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Injectable Ferric Carboxy Maltose Versus Oral Ferrous Fumerrate in Treatment of Iron Deficiency Anaemia in Pregnancy- A Randomized Controlled Trial

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Abstract

Background: Anemia in pregnancy is widespread and poses risks to both mother and fetus. This study aims to compare the efficacy of injection ferric carboxymaltose and oral iron supplementation in treating iron deficiency anemia during pregnancy. ***Aim:*** To compare the injection ferric carboxy maltose and oral iron in treating iron deficiency anaemia during pregnancy. ***Methods:*** This randomized control trial was conducted at department of Obstetrics & Gynecology, Institute of Child and Mother Health, for 9 months, following ethical clearance. A total of 156 pregnant women (16 to 34 weeks of gestation) diagnosed with anemia (Hb < 11 g%, low serum ferritin, and peripheral blood smear findings of IDA) were included after getting informed written consent and divided into Group-A (oral Ferrous Sulphate, n=78) and Group-B (Injection Ferric carboxy maltose, n=78). Data was collected in separated case-record form and analyzed by SPSS 26 version. ***Result:*** Demographic characteristics were similar across the two groups in terms of age and residence ($p>0.05$ in all cases). In both group-A and group-B, significant rise of Hb (mean difference= 1.018 and 1.664, respectively) and serum ferritin (mean difference= 205.22 and 227.37, respectively) were noted. However, TIBC was significantly decreased only in group-B (mean difference= -47.06, $p=0.013$), while group-A showed no significant improvement in TIBC ($p>0.05$). Overall, Hb≥ 11 gm% after 6-weeks of treatment was significantly higher in group-B than group-A (65.4% vs 44.9%, $p=0.010$). Besides, group-B patients had significantly lower gastrointestinal adverse events than group-A patients ($p<0.05$). ***Conclusion:*** Ferric carboxymaltose demonstrates superior effectiveness and safety compared to oral ferrous sulfate for treating anemia in pregnant women. However, further study is warranted.

Keywords: Iron deficiency anemia, Ferric carboxymaltose, Ferrous fumarate, Intravenous iron, Oral iron therapy, Hemoglobin, Serum ferritin.

INTRODUCTION

Anemia during pregnancy is a major global health issue with serious implications for both maternal and fetal outcomes. According to the World Health Organization, iron deficiency anemia (IDA) is the most widespread nutritional deficiency, affecting over two billion people globally [1]. Pregnant women are especially at risk, accounting for up to 40% of all anemia cases [2-4]. IDA is particularly prevalent in developing countries, where rates can reach as high as 80%, compared to 17–20% in developed nations [5-7]. This condition is linked to preterm birth, low birth weight, fetal growth restriction, and increased maternal and neonatal morbidity and mortality [8-9].

During pregnancy, the body's demand for iron increases due to expanded red cell mass and blood volume [5-7]. If this demand is not met, iron deficiency may occur, potentially affecting not only pregnancy outcomes but also long-term child development [10-12]. Despite routine use of oral iron, many women experience gastrointestinal side effects—such as nausea, vomiting, or diarrhea—that impair adherence and limit

effectiveness [9,13,14]. For women with severe IDA or those who cannot tolerate oral supplements, intravenous (IV) iron is often recommended [13-16].

Ferric carboxymaltose (FCM) is a newer IV iron preparation with high bioavailability and a favorable safety profile. It allows for a large single dose (up to 1000 mg) to be infused over a short period, reducing treatment time and improving compliance [17-18]. The FER-ASAP trial showed that FCM led to faster and more effective anemia correction than oral ferrous fumarate, with fewer gastrointestinal side effects [19]. This randomized controlled study is designed to compare the efficacy and safety of injectable ferric carboxymaltose with oral ferrous fumarate in treating iron deficiency anemia among pregnant women, aiming to inform better clinical decision-making and improve maternal outcomes.

OBJECTIVE

To compare the injection ferric carboxy maltose and oral iron in treating iron deficiency anaemia during pregnancy.

METHODS

This randomized controlled trial was conducted over nine months at the Department of Obstetrics and Gynecology, Institute of Child and Mother Health, following protocol approval. A total of 156 pregnant women, between 16 and 34 weeks of gestation, diagnosed with iron deficiency anemia (Hb <11 g%, low serum ferritin, and microcytic hypochromic anemia on peripheral smear), and meeting inclusion and exclusion criteria, were enrolled through purposive sampling and randomly allocated into two groups. Exclusion criteria included Hb >11 g% or <7 g%, serum ferritin ≥15 mcg/L, prior oral or injectable iron therapy, allergy history, non-IDA anemia, current myelosuppressive drugs, recent blood transfusion, or erythropoietin use. Baseline data on socio-demographic and clinical variables were collected using a semi-structured questionnaire, including obstetric and medical histories. Group A received oral ferrous fumarate (200 mg with 0.4 mg folic acid) twice daily for six weeks, instructed to avoid interfering substances like tea and dairy. Group B received a single dose of 1000 mg IV ferric carboxymaltose (FCM) diluted in 250 ml normal saline over 20 minutes, under supervision, with post-infusion observation for adverse events. Treatment outcomes were evaluated at six weeks by comparing changes in hemoglobin, serum ferritin, and TIBC. Adverse events were monitored and documented. Data were collected using a checklist and informed consent forms in Bengali and English. All collected data were verified and analyzed using SPSS version 26. Descriptive statistics (mean, SD, frequency, percentage) were used for variable presentation. Chi-square tests were used for categorical variables, independent and paired sample t-tests for continuous variables, and a p-value <0.05 was considered statistically significant. Ethical clearance was obtained from the Institutional Review Board, and informed consent was secured from each participant, ensuring confidentiality, voluntary participation, and the right to withdraw at any stage.

RESULTS

Table 1: Baseline socio-demographic and obstetric characteristics of study participants in Group A and Group B (n=156)

Variables	Group A (n=78) n (%)	Group B (n=78) n (%)	P value
Age (mean±SD)	26.19±6.08	27.10±5.8	0.340
Education			
Illiterate	4(5.1)	12(15.4)	0.105
Below SSC	20(25.6)	25(32.1)	
Secondary	29(37.2)	18(23.1)	
HSC	14(17.9)	15(19.2)	
Graduate and above	11(14.1)	8(10.3)	
Residence			
Urban	42(53.8)	32(41.0)	0.215
Rural	24(30.8)	34(43.6)	
Slum	12(15.4)	12(15.4)	
Parity			
Nullipara	26(33.3)	15(19.2)	0.101
Primipara	29(37.2)	27(34.6)	
Multipara	21(26.9)	31(39.7)	
Grand multipara	2(2.6)	5(6.4)	
Gravida			
Primi gravida	26(33.3)	16(20.5)	0.071
Multigravida	52(66.7)	62(79.5)	
History of previous delivery			
Vaginal delivery	29(37.2)	37(47.4)	0.125
Instrumental delivery	4(5.1)	1(1.3)	

LUCS	19(24.4)	24(30.8)	
No previous child	26(33.3)	16(20.5)	
Age of last child	3.9±2.37	3.8±2.4	0.885
Menstrual cycle			
Regular	45(57.7)	37(47.4)	0.200
Irregular	33(42.3)	41(52.6)	
Contraceptive history			
None	19(24.4)	27(34.6)	0.437
Barrier	22(28.2)	20(25.6)	
Oral	24(30.8)	17(21.8)	
Injectable	13(16.7)	14(17.9)	

Group A= Respondents receiving oral Ferrous Sulphate (FS)
Group B= Respondents receiving Injection Ferric carboxy maltose (FCM)

Table 1 shows that there were no statistically significant differences between Group A and Group B in terms of age, education level, residence, parity, gravidity, delivery history, menstrual regularity, or contraceptive use ($p > 0.05$ in all comparisons).

Table 2: Mean hemoglobin levels at baseline and after 6 weeks of treatment in ferrous fumarate and ferric carboxymaltose groups (n=156)

Groups	Hemoglobin		Mean Difference	*p*-value
	Baseline Mean±SD	After 6 weeks Mean±SD		
Group A FF (n=78)	9.117 ± 1.166	10.135 ± 1.027	1.018	<0.001*
Group B FCM (n=78)	9.690 ± 1.313	11.655 ± 1.262	1.664	<0.001*

p-value obtained using paired t-test

Both treatment groups showed a statistically significant increase in hemoglobin after 6 weeks ($p < 0.001$). The ferric carboxymaltose group had a greater mean rise (1.664 g/dL) compared to the ferrous fumarate group (1.018 g/dL), indicating a more effective response with injectable FCM.

Table 3: Mean serum ferritin levels at baseline and after 6 weeks of treatment in ferrous fumarate and ferric carboxymaltose groups (n=156)

Groups	Serum Ferritin		Mean Difference	*p*-value
	Baseline Mean±SD	After 6 weeks Mean±SD		
Group A FF (n=78)	11.627 ± 2.609	216.846 ± 39.111	205.219	<0.001*
Group B FCM (n=78)	11.287 ± 2.607	238.654 ± 61.447	227.367	<0.001*

p-value obtained using paired t-test

Serum ferritin levels significantly increased in both groups after 6 weeks of treatment ($p < 0.001$). The ferric carboxymaltose group showed a greater mean rise (227.367 ng/mL) compared to the ferrous fumarate group (205.219 ng/mL), indicating a more substantial replenishment of iron stores with FCM.

Table 4: Comparison of Total Iron Binding Capacity (TIBC) between baseline and 6 weeks in two Groups (n=156)

Groups	TIBC		Mean Difference	*p*-value
	Baseline Mean±SD	After 6 weeks Mean±SD		
Group A FF (n=78)	342.9 ± 134.2	313.24 ± 133.7	−29.67	0.084
Group B FCM (n=78)	344.6 ± 137.9	297.50 ± 123.6	−47.06	0.013*

p-value obtained using paired t-test

TIBC decreased in both groups after treatment, but the reduction was statistically significant only in the ferric carboxymaltose group (mean difference = −47.06, $p = 0.013$). The ferrous fumarate group showed a non-significant change ($p = 0.084$), suggesting more effective correction of iron deficiency with FCM.

Table 5: Assessment of Anemia Correction at 6 Weeks After Treatment Among FF and FCM Groups

Hemoglobin at 6 weeks	Group A FF (n =78) n (%)	Group B FCM (n = 78) n (%)	Total (n = 156) n (%)	*p*-value
≥ 11 gm%	35 (44.9%)	51 (65.4%)	86 (55.1%)	0.010
< 11 gm%	43 (55.1%)	27 (34.6%)	70 (44.9%)	
Total	78 (100%)	78 (100%)	156 (100%)	

p-value obtained using Chi-square test

After 6 weeks of treatment, a significantly higher proportion of participants in the ferric carboxymaltose group (65.4%) achieved hemoglobin ≥11 g/dL compared to the ferrous fumarate group (44.9%), with the difference being statistically significant (p = 0.010).

Table 6: Comparison of side effects observed during treatment of iron deficiency anemia in pregnancy between ferrous fumarate and ferric carboxymaltose groups (n=156)

Side effects*	Group A (n=78) n (%)	Group B (n=78) n (%)	p-value
Gastrointestinal disorders			
Vomiting	6 (7.7)	0	0.012
Diarrhea	5 (6.4)	0	0.023
Abdominal cramp	4 (5.1)	0	0.043
Unpleasant test	4 (5.1)	0	0.043
General disorders and administration-site conditions			
Injection site pain	0	3 (3.8)	0.081
Hyperpyrexia	0	2 (2.6)	0.155
Shivering	0	2 (2.6)	0.155

*Multiple responses were considered.
p-value obtained using Chi-square test
Group A= Respondents receiving oral Ferrous Fumerate (FF)
Group B= Respondents receiving Injection Ferric carboxy maltose (FCM)

Gastrointestinal side effects—including vomiting, diarrhea, abdominal cramps, and unpleasant taste—were reported exclusively in the ferrous fumarate group and were statistically significant (p < 0.05). Injection-related reactions (pain, hyperpyrexia, shivering) occurred only in the ferric carboxymaltose group but were not statistically significant. Overall, FCM was better tolerated than FF.

DISCUSSION

Anemia in pregnancy remains a major global health issue, with significant risks for both mother and fetus.[20] Iron supplementation is essential for managing iron deficiency anemia (IDA) during pregnancy. This study compared the effectiveness of injectable ferric carboxymaltose (FCM) and oral ferrous fumarate (FF) in treating IDA.

Participants in both groups were predominantly young, with a mean age around 27 years- consistent with the typical reproductive age range and findings by Jose *et al.,*[21], who reported similar age distributions. Most participants were from urban areas and had primary or secondary education, reflecting socio-demographic patterns commonly associated with anemia in pregnancy. This aligns with Suryanarayana *et al.,*[22], who noted higher prevalence among women aged 21–30 years with lower education levels. These characteristics underline the importance of targeted interventions for younger, less-educated pregnant women in urban and peri-urban settings.

Obstetrically, most participants in the oral iron group were primiparous, while the injectable ferric carboxymaltose group included more multiparous women. Delivery history varied across both groups, with a mix of vaginal and cesarean births. These findings align with a similar study where the mean gravidity was 3.66 ± 0.97 and 3.37 ± 0.74, and mean parity was 2.5 ± 0.88 in Group A and 2.2 ± 0.65 in Group B, respectively. [23] These demographic and obstetric profiles are crucial for designing appropriate treatment strategies for pregnant women with anemia.

Regarding menstrual history, 52.6% of women in the FCM group reported irregular cycles, while overall, 52.56% of all participants had regular cycles. Oral contraceptive use was more common among the oral iron group (30.8%), whereas most women in the FCM group reported no contraceptive use. Menstrual and reproductive history is important, as higher parity (p = 0.023) and prolonged menstrual bleeding (>5 days, p = 0.042) have been identified as risk factors for anemia during pregnancy.[24] Additionally, multigravidity,

short birth intervals, and gestational duration have also been linked to increased risk of anemia.[22]

The study found no significant differences in past medical history between the oral iron and FCM groups. However, comorbidities such as hypertension and diabetes were present in both groups-conditions commonly seen in pregnancy that can complicate the management of iron deficiency anemia (IDA). These findings emphasize the need for comprehensive antenatal care that includes screening and management of underlying health issues to optimize maternal outcomes. In terms of treatment efficacy, FCM demonstrated superior performance over oral ferrous fumarate. It resulted in a significantly greater increase in hemoglobin and a notable reduction in total iron-binding capacity (TIBC), which suggests more effective iron repletion. Although both groups showed improved serum ferritin levels after treatment, the FCM group had a higher mean increase, reflecting a stronger physiological response. At the 6-week follow-up, a greater proportion of participants in the FCM group achieved anemia correction compared to those receiving oral iron. These results are consistent with findings by Breymann *et al.,*[25], who reported that while both treatments improved hemoglobin levels, significantly more women in the FCM group reached the target Hb ≥11.0 g/dL (84% vs. 70%; p = 0.031) and in a shorter timeframe (median 3.4 vs. 4.3 weeks). Other studies have also reported higher increases in hemoglobin, serum ferritin, and improved iron-binding capacity with FCM compared to oral iron therapy. [26,27,28]

While FCM proved more effective in correcting anemia, it was associated with some mild adverse effects, indicating a trade-off between efficacy and tolerability. Gastrointestinal side effects—such as nausea, vomiting, diarrhea, abdominal cramps, and unpleasant taste—were reported only among participants receiving oral iron. In contrast, the FCM group experienced no gastrointestinal complaints but did report minor injection-related side effects, including injection site pain (3 cases), hyperpyrexia (2 cases), and shivering (2 cases). No such events were reported in the oral iron group. These findings are consistent with Breymann *et al.,*[25], who observed that treatment-related adverse events occurred in 14 FCM and 19 FS recipients, with gastrointestinal disorders significantly more frequent among FS users (16 vs. 3). Similarly, Vanobberghen *et al.,*[28] reported mild to moderate infusion-related reactions and a few serious adverse events in both treatment arms, reinforcing that while both therapies are generally safe, injectable iron may be better tolerated overall.

Injectable ferric carboxymaltose not only demonstrated superior efficacy in improving hematologic parameters but also caused fewer gastrointestinal side effects compared to oral iron therapy. While minor injection-related reactions were observed in the FCM group, the oral iron group experienced a higher rate of gastrointestinal discomfort. These findings support the use of ferric carboxymaltose as a more effective and better-tolerated option for the treatment of iron deficiency anemia during pregnancy.

CONCLUSION

This study demonstrates that ferric carboxymaltose is more effective and better tolerated than oral ferrous sulfate for treating iron deficiency anemia in pregnant women. Significant improvements in hemoglobin, serum ferritin, and TIBC were observed within 6 weeks of treatment, with fewer gastrointestinal side effects reported in the FCM group. These findings align with previous research and support the use of FCM as a preferred treatment option in pregnancy-related anemia, particularly when rapid correction is needed. Nonetheless, further large-scale, multicenter studies with extended follow-up are recommended to confirm these outcomes and assess long-term safety and efficacy.

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