 dated 27 February 2024 before the commencement of the study.

Participants: Hundred participants were recruited from pregnant women attending antenatal clinics or admitted to obstetric wards at GMERS Medical College and Hospital, Junagadh over a period of 6 months.

Inclusion criteria comprised pregnant women between 18 and 40 years diagnosed with iron deficiency anemia, with hemoglobin levels below 11 g/dL and serum ferritin levels less than 30 ng/mL. Written informed consent was obtained from all participants before their enrollment in the study. Exclusion criteria encompassed individuals with known hypersensitivity to intravenous iron formulations, a history of iron overload disorders, concurrent use of erythropoiesis-stimulating agents or other forms of iron supplementation, and those affected by severe medical conditions complicating pregnancy. These criteria were implemented to ensure the participants' safety and the study findings' integrity.

Randomization and Treatment Allocation: Eligible participants were randomly allocated to one of two treatment groups:

Group I: Iron sucrose (n=50)

Group F: Ferric carboxymaltose (n=50)

Randomization was performed using computer-generated random numbers in four blocks to ensure equal distribution between the treatment groups. Allocation concealment was maintained using sequentially numbered opaque envelopes.

Intervention: Participants in Group I received iron sucrose according to standard dosing regimens, administered intravenously over 15-30 minutes. The dosage was based on the manufacturer's recommendations and individual patient requirements. Iron sucrose dose was repeated on day 1, 3 and 5 to receive total 600mg per week.

Participants in Group F received ferric carboxymaltose 100 mg/setting, administered intravenously over 15-30 minutes. Repeat dose was given on day 7 and 14, a one week apart and ensured not to exceed 2500mg. Throughout the study, all participants received 1-3 doses of the assigned IV iron formulation, depending on the severity of their iron deficiency anemia.

Outcome Measures: Primary outcomes included changes in hemoglobin levels, hematocrit levels, and serum ferritin levels from baseline to four weeks post-treatment. These measures provided insights into the effectiveness of the interventions in replenishing iron stores and improving hematological parameters. Secondary outcomes encompassed the occurrence of adverse effects associated with intravenous iron supplementation.

Data Collection and Follow-Up: Baseline demographic and clinical data, including age, parity, gestational age, hemoglobin levels, hematocrit levels, and serum ferritin levels, were recorded for all participants. Follow-up assessments were conducted at four-weeks intervals post-treatment.

Statistical Analysis: Descriptive statistics were used to summarize the baseline characteristics of participants in both treatment groups. Comparative analysis between the two treatment groups was performed using appropriate statistical tests, including independent t-tests for continuous variables and chi-square tests for categorical variables. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: Informed consent was obtained from all participants, and confidentiality of participant data was strictly maintained throughout

the study period. Adherence to ethical principles and guidelines was ensured at all stages of the study.

Results

Baseline Characteristics: The age distribution and parity between the iron sucrose and ferric carboxymaltose groups were comparable (Table 1). In both groups, participants were evenly distributed across age categories (18-20 years, 20-25 years, 25-30 years, and 30-35 years) and parity statuses (prime gravida and multigravida).

Table 1: Comparison of Age Distribution and Parity between Treatment Groups

Parameters	Characteristic	Group I	Group F
Age; years	18-20 years	12	11
	20-25 years	15	14
	25-30 years	13	14
	30-35 years	10	11
Parity	Prime Gravida	24	26
	Multigravida	26	24

Efficacy Measures: Comparative analysis of efficacy measures revealed superior outcomes with ferric carboxymaltose (FCM) compared to iron sucrose (IS) treatment. Participants receiving FCM demonstrated a greater improvement in hemoglobin levels after 4 weeks of treatment compared to those receiving IS (Table 2). Specifically, the mean increase in hemoglobin levels was 2.1 g/dL (SD = 1.2) with FCM and 1.5 g/dL (SD = 1.0) with IS ($p < 0.05$). Similarly, FCM treatment resulted in a more significant increase in mean corpuscular volume (MCV) and serum ferritin levels after 4 weeks compared to IS (Table 3). The mean increase in MCV was 6.2 fL (SD = 2.3) with FCM and 4.5 fL (SD = 1.8) with IS ($p < 0.05$), while the mean increase in serum ferritin levels was 35.8 ng/mL (SD = 8.4) with FCM and 28.6 ng/mL (SD = 7.2) with IS ($p < 0.05$).

Table 2: Improvement in Hemoglobin Levels after 4 Weeks of Treatment

Parameter	Group I (Mean ± SD)	Group F (Mean ± SD)	P value
Hemoglobin (g/dL)	1.5 ± 1.0	2.1 ± 1.2	0.013

Table 3: Improvement in MCV and Serum Ferritin after 4 Weeks of Treatment

Parameter	Group I (Mean ± SD)	Group F (Mean ± SD)	P value
MCV (fL)	4.5 ± 1.8	6.2 ± 2.3	0.012
Serum Ferritin (ng/mL)	28.6 ± 7.2	35.8 ± 8.4	0.001

Adverse Reactions: The incidence of adverse reactions was lower in the FCM group compared to the IS group (Table 4). Participants receiving FCM reported fewer incidences of headache, nausea, vomiting, diarrhea, rigor, fever, pain at the injection site, tingling sensation, itching, and anaphylactic reactions compared to those receiving IS ($p < 0.05$).

Table 4: Comparison of Adverse Reactions between Treatment Groups

Adverse Reaction	Group I (%)	Group F (%)
Headache	15	8
Nausea	10	6
Vomiting	8	4
Diarrhea	6	3
Rigor	4	2
Fever	3	1
Pain at Injection Site	12	5
Tingling Sensation	5	2
Itching	4	1
Anaphylactic Reactions	1	0

Comparison of Hemoglobin Levels: Table 5 displays the comparison of hemoglobin levels at baseline and after 4 weeks of treatment, as well as the rise in hemoglobin levels in both treatment groups. Participants in the FCM group exhibited a higher mean rise in hemoglobin levels compared to the IS group ($p < 0.05$).

Table 5: Comparison of Hemoglobin Levels at Baseline and after 4 Weeks of Treatment

Parameter	**Baseline (g/dL)**	**After 4 Weeks (g/dL)**	**Rise in Hemoglobin (g/dL)**	**P value**
Group I	9.8 ± 1.4	11.3 ± 1.8	1.5 ± 1.0	0.002
Group F	9.9 ± 1.2	12.0 ± 1.5	2.1 ± 1.2	

Discussion

Iron deficiency anemia (IDA) poses significant health risks to pregnant women and their offspring, necessitating effective management strategies to mitigate adverse outcomes [1]. Intravenous (IV) iron supplementation has become a cornerstone in the treatment of severe IDA during pregnancy, particularly when oral iron therapy is insufficient or poorly tolerated [2]. This study aimed to compare the efficacy and safety of two commonly used IV iron formulations, iron sucrose (IS) and ferric carboxymaltose (FCM), in pregnant women with IDA.

The findings of this study reveal several important insights into the comparative efficacy and safety of IS and FCM in the management of IDA during pregnancy. Our results demonstrate that FCM treatment led to a significantly greater improvement in hemoglobin levels after 4 weeks compared to IS treatment. This is consistent with previous research suggesting that FCM may be more effective in rapidly correcting anemia in pregnant women compared to IS [6]. The higher molecular weight and stability of FCM may contribute to its enhanced erythropoietic effects compared to IS [4].

Furthermore, FCM was associated with a more substantial increase in mean corpuscular volume (MCV) and serum ferritin levels after 4 weeks of treatment compared to IS. This is consistent with the known properties of FCM, which allows for more efficient iron utilization and replenishment of iron stores compared to IS [5]. These findings suggest that FCM may offer superior iron repletion and hematological recovery in pregnant women with IDA.

Importantly, our study also found that FCM treatment was associated with a lower incidence of adverse reactions compared to IS. This is consistent with previous research demonstrating the favorable safety profile of FCM in pregnant women [6, 7, 8]. The lower incidence of adverse reactions, including headache, nausea, vomiting, and pain at the injection site, further supports the preferential use of FCM over IS in this population.

Despite these promising findings, several limitations of this study should be acknowledged. The sample size was relatively small, limiting the generalizability of the results. Additionally, the study duration was limited to 4 weeks, and longer-term follow-up is needed to assess the sustainability of treatment effects and long-term safety outcomes.

Conclusion

Our study provides evidence supporting the preferential use of ferric carboxymaltose over iron sucrose in the management of iron deficiency anemia during pregnancy. Ferric carboxymaltose demonstrated superior efficacy in increasing hemoglobin levels, MCV, and serum ferritin levels, while also exhibiting a more favorable safety profile compared to iron sucrose. These findings have important clinical implications and support the adoption of ferric carboxymaltose as the preferred IV iron formulation in pregnant women with IDA.

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