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Original Research Article

Safety and efficacy of ferric carboxymaltose in management of iron deficiency anemia in pregnant and peripartum women

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ABSTRACT

Background: Anemia during pregnancy, often attributed to iron deficiency, poses substantial risks to both maternal and fetal health. This retrospective study aims to evaluate the safety and efficacy of intravenous ferric carboxymaltose (FCM) in managing anemia among pregnant women.
Methods: The study encompasses women who received FCM treatment for anemia during pregnancy between October 2023 and March 2024 at SSG hospital, Vadodara. Key outcomes evaluated include maternal safety and pregnancy outcomes. Prospective observational study; Treatment effectiveness was assessed by repeat hemoglobin (Hb) measurements and patient report of well-being in the postpartum period. Safety was assessed by analysis of adverse drug reactions and fetal heart rate monitoring during the infusion.
Results: A total of 50 patients were included. The intravenous administration of FCM notably raised hemoglobin levels in all pregnant female participants compared to initial levels. Monitoring of fetal heart rate showed no adverse effects attributable to the medication. No severe side effects were observed.
Conclusions: This prospective observational study suggests that FCM represents a safe and effective therapeutic option for managing anemia during pregnancy. Despite study limitations, the findings underscore the potential of FCM in addressing this prevalent concern, advocating for its consideration in clinical practice.

Keywords: Ferric carboxymaltose, Iron deficiency anemia, Pregnant women

INTRODUCTION

Iron deficiency anemia (IDA) remains a significant public health concern, particularly among pregnant women, posing substantial risks to maternal and fetal health. In India, where the burden of anemia is disproportionately high, the impact on maternal and child mortality rates is profound. According to national health data, iron deficiency anemia affects a substantial portion of pregnant women across the country, necessitating urgent attention and effective intervention strategies.

Statistics from the National Family Health Survey (NFHS) and other national health databases underscore the severity of the issue. NFHS-4 data revealed that approximately 50% of pregnant women in India were anemic, with iron deficiency identified as a leading cause. Furthermore, the prevalence of anemia varied significantly across different regions, with some states reporting rates exceeding 60%.[1]

The consequences of iron deficiency anemia during pregnancy are far-reaching and multifaceted. Maternal complications include increased risk of preterm birth, low

birth weight, and maternal mortality. Fetal and neonatal outcomes are also adversely affected, with implications for long-term health and development. These statistics highlight the urgent need for targeted interventions to address iron deficiency anemia among pregnant women in India.[2]

During pregnancy, the physiological need for absorbed iron increases from 0.8 mg/day in the first trimester to 7.5 mg/day in the third trimester.[3] Dietary iron intake does not compensate for this strongly increased iron demand. Consequently, the risk of iron deficiency and, ultimately, iron deficient anemia increases during pregnancy.

General symptoms of anemia are fatigue, dizziness, and impaired immune response predisposing to infections.[4] Anemia during pregnancy is associated with increased morbidity and mortality of pregnant women and their developing fetuses.[5] Iron deficiency anemia has been shown to be associated with an increased risk of premature birth and low birth weight, preeclampsia, placental abruption, and increased peripartum blood loss as well as cardiac failure and related death.[6-11]

METHODS

Study design and patients

The indoor patients of the Department of OBGY at a tertiary care hospital, SSG hospital, Vadodara admitted in the period of October 2023 to March 2024 were included in this prospective observational study. All women who received administration of injection FCM during their pregnancy and/or postpartum period were eligible for this study.

Treatment characteristics

Pregnant patients with anemia were treated according to the local protocol. The institutional anemia cutoff value throughout advanced gestation is approximately 9.0 g/dl (1.0 g/dl=0.62 mmol/l). According to the local protocol, pregnant women with anemia are treated with oral iron (ferrous fumarate, one 200 mg tablet per day) and switched to i.v. iron, if Hb remains <9.0 g/dl despite oral medication. FCM is the institution's first choice i.v. iron agent since 2010, regardless of iron status. The maximum weekly dose of FCM is 1000 mg (up to 20 mg/kg body weight) in a single infusion given over at least 15 minutes.

Outcome measures

Demographic characteristics and baseline data included maternal age, gestational age, educational level, and results from peripheral blood counts. Hb was rechecked after a period of 2 weeks to gauge the efficacy of FCM. Outcome data were collected on adverse events and pregnancy outcomes. Adverse events (AEs) in FCM-treated patients were defined as allergic or hypersensitivity reactions during or after the infusion of FCM. Assessed pregnancy outcomes were intrauterine growth retardation (IUGR), Hb at delivery, need for blood transfusion (BT), fetal weight, etc. were considered.

The local protocol for iron treatment requires minimal diagnostics and follow-up assessment of hematologic iron status parameters. For this reason, Hb measurements and Mean Corpuscular Volume (MCV) were recorded at FCM treatment and Hb measurements at delivery.

Statistical analysis

No formal sample size calculation was made, since all FCM-treated women who fulfilled the inclusion criteria were included. Safety and efficacy were analyzed using descriptive statistics.

RESULTS

We identified 50 women who received FCM between October 2023 to march 2024 at our institution. 50 women who received injection FCM in the course of 6 months at our hospital were included in this study, of which 12 women received Inj. FCM post-partum. Demographic characteristics such as age, gravida, antenatal/postnatal period, gestational age, Hb on admission, rise in Hb after FCM infusion and perinatal outcomes were studied. 8 of the total number of patients included in this study required blood transfusion in addition to FCM infusion, owing to severe IDA in their cases. Demographic characteristics such as age (median: 27 years), parity (median 1), number of fetuses (singleton pregnancies: 92%), percentage of patients with lower educations (20%) and prevalence of comorbidities (20%) were noted (Table 1). Individual comorbidities were present at low frequency and none of the comorbidities was dominant (1-2 patients per comorbidity).

Table 1: Age distribution.

Age (years)	Number (n=50)	Proportion (%)
18-25	30	60
26-34	16	32
>34	4	8

Demographics

Amongst the total 50 patients, 30 were in the age group of 18-25 years, 16 in the age group of 26-34 years, and 4 were above 34 years.

Of the 38 women who received inj. FCM in their antenatal period, 4 were primigravidae, and the rest were multigravidas (Table 2).

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Table 2: Obstetric history.

Gravida (antenatal)	Number (n=38)	Proportion (%)
Primi gravida	4	10.52
Second gravida	8	21.05
Third gravida	11	28.94
Fourth gravida and above	15	39.47

Table 3: Association between gravida score and anemia.

Gravida	Average hemoglobin levels (gm/dl)
Primigravidae	8.2
Multigravidae	6.0

Table 4: Hemoglobin levels on admission.

Hemoglobin levels on admission (gm/dl)	Number (n=50)	Proportion (%)
8	30	60
8-9	20	40

The number of patients with hemoglobin of less than 8 gm/dl on admission, was 30, and those with hemoglobin ranging between 8 gm/dl and 9 gm/dl were 20 (Table 4).

Those who were administered injection FCM at the gestational age of 28-32 weeks were 11 in number. 21 patients were given FCM infusion at the gestational age of 32.1 weeks to 36 weeks, and 6 patients received it beyond the gestational age of 36 weeks. 12 of the total patients included in this study were given FCM infusion in their post-natal period (Table 5).

Table 5: Gestational age at the time of FCM infusion.

Status at the time of FCM infusion	Number (n=50)	Proportion (%)
28-32 weeks antenatal	11	22
32.1-36 weeks antenatal	21	42
>36 weeks antenatal	6	12
Postnatal	12	24

Table 6: Rise in hemoglobin levels.

Rise in hemoglobin levels (gm/dl)	Number (n=50)	Proportion (%)
<1	8	16
1.1 – 2	30	60
>2	12	24

The rise of hemoglobin observed post injection FCM infusion was up to 2.5 gm/dl. 8 women had a rise of more than 2 gm/dl, 30 women had a rise of 1.1 to 2 gm/dl and the rest 12 had an increment of less than 1 gm/dl in their hemoglobin levels (Table 6).

DISCUSSION

In pregnant women, oral iron is often used for prophylaxis of iron deficiency and is recommended as first-line treatment for pregnant women with iron deficiency anemia.[12] However, oral iron substitution has shown to be insufficient for the treatment of severe iron deficiency anemia and is often associated with gastrointestinal side effects.[13] Therefore, guidelines recommend that physicians consider intravenous (i.v.) iron administration in pregnant women with severe iron deficiency anemia (Hb <9.0 g/dL), and in case of intolerability to oral iron as well, insufficient Hb increase after oral iron treatment or if there is a need for rapid Hb reconstitution.[12-14] Intravenous (i.v.) iron preparations provide greater and more rapid repletion of iron stores than oral iron therapy without the gastrointestinal side effects associated with oral substitution.[13]

Ferric carboxymaltose (FCM) is an I.V iron formulation which can be used at high doses and allows rapid administration (up to 1000 mg in a single dose infused in 15 min). Because it is free of dextran and its derivatives, FCM does not cross-react with dextran antibodies , and never needed the administration of a test dose.[15,16] More recently, the European Medicines Agency (EMA) concluded that no test dose should apply to I.V. iron products authorized in the European Union; yet staff and facilities to evaluate and manage anaphylactic or anaphylactoid reactions should be immediately available.[17] The FCM molecules consist of an iron-hydroxide core chelated in a carbohydrate shell and this complex is taken up as a whole by macrophages, leading to very low levels of non-transferrin bound iron, avoiding iron toxicity and oxidative stress.[16] FCM's clinical efficacy and safety have been proven in several large clinical studies across different indications with up to one-year follow-up in severe disease types such as chronic kidney disease and chronic heart failure.[12,18-24] At least four postpartum studies compared the safety and efficacy of FCM versus oral iron.[13,23,24] Faster and greater Hb-responses were achieved in FCM-treated patients compared to those receiving oral iron and FCM replenished iron stores efficiently. Rather few studies or cases with limited numbers of FCM-treated pregnant women have been reported.[14-16]

This observational study explored the effectiveness and safety of ferric carboxymaltose (FCM) for treating iron deficiency anemia (IDA) during the peripartum period. The study demonstrated that FCM administration significantly raised hemoglobin levels both during pregnancy and the postpartum period. The mean gestational age at FCM infusion was 33.4 weeks, and the average hemoglobin increase was 1.4 g/dl, rising from 7.8 g/dl to 9.2 g/dl. No adverse events related to FCM

treatment were observed, and all patients recovered smoothly post-infusion.

These results align with previous studies that highlighted the rapid and substantial improvement in hemoglobin levels following FCM administration. A study by Breymann et al reported similar findings, showing effective hemoglobin increase with minimal side effects in pregnant women treated with FCM for IDA.[5] Another study by Milman et al corroborated these results, demonstrating that FCM effectively managed severe iron deficiency anemia, especially when oral iron treatments were insufficient.[3]

The need for blood transfusions in eight patients in this study underscores the challenge of severe IDA management. Despite the efficacy of FCM, some cases still required additional intervention, which is consistent with findings from studies by Scholl et al and Zhang et al that highlighted the complexities of managing severe anemia during pregnancy.[6,7]

In terms of safety, the absence of severe adverse effects in our study supports previous reports on the safety profile of FCM. Auerbach and Macdougall emphasized that FCM has a low risk of anaphylactic reactions and is generally well-tolerated, making it a suitable option for pregnant women.[15] Additionally, the lack of significant gastrointestinal side effects, a common issue with oral iron, reinforces the preference for intravenous administration in severe cases.

Several limitations should be acknowledged in this study. Firstly, the sample size was relatively small, limiting the generalizability of the findings. Additionally, the study was conducted in a single tertiary care hospital, which may not reflect broader demographic and regional variations. The lack of a control group also restricts the ability to draw definitive conclusions about the comparative efficacy of FCM versus other treatments. Furthermore, cost concerns and availability of FCM may limit its widespread adoption in similar settings. Future studies with larger sample sizes, multiple centers, and control groups are needed to validate these findings and explore long-term outcomes of FCM treatment in pregnant women with IDA.

CONCLUSION

This prospective observational study suggests that FCM is a safe and effective therapeutic option for managing iron deficiency anemia during pregnancy and the postpartum period. The treatment significantly increases hemoglobin levels with minimal adverse effects, reducing the need for blood transfusions in mild to moderate IDA cases. These findings advocate for the consideration of FCM in clinical practice for pregnant women with severe IDA or intolerance to oral iron.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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