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EFFICACY OF INTRAVENOUS FERRIC CARBOXYMALTOSE VERSUS IRON SUCROSE COMPLEX FOR THE TREATMENT OF IRON DEFICIENCY ANEMIA IN PREGNANCY

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ABSTRACT

Background: Iron deficiency anemia (IDA) is common during pregnancy and may adversely affect maternal and fetal health. Intravenous iron is useful when rapid iron replacement is required or oral iron is poorly tolerated. Ferric carboxymaltose (FCM) permits administration of larger iron doses over a shorter infusion period than conventional iron sucrose.

Objective: To compare the efficacy of intravenous ferric carboxymaltose with intravenous iron sucrose complex for treatment of IDA during pregnancy.

Methods: This randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology, Memon Medical Institute Hospital, Karachi, from 15 November 2022 to 15 May 2023. One hundred pregnant women aged 18–40 years, at ≥16 weeks' gestation, with IDA were enrolled and allocated equally to iron sucrose (n=50) or FCM (n=50) using opaque sealed envelopes. Iron sucrose was administered at 100–200 mg weekly, diluted in 250 mL normal saline, with treatment stopped after a total of 400 mg. FCM was administered at 15 mg/kg, not exceeding 1000 mg per dose, intravenously over approximately 15 minutes and given weekly for three weeks. Efficacy was assessed on day 21 according to the study definition. Data were analyzed using SPSS version 25; categorical comparisons used chi-square/Fisher exact testing.

Results: Mean age was 35.40±4.33 years in the iron sucrose group and 36.20±2.74 years in the FCM group. Efficacy was achieved in 15/50 (30.0%) participants receiving iron sucrose compared with 40/50 (80.0%) receiving FCM (p=0.001). The absolute difference in efficacy was 50 percentage points; the calculated risk ratio was 2.67 (95% CI 1.71–4.16). Stratified analyses also demonstrated higher efficacy with FCM across several age, BMI, gestational-age, residence, parity and gravida categories.

Conclusion: Within this study population, intravenous FCM was associated with substantially greater treatment efficacy at day 21 than iron sucrose. The findings support FCM as a useful intravenous iron option for pregnant women with IDA when rapid iron repletion is clinically indicated, while larger studies with detailed safety, cost-effectiveness and longer-term maternal and neonatal outcomes are warranted.

KEYWORDS: ferric carboxymaltose; iron sucrose; iron deficiency anemia; pregnancy; intravenous iron; hemoglobin

INTRODUCTION

Iron deficiency anemia is an important and potentially modifiable cause of maternal morbidity. Pregnancy substantially increases iron requirements because iron is needed for expansion of maternal red-cell mass and for fetal and placental development. Inadequate dietary intake, limited bioavailability, previous blood loss and the increased physiological requirements of pregnancy may contribute to depletion of iron stores. [1–4]

Oral iron remains an important treatment strategy, but gastrointestinal adverse effects and poor adherence can limit its effectiveness. Intravenous iron is particularly relevant in women with moderate or severe anemia, intolerance or non-adherence to oral therapy, or a need for relatively rapid restoration of iron stores. [5,6]

Iron sucrose has been widely used during pregnancy because of its established safety profile and lack of requirement for a test dose. However, its practical limitation is the need for repeated administrations because only relatively small amounts can be given during an individual infusion. Ferric carboxymaltose is a newer dextran-free intravenous formulation that permits administration of a larger iron dose over a short infusion period. [7,8]

Previous comparative studies have reported higher or faster correction of iron deficiency with ferric carboxymaltose than with iron sucrose, including evidence from South Asian populations. [7–9] Nevertheless,

local evidence remains limited. The present study was therefore undertaken to compare the efficacy of ferric carboxymaltose and iron sucrose complex in pregnant women with IDA attending a tertiary-care hospital in Karachi.

MATERIALS AND METHODS

Study design and setting

This randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology, Memon Medical Institute Hospital, Karachi, Pakistan. The study period was 15 November 2022 to 15 May 2023. The dissertation reports that permission was obtained from the institutional ethical review committee and CPSP before recruitment, and informed consent was obtained from participants.

Participants

Women aged 18–40 years with a gestational age of 16 weeks or more on ultrasound and a confirmed diagnosis of IDA were eligible. Participants were included irrespective of booking status, parity and gravida, provided they were willing to participate. Women with known allergy to study-drug ingredients, bacterial or viral infection, intravenous iron treatment or blood transfusion during the preceding four weeks, or known hematological disorders were excluded.

Sample size and sampling

Sample-size calculation based on previously reported efficacy rates of 81.2% for ferric carboxymaltose and 22.5% for iron sucrose, with 80% power and a 95% confidence level, yielding 22 participants (11 per group). To improve reliability, 100 women were ultimately enrolled, with 50 participants assigned to each treatment group. Consecutive non-probability sampling was used for recruitment.

Randomization and interventions

After baseline assessment and informed consent, participants were randomly allocated to two groups using an opaque sealed-envelope technique. Group A received iron sucrose complex 100–200 mg once weekly, diluted in 250 mL of 0.9% sodium chloride and infused slowly over approximately two hours; treatment was stopped after a total dose of 400 mg. Group B received ferric carboxymaltose at 15 mg/kg, not exceeding 1000 mg per dose, intravenously over approximately 15 minutes, weekly for three weeks. Participants receiving either preparation were monitored after infusion for clinically relevant reactions, including hypersensitivity manifestations, hypotension, headache, chest pain, dyspnea, tachycardia, skin rash and facial flushing.

Outcome definition

Defined IDA using hemoglobin <11.0 g/dL and a serum ferritin criterion reported as 15 µg/L. Efficacy was defined as hemoglobin >12.0 g/L after 21 days of treatment in the source dissertation. Because the dissertation contains this unit wording, it has been retained here rather than introducing an unsupported correction.

Data collection and statistical analysis

At baseline, demographic and clinical information including age, residence, parity, gravida, height, weight, body mass index (BMI), gestational age, booking status and previous IDA history was recorded. A 5-mL blood sample was collected for assessment of iron status. Quantitative variables were summarized as mean±standard deviation or median (interquartile range), while categorical variables were presented as frequencies and percentages. SPSS version 25 was used for analysis. Chi-square or Fisher exact testing was used for comparisons of efficacy, with $p \leq 0.05$ considered statistically significant. Efficacy was additionally stratified by age, residence, gestational age, BMI, family monthly income, parity, gravida, baseline hemoglobin, ferritin and previous IDA history.

RESULTS

A total of 100 pregnant women were included, with 50 participants in each treatment group. Baseline demographic and laboratory characteristics reported in the dissertation are summarized in Table 1. Mean age was similar between groups (35.40±4.33 versus 36.20±2.74 years). Baseline hemoglobin was also similar (8.40±1.57 versus 8.50±1.92 g/dL), supporting comparability of the two groups with respect to the principal hematologic parameter before treatment.

Variable	Iron sucrose (n=50)	Ferric carboxymaltose (n=50)
Age, years	35.40±4.33	36.20±2.74
Height, cm	154.30±11.35	153.70±13.70
Weight, kg	59.20±10.84	57.60±8.93
BMI, kg/m²	29.00±3.49	25.90±5.21
Hemoglobin	8.40±1.57	8.50±1.92
Hematocrit	31.90±1.77	31.10±1.88
MCV	66.60±4.54	67.30±5.57
MCH	25.00±1.62	24.80±2.33
MCHC	28.50±1.51	28.20±1.90
Serum ferritin	9.60±0.92	9.50±0.93
Transferrin saturation*	216.50±19.69	208.50±15.65

*The transferrin saturation values are reproduced exactly as reported in the dissertation; the source table appears to contain a possible transcription/unit issue, so no unsupported correction has been made.

The distribution of residence, parity, gravida, booking status, previous history of IDA and selected comorbidities is shown in Table 2. Urban residence was reported in 35 participants in each group. Parity was evenly distributed, with 25 primiparous and 25 multiparous women in each group. The iron sucrose group included 40 primigravidas and 10 multigravidas, whereas the FCM group included 35 primigravidas and 15 multigravidas. The dissertation also reported differences in booking status and several comorbidities; these descriptive distributions are presented without modification.

Characteristic	Category	Iron sucrose n	FCM n
Residence	Urban	35	35
	Rural	15	15
Parity	Primipara	25	25
	Multipara	25	25
Gravida	Primigravida	40	35
	Multigravida	10	15
Booking	Booked	10	0
	Unbooked	40	50
Previous IDA	Yes	15	10
	No	35	40
Diabetes	Yes	10	5
	No	40	45
Hypertension	Yes	5	10
	No	45	40
Asthma	Yes	30	20
	No	20	30
Hyperthyroidism	Yes	20	10
	No	30	40
Chronic kidney disease	Yes	10	10
	No	40	40

The primary comparison demonstrated a marked difference in efficacy. Fifteen of 50 women (30.0%) in the iron sucrose group met the study's efficacy criterion compared with 40 of 50 women (80.0%) in the FCM group (p=0.001). Thus, the absolute difference was 50 percentage points. Based on the reported counts, the calculated risk ratio for efficacy was 2.67 (95% CI 1.71–4.16).

Treatment group	Efficacy achieved	Efficacy not achieved	p value
Iron sucrose (n=50)	15 (30.0%)	35 (70.0%)	0.001
Ferric carboxymaltose (n=50)	40 (80.0%)	10 (20.0%)	
Total (n=100)	55 (55.0%)	45 (45.0%)	

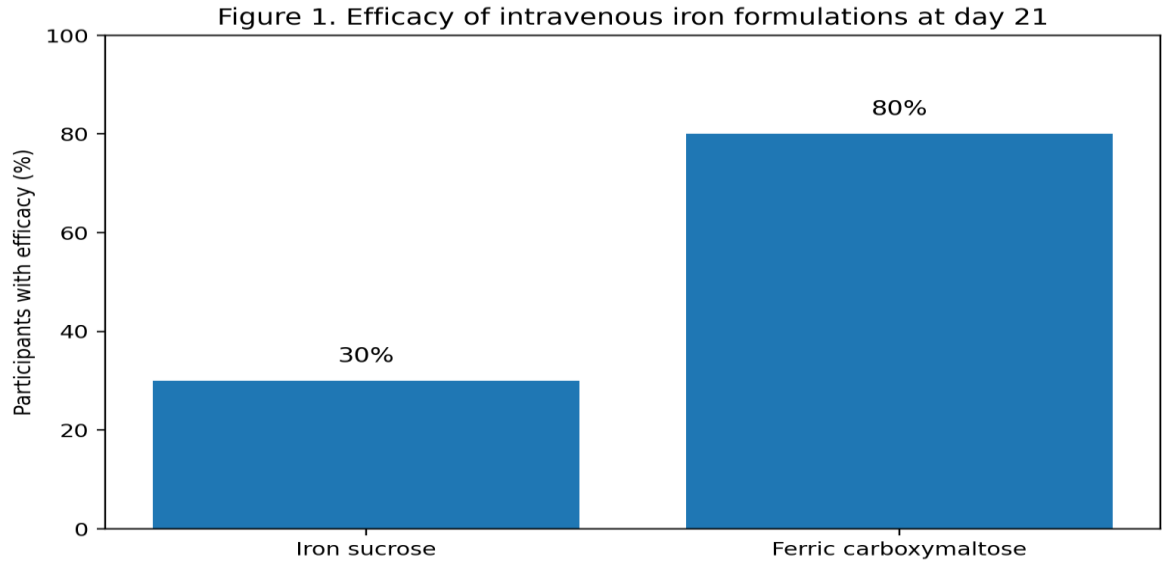

Figure 1 demonstrates the substantially higher proportion of participants achieving efficacy in the FCM group.

Stratified analysis suggested that the advantage of FCM was maintained across several participant subgroups. Among women aged 31–40 years, efficacy was achieved in 10/45 women receiving iron sucrose versus 35/45 receiving FCM (p=0.001). For BMI categories, significant between-treatment differences were reported among overweight and obese participants (p=0.002 for each), whereas the difference in the normal-BMI category was not statistically significant (p=0.140). For gestational age, the reported difference was not statistically significant at 16–25 weeks (p=0.101) but was significant at 26–42 weeks (p=0.001).

Stratum	Iron sucrose: Yes/No	FCM: Yes/No	p value
Age 18–30 years	5 / 0	5 / 0	—
Age 31–40 years	10 / 35	35 / 10	0.001
Normal BMI	10 / 0	15 / 5	0.140
Overweight	0 / 10	15 / 0	0.002
Obese	5 / 25	10 / 5	0.002
Gestational age 16–25 weeks	0 / 5	5 / 5	0.101
Gestational age 26–42 weeks	15 / 30	35 / 5	0.001

Residence and parity also showed a higher proportion of efficacy with FCM. In urban participants, efficacy was reported in 10/35 women receiving iron sucrose compared with 30/35 receiving FCM (p=0.001), whereas the rural comparison did not reach statistical significance (p=0.143). Among primiparous women, efficacy was 10/25 versus 20/25 (p=0.009), and among multiparous women it was 5/25 versus 20/25 (p=0.001) for iron sucrose and FCM, respectively. Among multigravidas, efficacy was 5/10 with iron sucrose and 15/15 with FCM (p=0.005).

Stratum	Iron sucrose: Yes/No	FCM: Yes/No	p value
Urban residence	10 / 25	30 / 5	0.001
Rural residence	5 / 10	10 / 5	0.143
Primipara	10 / 15	20 / 5	0.009
Multipara	5 / 20	20 / 5	0.001
Primigravida	10 / 30	25 / 10	0.101
Multigravida	5 / 5	15 / 0	0.005

DISCUSSION

The present randomized controlled trial found a substantially greater proportion of pregnant women meeting the study-defined efficacy endpoint after treatment with ferric carboxymaltose than with iron sucrose complex. Efficacy was observed in 80.0% of women in the FCM group compared with 30.0% in the iron sucrose group, with a statistically significant between-group difference (p=0.001). This finding is directionally consistent with previous comparative studies cited in the dissertation, which have reported greater or more rapid iron replenishment with FCM. [7–9]

A plausible explanation is the dosing and administration characteristics of FCM. The formulation permits administration of a larger quantity of iron in a shorter infusion, whereas iron sucrose generally requires multiple smaller administrations. In the present study, iron sucrose was given in weekly doses of 100–200 mg until a total of 400 mg, while FCM was prescribed at 15 mg/kg, up to 1000 mg per dose. The resulting difference in cumulative delivery and infusion burden may have contributed to the observed difference in the day-21 efficacy endpoint. [7,8]

Earlier evidence has also emphasized the practical advantages of intravenous iron when oral therapy is limited by gastrointestinal intolerance or inadequate adherence. [5,6] Iron sucrose has a well-established role in pregnancy and is generally considered safe, but repeated infusions may increase the treatment burden. FCM was developed to permit higher-dose replacement over a short infusion period, potentially improving convenience and allowing more rapid correction when time to delivery is limited. [7,8]

The subgroup findings were generally consistent with the primary result. The advantage of FCM was statistically significant among women aged 31–40 years, those who were overweight or obese, women at 26–42 weeks' gestation, urban participants, and both primiparous and multiparous women. Some strata, including women with normal BMI, gestational age 16–25 weeks, rural residence and primigravidity, did not show statistically significant differences. These findings should be interpreted cautiously because the subgroup sample sizes were small and the study was not primarily powered for interaction or subgroup effects.

The study is also relevant to local clinical practice. The dissertation identified limited local consensus regarding the preferred intravenous iron preparation and cited previous Pakistani data showing higher efficacy with FCM than iron sucrose. [9] The current findings add another local dataset supporting the use of FCM for rapid correction of IDA during pregnancy.

Safety and tolerability are important considerations when selecting intravenous iron. The dissertation reports that both groups were monitored after infusion for hypersensitivity and other acute reactions. However, the study's results section does not provide a comparative numerical table of adverse events. Therefore, no

unsupported safety comparison is made in this manuscript. Existing literature cited in the dissertation describes FCM as a generally well-tolerated dextran-free preparation, while emphasizing the need for appropriate infusion technique and monitoring. [8,13,14]

Several limitations should be considered. First, the study was conducted at a single center and included only 100 participants, limiting generalizability. Second, consecutive non-probability sampling may introduce selection bias. Third, efficacy was assessed at a single early follow-up point (day 21), so durability of hematologic response and longer-term replenishment of iron stores cannot be determined. Fourth, detailed adverse-event frequencies and maternal or neonatal clinical outcomes were not reported in the study results available in the dissertation. Finally, the source document contains apparent transcription/unit inconsistencies in some operational definitions and baseline laboratory reporting; these have not been replaced with invented values.

CONCLUSION

In this randomized controlled trial of 100 pregnant women with iron deficiency anemia, ferric carboxymaltose demonstrated significantly greater study-defined efficacy at day 21 than iron sucrose complex (80.0% versus 30.0%; p=0.001). The findings suggest that FCM may be a useful option when rapid intravenous iron replacement is required during pregnancy. Larger multicenter studies should evaluate longer-term hematologic and ferritin responses, treatment-related adverse events, cost-effectiveness, and maternal and neonatal clinical outcomes before broader conclusions are made.

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