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Original Research Article

# Comparison of Intravenous Iron Sucrose and Intravenous Ferric Carboxymaltose for Treatment of Iron Deficiency Anemia in Pregnant Women: A Study from A Tertiary Care Hospital in Central India

**Mohit Garg[1], Pankaj Kumar Jain[1], Rounak Munshi[2], Utkarsh Tripathi[3]**

[1]Assistant Professor, Department of Medicine, NSC Government Medical College, Khandwa, Madhya Pradesh, India

[2]Senior Resident, Department of Obstetrics and Gynaecology, NSC Government Medical College, Khandwa, Madhya Pradesh, India

[3]Senior Resident, Department of Medicine, NSC Government Medical College, Khandwa, Madhya Pradesh, India

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**Corresponding author: Dr Utkarsh Tripathi**

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**Abstract**

**Background and Objectives:** Iron deficiency is a prevalent global nutritional insufficiency that often leads to antenatal anemia. This study aims to evaluate the effectiveness and safety of intravenous Ferric Carboxymaltose (FCM) compared to intravenous Iron sucrose complex (ISC) in managing iron deficiency anemia during pregnancy, as per the classification of the World Health Organization (WHO) based on hemoglobin levels below 11 g/dL, with severe anemia defined by hemoglobin levels below 9 g/dL.

**Materials & Methods:** An interventional prospective study was conducted at the Department of Obstetrics and Gynecology, Government Medical College from Central India. The study enrolled a total of 100 antenatal patients diagnosed with anemia, characterized by hemoglobin levels ranging from 5 to 9.5 g/dL. The participants were randomly assigned to two groups: the first group received a total of 1000 mg of intravenous iron sucrose administered in five divided doses on alternate days (200 mg per dose), while the second group received 1000 mg of intravenous ferric carboxymaltose.

**Results:** The majority of patients in our study belonged to the low socioeconomic group. A significantly higher number of women in the ferric carboxymaltose (FCM) group achieved a rise in hemoglobin levels of more than 2 g/dL, which was highly significant. The mean rise in hemoglobin was 2 g/dL in the FCM group and 1.7 g/dL in the iron sucrose group, which was also statistically significant. Furthermore, the ferric carboxymaltose group exhibited a greater increase in serum ferritin levels compared to the iron sucrose group.

**Conclusion:** Ferric carboxymaltose emerges as an effective and preferable alternative to Iron Sucrose in the treatment of iron deficiency anemia during pregnancy. It offers the advantage of a single-dose regimen with reduced incidence of side effects.

**Keywords:** Iron sucrose, Pregnancy, Ferric carboxymaltose, Iron deficiency anemia, India.

## Introduction

Iron deficiency is a prevailing nutritional insufficiency that has a significant global impact, affecting approximately 1.6 billion individuals, which accounts for nearly a quarter of the world's population [1]. It is commonly observed in various population groups, including children, women with abnormal uterine bleeding (AUB), pregnant women, and individuals in the postpartum period [2, 3]. Iron deficiency (ID) and iron deficiency anemia (IDA) are frequently encountered in these populations, highlighting the importance of addressing this issue to promote optimal health outcomes.

Iron plays a crucial role as the functional component of hemoglobin and is an essential constituent of numerous enzymes involved in key metabolic pathways [4]. Therefore, reduced iron levels can impair energy production, leading to various symptoms. Common manifestations of iron deficiency (ID) include fatigue, exhaustion, increased susceptibility to stress, and decreased performance. Additionally, ID has been associated with diminished mental and cognitive function, difficulties with concentration, and heightened vulnerability to infections. These detrimental effects highlight the importance of maintaining adequate iron levels for optimal physiological functioning and overall well-being [5–8].

To ensure the bioavailability of a parenteral iron formulation, it is necessary to incorporate iron (III) oxyhydroxide complexed with a protein or carbohydrate molecule. This complexation serves to prevent the release of free iron, which has the potential to induce oxidative damage to body tissues. The iron complex functions similarly to ferritin, which is the natural carrier of iron in the body. Like ferritin, this iron complex contains iron (III) hydroxide at its core within the Apo ferritin molecule. By resembling ferritin, these iron complexes enable the delivery of iron to the physiological transport system at a neutral pH level [9].

FCM (Ferric Carboxymaltose), classified as a Type I complex, exhibits a gradual and targeted delivery of iron primarily to the reticuloendothelial system (RES) of the liver. This controlled and slow release mechanism contributes to the low toxicity of FCM and ensures a significant safety margin, with recommended clinical dosing reaching up to 66 times the maximum weekly dose and 5 times greater than the lethal dose for iron sucrose. Furthermore, the formulation of FCM is characterized by its neutral pH and physiological osmolarity, allowing for high doses to be administered while maintaining good local tolerance. As long as the iron dose is individually calculated based on each patient's requirements, the likelihood of toxicity during the clinical use of FCM is minimal. Unlike iron dextran, ferumoxytol, and iron isomaltoside 1000, FCM does not contain dextran or its derivatives, thereby significantly reducing the risk of dextran-induced anaphylactic reactions. Additionally, FCM exhibits a very low potential for immunogenicity, further contributing to its excellent safety profile. This advantageous characteristic not only ensures convenience for both patients and medical professionals but also enhances the cost-effectiveness of iron replacement therapy. Furthermore, the ability to administer large doses in a single session adds to the overall convenience and efficiency of treatment [10].

## Material & Methods

The study was conducted as a prospective comparative interventional analytical study in the department of Obstetrics and Gynecology at a Government medical college in Central India. The study spanned a period of one year, from October 2020 to August 2021. The study was done in a adhering to the principles outlined in the Declaration of Helsinki [11]. All procedures conducted during this study

were in full compliance with the guidelines and regulations set forth by the Institutional Ethics Committee for Human Research (IECHR). Prior to their participation, informed consent was obtained from all patients, ensuring that they were fully informed about the study's objectives, procedures, potential risks, and benefits. The informed consent process ensured that the patients voluntarily agreed to participate in the study based on their understanding of the information provided. Respecting the principles of autonomy and patient rights, informed consent was a crucial step in ensuring ethical conduct throughout the study.

The study participants were purposively classified into two groups using Epi info version 3.1 software. Each group consisted of 50 pregnant women with a gestational age between 28-32 weeks who had been diagnosed with iron deficiency anemia, with hemoglobin levels ranging from 5-9.5 g%. Group 1 comprised of 50 cases who received intravenous iron sucrose therapy, while Group 2 included 50 cases who received intravenous iron carboxymaltose therapy.

**Inclusion & Exclusion criteria:**

The inclusion criteria for the study involved 100 pregnant women at a gestational age of 28-32 weeks with hemoglobin levels ranging from 5 to 10 gm% and diagnosed with iron deficiency anemia during pregnancy. The exclusion criteria for this study involved the careful selection of participants. Individuals with anemia not caused by iron deficiency were excluded, ensuring that the focus remained on iron deficiency anemia specifically. Moreover, individuals with a known hypersensitivity or allergic reaction to Ferric Carboxymaltose (FCM) or Iron Sucrose were excluded to prevent any potential adverse reactions. Participants with sickle cell disease, a genetic disorder affecting the red blood cells, were also excluded to maintain a homogeneous study population. Lastly, individuals who did not provide informed consent were not included in the study, emphasizing the importance of ethical considerations and voluntary participation

**Iron therapy:** Group 1 received intravenous injections of iron sucrose complex. The iron sucrose complex was administered as 200 mg of elemental iron, which was prepared by combining two ampules of 5 ml each, in 100 ml of 0.9% normal saline. The infusion was given over a duration of 30 minutes, and this treatment was repeated every alternate day for a total of five doses. On the other hand, Group 2 received intravenous injections of iron carboxymaltose complex.

In addition to the iron interventions, all the women in the study were also prescribed a daily dose of 5 mg of folic acid. Throughout the study, any minor or major adverse effects experienced by the participants were carefully observed and recorded. Follow-up assessments were conducted at 4 weeks and 90 days after the initiation of treatment. During these follow-up visits, hemoglobin levels, red blood cell (RBC) indices, and serum iron studies were measured. Patients reported any adverse events they experienced during these visits. The primary outcome of the study was the change in hemoglobin levels from baseline after 90 days. Secondary outcomes included changes in ferritin levels, improvements in serum iron studies and RBC indices, evaluation of the safety and side effects of the treatments, and assessment of perinatal outcomes. These measures allowed for a comprehensive evaluation of the effectiveness, safety, and impact of the interventions on the participants' health and well-being.

Statistical Analysis:

The data obtained from the study were presented in the form of number (%) for categorical variables and mean ± standard deviation for continuous variables, depending on the nature of the data. To compare baseline categorical variables

between the groups, the Chi-square test or Fisher's exact test was used. Continuous variables were compared using Student's t-test. A p-value of less than 0.05 was considered statistically significant.

## Results

Table 1 shows severity wise distribution of study population. The study found that the mean hemoglobin level in the Ferric carboxymaltose group was 10.10 ± 0.64 gm%, while in the Iron sucrose group it was 9.85 ± 0.76 gm%. There was a statistically significant difference in the distribution of hemoglobin between the two groups ($p < 0.05$), as indicated in Table 2. This finding suggests that the use of Ferric carboxymaltose was associated with a higher mean hemoglobin level compared to the use of Iron sucrose in the treatment of iron deficiency anemia.

The study revealed that the mean serum ferritin level in the Ferric carboxymaltose group was 97.55 ± 22.18 (mg/L), whereas in the Iron sucrose group it was 23.15 ± 3.75 (mg/L). The distribution of serum ferritin between the two groups showed a statistically significant difference ($p < 0.05$), as indicated in Table 3. This finding suggests that the use of Ferric carboxymaltose was associated with a higher mean serum ferritin level compared to the use of Iron sucrose in the treatment of iron deficiency anemia. Table 4 shoes the adverse drug reaction profile of both drugs.

**Table 1: Severity of Anaemia cases**

| Hemoglobin (gm/dl) | Severity of Anaemia | IV Iron Sucrose | IV Ferric Car boxy Maltose (FCM) | Total | P value |
|---|---|---|---|---|---|
| < 6 | Severe | 1 | 4 | 5 | > 0.05 |
| 6 -7.9 | Moderate | 29 | 15 | 44 | |
| 8-9.5 | Mild | 20 | 31 | 51 | |
| **Total** | | **50** | **99** | **100** | |

**Table 2: Mean Haemoglobin (gm/dl) values in both groups**

| Hemoglobin (gm/dl) | IV Iron Sucrose | IV Ferric Car boxy Maltose (FCM) | P value |
|---|---|---|---|
| Before treatment | 7.56 | 7.45 | **< 0.05** |
| 4 weeks pot treatment | 9.45 | 9.76 | |
| 90 days post treatment | 10.1 | 9.95 | |

**Table 3: Mean serum ferritin values in both groups**

| Serum ferritin (mg/dl) | IV Iron Sucrose | IV Ferric Car boxy Maltose (FCM) | P value |
|---|---|---|---|
| Before treatment | 20.25 | 19.77 | > 0.05 |
| 90 days post treatment | 97.55 | 23.15 | **< 0.05** |

**Table 4: Adverse drug reactions in both groups**

| ADRs | IV Iron Sucrose | IV Ferric Car boxy Maltose (FCM) | Total |
|---|---|---|---|
| Pain/burning at injection site | 8 | 5 | 13 |
| Swelling at injection site | 4 | 1 | 5 |
| Blackening at injection site | 0 | 0 | 0 |
| Nausea/vomiting | 5 | 1 | 6 |
| Gastritis | 3 | 1 | 4 |
| Giddiness/hypotension | 1 | 1 | 2 |
| Other | 0 | 0 | 0 |
| **Total** | **21 (42%)** | **9 (18%)** | **30 (30%)** |

## Discussion

The present study demonstrated that both iron sucrose complex and ferric carboxymaltose are effective in treating iron deficiency anemia during pregnancy. These treatments not only corrected the deficit in hemoglobin levels but also replenished iron stores. Both modalities showed an increase in hemoglobin levels after 4 weeks and after 90 days, consistent with findings from previous studies [12-16]. These results highlight the potential of both iron sucrose complex and ferric carboxymaltose as viable options for managing iron deficiency anemia in pregnant patients, providing evidence for their efficacy in improving hemoglobin levels and iron status.

In the present study, it was observed that the increment in hemoglobin levels was slightly higher in patients treated with ferric carboxymaltose (FCM) compared to those treated with iron sucrose. Similarly, serum ferritin levels showed a greater increase in patients receiving FCM. Adverse events reported during the study were mild and reversible, mainly limited to local reactions at the infusion site. No serious adverse events related to the treatment were recorded, and there were no instances of anaphylactic reactions or venous thrombosis. None of the adverse events required additional medical intervention. Apart from the hematological effectiveness, the study also highlighted several additional advantages of FCM over iron sucrose.

FCM demonstrated a significantly reduced burden of treatment compared to iron sucrose. Despite achieving comparable improvements in hemoglobin levels, FCM required a much lower total dose and shorter duration of exposure. This finding is particularly important as it suggests that FCM offers a more convenient treatment option for patients, potentially improving their compliance with medication. In real-world settings, a high burden of treatment can often lead to low patient compliance, resulting in the exacerbation of the disease and increased healthcare costs. Therefore, the reduced burden of treatment associated with FCM has the potential to positively impact patient outcomes and healthcare resources.

In certain patients, the administration of a single dose of FCM may effectively address iron deficiency anemia (IDA) without the need for multiple administrations, offering a more convenient alternative to iron sucrose. The pioneering study conducted by Christoph P et al. [17] was the first to explore the use of FCM for the treatment of IDA in pregnancy. The study concluded that FCM exhibited comparable safety and tolerability to ISC (iron sucrose complex) while providing the advantage of higher iron dosage in a single administration. This characteristic reduces the necessity for repeated applications and enhances patient comfort during the treatment process. In contrast to the previous study by Christoph P et al. [17], the current study demonstrated significantly higher hemoglobin levels in the FCM group compared to the ISC group after a duration of 90 days. This finding indicates that FCM was more effective in raising hemoglobin levels in the study participants. The results of the current study diverge from the previous findings, possibly due to differences in patient characteristics, treatment protocols, or other factors that may have influenced the outcomes.

In the present study, serum ferritin levels were similar between the two groups at baseline and at the end of the study after 12 weeks. This suggests that while FCM leads to a rapid increase in iron stores, over the long term, ISC is equally effective in providing comparable supplementation for the replenishment of iron stores. The study indicates that both FCM and ISC can effectively address iron deficiency and contribute to the restoration of iron stores in the body.

**Limitations:** Our study had several limitations, including a small sample size in

both the treatment and control groups. Additionally, certain confounding variables were not accounted for in our analysis. To obtain more robust and reliable results, larger-scale trials are needed to compare the safety and efficacy of intravenous ferric carboxymaltose with iron sucrose therapy in the specific context of the Indian population. These larger trials would provide more comprehensive insights and help establish a stronger evidence base for guiding clinical practice in this setting.

## Conclusions

This prospective study confirms that intravenous ferric carboxymaltose is a safe and effective alternative to iron sucrose for treating iron deficiency anemia in pregnant women. Ferric carboxymaltose leads to a faster increase in hemoglobin levels and iron stores compared to iron sucrose. No serious adverse effects were observed. The convenience of administering a larger dose per session reduces the number of required doses, hospital visits, and associated costs for the patient.

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