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Original Research Article

# A Comparative Study of Effectiveness and Safety of Ferric Carboxymaltose and Iron Sucrose in Treating Iron Deficiency Anemia in Pregnant Women

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**Abstract**

**Background:** The most frequent cause of anaemia in the world is iron deficiency, which has serious negative effects on both pregnant women and their unborn children. Currently available options for treatment include red blood cell transfusions, which have an inherent risk and should be avoided, oral iron supplementation, which can be ineffective and poorly tolerated, and intravenous iron, which can be used in patients who are unable to tolerate or respond to oral iron. Iron treatment administered intravenously may lessen the need for allogenic blood transfusions. A novel intravenous iron formulation called ferric carboxymaltose claims to be equally safe and effective as iron sucrose. Given that it allows for the administration of a considerably bigger iron dosage at once, it may even have better compliance. The goal of the study was to assess the effectiveness and safety of IV ferric carboxymaltose versus iron sucrose in treating mild iron deficiency anaemia in second and third trimester pregnant women.

**Methods:** From November 2021 to October 2022, the Obstetrics and Gynecology department at Darbhanga Medical College and Hospital, Laheriasarai, Bihar, conducted a hospital-based, randomised prospective study. To identify iron deficiency anaemia, baseline haemoglobin, peripheral smear, and serum ferritin levels were assessed. 120 pregnant women who met the study inclusion requirements were divided randomly into two groups, with 60 in Group C receiving ferric carboxymaltose and 60 in Group S receiving saline (Received iron sucrose). Three weeks following therapy, haemoglobin levels were measured to evaluate the outcome and compare the two groups safety and efficacy.

**Results:** The age range with the highest prevalence in the current study was 21 to 30 years, which was represented by 80% in group C and 73.3% in group S. The mean age of the study population in groups C and S was similar (25.2±3.54 vs. 24.8±4.58 years). Both groups sociodemographic traits, obstetric history, vital signs, and pretreatment haemoglobin levels were equivalent ($p>0.050$). 63.3% of the women in group C had post-treatment haemoglobin levels of 11 or greater, compared to 46.7% of the women in group S, and the mean post-treatment haemoglobin levels were similar in group C and group S (11.016±0.789 vs. 10.73±0.821 gm%; $p=0.174$). In this study, 43.3% of the women in group C had a post-treatment mean increase in haemoglobin levels between 2.0 and 2.5 gm%, compared to 50.0% of the women in group S.

**Conclusion:** Administration of ferric carboxymaltose during the second and third trimesters of pregnancy is well tolerated and has no known clinical safety issues. Even when ferric

carboxymaltose was delivered in a significantly higher dosage than iron sucrose, both ferric carboxymaltose and iron sucrose have a comparable safety profile. If intravenous iron therapy is required in the second or third trimester of pregnancy, ferric carboxymaltose should be taken into consideration as the preferred medication.

**Keywords:** Ferric Carboxymaltose, Iron Sucrose, Haemoglobin, Iron Deficiency Anemia.



## Introduction

For all types of cells in the body to operate properly, iron is a necessary ingredient. It is essential for the control of the cell cycle, respiratory chain electron transport, DNA synthesis, and other metabolic processes. The availability of iron is a key factor in how well oxygen-binding molecules like haemoglobin operate. Anaemia is a condition where there are not enough red blood cells or that they are not able to carry enough oxygen to meet physiologic requirements.[1–3] In India, it is among the most prevalent medical conditions affecting expectant mothers. Depleted iron reserves and indications of a hampered delivery of iron to the tissues accompany iron deficiency anaemia.1 Haemoglobin levels vary physiologically throughout pregnancy; at the start of a pregnancy, there is a typical decrease in haemoglobin levels, which is followed by a little rise as the pregnancy progresses due to increasing haemoconcentration.[2] The initial decline has been attributed to the fetus's demands for iron, which are greater than the mother's iron intake, leading to a decrease in the woman's body's iron reserves. [2]

The most prevalent disorder associated with nutritional deficiency is anaemia. According to estimates from the World Health Organization (WHO), the prevalence of anaemia in pregnant women in developed and developing countries is 14% and 51%, respectively. Knowing that prevalence in India is between 65 and 75 percent is concerning. [ 4]

South Asian nations have the highest prevalence of anaemia when compared to other nations. According to WHO estimations, India has the greatest prevalence of anaemia among the South Asian nations. Even more significant is the fact that South Asian nations account for nearly 50% of all maternal deaths worldwide caused by anaemia. [5]

It is clear that India contributes more than its population would suggest to the prevalence of anaemia in pregnancy and maternal fatalities caused by anaemia. 3 According to figures at hand, India experienced a smaller decline in the prevalence of anaemia during the 1990s than its South East Asian neighbours. In order to determine the prevalence of anaemia in the nation, five major surveys the National Family Health Survey (NFHS) [6] 2 and 3, the District Level Household Survey 2 (DLHS), the Indian Council of Medical Research (ICMR) [7,8] Micronutrient Survey, the National Nutrition Monitoring Bureau (NNMB) Micronutrient Survey, and the National Family Health Survey (NFHS) [9] Micronutrient Survey were carried out. The results of these surveys showed that over 70% of pregnant women and adolescent girls in the country were anaemic. Our study compares the effectiveness and safety profiles of intravenous iron sucrose and intravenous ferric carboxymaltose during pregnancy.

## Materials and Methods

From November 2021 to October 2022, this randomised prospective study was carried out at the Darbhanga Medical College and Hospital, Laheriasarai, Bihar, in the department of obstetrics and gynaecology.

Participants needed to be pregnant women between the ages of 12-36 weeks of gestation, have iron deficiency anaemia, and have haemoglobin levels between 7.0 and 9.9 gm%.

Anemia not due to iron shortage, past blood transfusions, known allergy to i.v. iron preparations, and any signs of major anomalies on anomaly ultrasonography were all exclusion criteria.

120 patients were randomly selected by computer-generated randomization from the hospital's prenatal clinic.

The subject was maskedly assigned to either the iron sucrose or iron carboxymaltose groups using a random sequence list. 60 patients received iron sucrose intravenously, while 60 patients received iron carboxymaltose intravenously.

Haemoglobin, peripheral smear and serum ferritin was estimated to diagnose iron deficiency anaemia and the iron deficit was calculated according to the formula:

Deficit = (12-Hemoglobin of the patient) × 2.4 x Weight + 500 (storage)

Group C will receive i.v. ferric carboxymaltose, whereas Group D will receive i.v. iron sucrose (Group S).

Up to the prescribed total dose, 200 mg of iron sucrose was supplied intravenously in 200 ml of normal saline over the course of 15–20 minutes on alternate days, with a weekly maximum dose of 1000 mg/week.

Ferric Carboxymaltose was administered as needed, diluted in normal saline over the course of 15-20 minutes, in a single dosage, keeping the dose under the weekly maximum of 1000 mg/day/week.

Every dose was administered in the ward, which had cardiac resuscitation equipment on hand. Patients were monitored before, during, and after the transfusion for any early or delayed adverse reactions. After three weeks, they were checked in order to estimate their haemoglobin levels and identify any changes.

In this study, the major end measure was the increase in haemoglobin levels three weeks following therapy, while the secondary outcome measures were drug side effects and treatment compliance.

Software called SPSS was used to do the statistical analysis. While continuous data was expressed as mean±standard deviation, categorical data was expressed in terms of frequencies and percentages (SD). For categorical data, the chi-square test was used to compare the two groups, and the independent sample 't' test was used to compare the means of various parameters. A "p" value ≤0.050 or less was regarded as statistically significant.

## Results

The trial had a total of 120 patients, and administered iron sucrose and ferric carboxymaltose intravenously to 60 of them. The baseline statistics and demographics did not indicate any statistical significance (Table 1).

Most of the women in the study were between the ages of 21 and 30; hence, 80% in group C and 73.3% in group S; nevertheless, this difference was not statistically significant (p= 0.581).

In groups C and S, the study population's mean ages were similar (25.2± 3.54 vs. 24.8± 4.58), with a p-value of 0.70.

**Table 1: Demographic characteristics and base data**

| | Ferric carboxymaltose (n=60) Mean±SD | Iron sucrose (n=60) Mean±SD | p-value |
|---|---|---|---|
| Age (years) | 25.2±3.547 | 24.8±4.582 | 0.707 |
| Gestational age (week) | 31.63±2.71 | 31.0±2.319 | 0.335 |
| Weight (kg) | 56.2±6.305 | 5.23±5.296 | 0.982 |
| Pre-treatment Hemoglobin (gm%) | 8.5±0.6761 | 8.38±0.7893 | 0.530 |
| Packed cell volume | 27.07±1.617 | 27.33±1.749 | 0.542 |
| Mean corpuscular volume (fl) | 75.43±3.766 | 75.93±3.805 | 0.611 |
| Mean corpuscular hemoglobin (pg) | 29.13±2.27 | 29.17±2.692 | 0.959 |
| Mean corpuscular hemoglobin concentration (g/dL) | 29.73±2.449 | 30.73±2.377 | 0.114 |
| Serum ferritin (ng/L) | 11.63±1.217 | 11.43±1.223 | 0.528 |
| Mean iron requirement (gms) | 843±101.848 | 894.2±126.397 | 0.092 |

**Table 2: Hemoglobin values after treatment**

| | Ferric carboxymaltose (n=60) Mean±SD | Iron sucrose (n=60) Mean±SD | p-value |
|---|---|---|---|
| Mean post-treatment hemoglobin (gm%) | 11.016±0.7896 | 10.73±0.8217 | 0.174 |
| Increase in hemoglobin (gm%) | 2.516±0.4218 | 2.350±0.4868 | 0.162 |

73.3% vs. 76.7% the majority of the women in groups C and S were unemployed. The study population's educational status in groups C and S was comparable (p = 0.346). The majority of the women belonged to the upper middle class; 36.7% of those in group C and 46.7% of those in group S; however, this was not statistically significant (p = 0.628). These results imply that the study population's sociodemographic traits were comparable.

In terms of obstetric history, group C (56.7%) and group S (46.7%) had the majority of primigravidae women. Nonetheless, the research population's parity status was comparable between the two groups (p = 0.314). The majority of the women in groups C (80.0%) and S (83.3%) made their appearances between 29 and 36 weeks of pregnancy (p = 0.739). Both groups mean gestational periods (31.63±2.71 in group C and 31.0±2.319 in group S) were comparable (p=0.335). These results exclude any potential bias resulting from group C and S's obstetric history.

The mean weight in the current study, which was based on a clinical examination, was comparable in both groups (p=0.982); it was 56.2±6.305 in group C and 56.23±5.296 in group S. The mean pulse rate (p = 1.000), systolic blood pressure (p = 1.000), and diastolic blood pressure (p = 1.000) on general physical examination were comparable in both groups, indicating the clinical.

Pre-treatment mean haemoglobin levels in this trial were similar in both groups (8.5±0.676 vs. 8.38±0.789 gm%; p=0.53). The mean corpuscular volume levels, mean corpuscular haemoglobin levels, and mean packed cell volume levels were equivalent between the two groups (27.07±1.617 vs. 27.33±1.749; p=0.542, 75.43±3.766 vs. 75.93±3.805 fl; p=0.611, and 29.13±2.27 vs. 29.17±2.692 pg, respectively; p=0.959, and 0. Also comparable between the two groups

were the serum ferritin concentrations (11.63±1.217 vs. 11.43±1.223 ng/L; p=0.528). In comparison to group B, group C had a lower mean iron need of 843.47±101.848, which was statistically insignificant (p=0.092).

After receiving treatment, 63.3% of the women in group C and 46.7% of the women in group S had haemoglobin levels of 11gm% or higher. Statistically speaking, this difference was not significant (p = 0.292). The mean post-treatment haemoglobin levels were similar in both groups (p = 0174); group C had a value of 11.016±0.789 and group S had a value of 10.73±0.821. In 43.3% of the women in group C, compared to 50.0% in group S, the mean increase in haemoglobin levels was detected between 2.0 and 2.5 gm% after treatment; however, this difference was statistically insignificant (p = 0.437).

After treatment, both groups' mean increases in haemoglobin levels were comparable (p = 0.162); group C mean rise was 2.51±0.421 and group S was 2.35±0.486. In comparison to group S, which had a haemoglobin percentage increase of 66.7%, 53.3% of the women in group C had one between 15 and 30 percent. The distinction was not, however, statistically significant (p = 0.292). The mean percentage change in haemoglobin levels after treatment was similar in both groups (p = 0.415); group C had a change of 29.797±5.60 and group S had a change of 28.424±7.247.

There were no side effects noted in either groups.

## Discussion

These results imply that iron sucrose and ferric carboxymaltose, two i.v. iron preparations, are equally efficient in treating iron deficiency anaemia in pregnant women. After the first trimester, iron insufficiency in pregnant women is treated with IV iron sucrose (IS). However, because adverse effects occur at greater levels, its usage is restricted by a low maximum dose. Higher doses of IV ferric carboxymaltose (FCM) can be delivered, and its side-effect profile is favourable. For use in the second and third trimesters of pregnancy, ferric carboxymaltose is allowed. [11,12]

Over existing i.v. iron formulations with low dosage restrictions, like iron sucrose, the quick delivery option of a high single dose of ferric carboxymaltose offers a viable therapeutic strategy for pregnant women who need correction of iron shortage and anaemia (200 mg).

In order to determine the safety and tolerability for the mother as well as to rule out any concerns for the safety of the foetus, Christoph *et al*. [11] conducted a retrospective examination of 206 pregnant women who were either treated with FCM (n=103) or IS (n=103). In all groups, the frequency of drug-related adverse events was low and largely moderate; patients receiving FCM experienced fewer side effects (FCM, 7.8%; IS, 10.7%, NS). For FCM and IS, respectively, the mean increase in haemoglobin was 15.4 and 11.7 g/L.

Yet, this trial demonstrated that FCM is well tolerated in pregnancy and that adverse effects are uncommon, even when given at considerably greater doses than IS. It also has the advantage of requiring fewer administrations, which improves patient comfort. The authors came to the conclusion that if IV iron treatment is required in the second or third trimester of pregnancy, FCM would appear to be the medication of choice.

The results of the present study agreed with those of Christoph *et al*.[11], with the exception of the mean haemoglobin levels, which were 11.016±0.789 in the present study compared to 15.4 g/L in the FCM group and 10.73±0.821 compared to 11.7 g/L in group S. In the present study, no side effects were noted in either group.

Ferric carboxymaltose up to 15 mg/kg was given to anaemic pregnant women between 24 and 40 weeks of pregnancy in a prospective observational research conducted by Bernd Froessler *et al*.[13] in Australia [14]. All women's Hb readings were considerably raised ($p<0.01$) over baseline levels by intravenous infusion of ferric carboxymaltose. Between 3 and 6 weeks after the infusion as well as up to 8 weeks after the infusion, higher Hb values were seen. Monitoring of the foetus' heart rate did not reveal any drug-related adverse effects. Minor side effects were experienced by 13 (20%) patients, however no significant adverse effects were discovered. Although the increase in haemoglobin in our trial was comparable to that in this investigation, no adverse effects were found.

Retrospective examination of pregnant women given iron dextran and ferric carboxymaltose by Myers B *et al*. 44 of the 92 women received intravenous FCM, while 48 were given intravenous Iron Dextran. The mean Hb rise at two weeks was 1.73 g/dL in the FCM group and 1.34 g/dL in the Iron Dextran group. The total increase in Hb at four weeks was 2.57 g/dL FCM and 2.34 g/dL Iron Dextran. The increases were 3.01 g/dL and 3.2 g/dL, respectively, at six weeks. The increase in Hb after four weeks was equivalent to what we saw in our trial.

Although while iron sucrose costs more per infusion than ferric carboxymaltose does, the cost of the treatment as a whole was higher with iron sucrose due to the greater number of infusions.

In the present study, no side effects were noted in either groups.

Ferric carboxymaltose has been shown to be tolerable and effective in a number of studies for various patient populations with iron-deficiency anemia [16–20], with comparable outcomes. In a review publication, Bailie GR17 shown that ferric carboxymaltose had an excellent tolerance and efficiency profile, citing nine randomised studies with more than 3000 patients. There has been a lot of research done on the usage of ferric carboxymaltose for the treatment of postpartum anaemia.[15-17,21,22] The safety of breastfed children whose moms took ferric carboxymaltose has not been questioned. [16]

In the three cohort studies [23–25], ferric carboxymaltose IV was administered to 345 individuals. Of these, 14 (4%), due to unfavourable occurrences, and 75 (21%) for any reason, withdrew. 197 patients (56%), 35 patients (10%) had significant adverse events, and 10 patients (3%), had hypotension. Overall, this study's findings support prior research showing that giving pregnant women intravenous iron carboxymaltose is probably both safe and efficient.

The study was limited, though, in that individuals were only followed up with after three weeks. In order to properly observe the pattern in the growth of haemoglobin values, serial follow-ups at the ends of two, three, six, and eight weeks would have been preferable.

When compared to other parentral iron preparations that are currently on the market, the price of ferric carboxymaltose is very high. When the number of trips and days spent in the hospital are considered, the high expense of the medication is more than made up for. However, research needs to be done to determine how affordable the treatment is. The effectiveness, safety, and efficacy of intravenous ferric carboxymaltose in the treatment of iron deficiency anaemia in pregnancy would be extended by more research involving a large number of women in a randomised controlled trial as well as the long term follow up of the neonates.

## Conclusion

The study findings suggest that both intravenous iron formulations are equally helpful in treating iron deficiency anaemia in pregnancy. This study demonstrates that even when supplied at significantly larger iron doses than iron sucrose, ferric carboxymaltose in pregnancy has excellent tolerance and no adverse effects. Contrary to iron sucrose, ferric carboxymaltose has the benefit of delivering a significantly greater dose of iron at once, which eliminates the need for repeated administrations and improves patient comfort. Despite the fact that FCM and IS are practically equally expensive, the dosing schedule for IS makes it more difficult and unpleasant for the patient, which lowers compliance.

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