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# COMPARING THE EFFICACY OF IRON SUCROSE AND FERRIC CARBOXYMALTOSE IN TREATING IRON DEFICIENCY ANEMIA IN HEMODIALYSIS PATIENTS

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## Abstract

***Objective:*** *To compare the effectiveness of iron sucrose and ferric carboxymaltose in treating iron deficiency among patients suffering from chronic kidney disease who were undergoing maintenance hemodialysis.*

***Methods:*** *In this comparative study, we included 100 patients with chronic kidney disease (CKD) on maintenance hemodialysis for more than 6 months. The patients were recruited from September 2024 to February 2025. The patients receiving ferric carboxymaltose (FCM) therapy (group A) were administered a single intravenous infusion ranging from 10 to 15 mg/kg, not exceeding a total of 1000 mg. In group B, intravenous IS was given in a total dose of 1000 mg in 14 days, a 200 mg undiluted injection over five minutes was given after every alternate day. Mean increase in Hb and ferritin levels from baseline value were the primary study outcomes. Hb and ferritin levels were measured after 4 weeks of treatment and then after 3 months to determine mean increase.*

***Results:*** *The average age of individuals in the FCM group was 57.5 years (±7.8), while those in the IS group had a slightly higher average age of 58.3 years (±8.1). At baseline, hemoglobin levels were similar between the groups. After four weeks, Group FCM exhibited an increase in hemoglobin to 9.9±1.2 g/dL, while Group IS reached 9.4±1.3 g/dL (p-value 0.04). By the three-month mark, Group FCM significantly improved their hemoglobin levels to 11.1±1.4 g/dL compared to Group IS at 9.9±1.2 g/dL (p-value <0.0001). y three months, Group FCM recorded an impressive serum ferritin level of 84.8±17.4 mg/L, while Group IS only reached 27.4±5.3 mg/L (p-value <0.0001).*

***Conclusion:*** *In hemodialysis patients, intravenous ferric carboxymaltose (FCM) is more effective than intravenous iron sucrose (IS) in treating iron deficiency*

*anemia. This research supports the use of FCM as an innovative option for treating IDA. It provides patients with a highly effective iron supplement that is also characterized by a favorable safety record.*

## INTRODUCTION

Anemia frequently occurs in individuals with chronic kidney disease (CKD) and has been linked to higher rates of illness and death (Madu and Ughasoro, 2017). It is estimated that 32.9% of the global population suffered from anemia, contributing to approximately 68.36 million years of life lost to disability, with a significant portion attributed to CKD (Safiri et al., 2021). The occurrence and intensity of anemia correspond closely with the level of kidney dysfunction. In the context of CKD, anemia arises due to a range of complex and interrelated factors (Shiferaw et al., 2020).

The Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend initiating iron therapy prior to the commencement of erythropoiesis-stimulating agents (ESAs) for addressing iron deficiency (Ku et al., 2023). Iron replacement therapy may involve either oral or intravenous iron formulations. However, oral iron supplements often have suboptimal absorption rates and can lead to gastrointestinal side effects that limit their use. To mitigate these issues, intravenous iron preparations were created, particularly suited for situations where iron absorption is impaired or when there is a need for rapid replenishment (Del Vecchio et al., 2021; Auerbach and Macdougall, 2017).

Intravenous iron formulations come in various types, each with distinct administration schedules and varying risk profiles for side effects. Currently, multiple options are available for intravenous iron supplementation. Iron sucrose (IS) and the more recent addition of ferric carboxymaltose (FCM) are commonly utilized in clinical practice (Pandey et al., 2016).

Iron sucrose, a formulation that does not contain dextran, is typically given through a 15–30 minute intravenous infusion in doses ranging from 200 to 300 mg. It is advised that the total weekly administration of iron sucrose should not exceed 600 mg, which often necessitates several infusions for patients to reach the desired iron levels. When administered at the recommended dosages, iron sucrose is generally considered safe and well tolerated, with a low occurrence of side effects or allergic reactions (Macdougall et al., 2020; Yan et al., 2023). On the other hand, Ferric carboxymaltose (FCM) consists of a colloidal solution featuring a polynuclear iron (III)-hydroxide core that is stabilized by carboxymaltose. FCM allows for the administration of a single dose of 1000 mg within a quick 15-minute infusion. This formulation is specifically approved for the rapid replenishment of significant iron deficits (Laso-Morales et al., 2022; Aiello et al., 2020). The purpose of the current study was to evaluate and compare the effectiveness of iron sucrose and ferric carboxymaltose in treating iron deficiency among patients suffering from chronic kidney disease who are undergoing maintenance hemodialysis.

## METHODS:

In this comparative study, we included 100 patients with chronic kidney disease (CKD) on maintenance hemodialysis for more than 6 months. The patients were recruited from September 2024 to February 2025. Patients of age ≥18 years, on hemodialysis, and having IDA were included. Patients with a history of recent Gastrointestinal bleed or bleeding from other organs and a history of recent iron therapy before enrollment in the study were excluded.

The sample size is calculated by taking estimated mean Hb levels of 10.08±0.69 g/dL in FCM group and 9.54±0.66 g/dL in IS group,[12] after 4 weeks of treatment by taking power of test (1-β)=80% and level of significance (α)=5.0%. the calculated sample size was 25 patients in each and we included 50 patients in each group.

Patients who qualified for the study were classified into two categories based on whether they were undergoing iron treatment at the moment of enrolment. Those receiving ferric carboxymaltose (FCM) therapy (group A) were administered a single intravenous infusion ranging from 10 to 15 mg/kg, not exceeding a total of 1000 mg, as outlined in the product guidelines, over a period of 20 minutes. The

dose was given through the HD catheter before 1 hour of hemodialysis for a maximum of 2 to 3 times per week. In group B, intravenous IS was given in a total dose of 1000 mg in 14 days, a 200 mg undiluted injection over five minutes was given after every alternate day from day 1.

Mean increase in Hb and ferritin levels from baseline value were the primary study outcomes. Hb and ferritin levels were measured after 4 weeks of treatment and then after 3 months to determine mean increase.

Data was analyzed using SPSS v25. Comparison of mean hemoglobin and ferritin levels was made using independent sample t-test taking p-value ≤0.05 as significant difference.

**RESULTS:**

The baseline characteristics of the study participants are summarized in Table 1. The average age of individuals in the FCM group was 57.5 years (±7.8), while those in the IS group had a slightly higher average age of 58.3 years (±8.1), with a non-significant p-value of 0.61 indicating comparable age distribution between the two groups. In terms of gender distribution, 46% of the FCM group were male, compared to 44% in the IS group, which also resulted in a non-significant p-value of 0.84. The body mass index (BMI) was similar across both groups, with the FCM group showing a mean BMI of 24.3 kg/m² (±3.5) and the IS group at 24.9 kg/m² (±4.3), yielding a p-value of 0.44. The prevalence of hypertension and diabetes was relatively alike, with 58% of participants in the FCM group and 54% in the IS group reporting hypertension, and 32% in the FCM group versus 34% in the IS group reporting diabetes. The corresponding p-values of 0.68 and 0.83 suggest that there were no significant differences in these conditions between the two groups. Regarding dialysis duration, the FCM group had an average of 23.5 months (±12.4), while the IS group averaged 25.7 months (±11.9), with a p-value of 0.37 indicating similar duration between groups. Lastly, pre-dialysis urea levels averaged 24.1 mg/dL (±6.3) in the FCM group and 23.8 mg/dL (±6.7) in the IS group, while pre-dialysis creatinine levels were 708 µg/dL (±145) for the FCM group and 743 µg/dL (±165) for the IS group; both parameters showed non-significant p-values of 0.81 and 0.26, respectively. Overall, these findings indicate that the baseline characteristics of the study population were well-matched between the two groups (Table 1).

At baseline, hemoglobin levels were similar between the groups, with Group FCM showing a mean of 7.45±0.8 g/dL and Group IS at 7.38±0.9 g/dL, resulting in a p-value of 0.68. After four weeks, Group FCM exhibited an increase in hemoglobin to 9.9±1.2 g/dL, while Group IS reached 9.4±1.3 g/dL, yielding a statistically significant p-value of 0.04. By the three-month mark, Group FCM significantly improved their hemoglobin levels to 11.1±1.4 g/dL compared to Group IS at 9.9±1.2 g/dL, with a p-value of less than 0.0001. Serum ferritin levels also demonstrated notable differences. At baseline, Group FCM had a serum ferritin level of 21.4±3.5 mg/L, while Group IS was at 22.8±4.1 mg/L, with a p-value of 0.06. After four weeks, Group FCM's serum ferritin surged to 56.3±15.3 mg/L, contrasting sharply with Group IS's 25.3±5.5 mg/L, and this change was highly significant with a p-value of less than 0.0001. By three months, Group FCM recorded an impressive serum ferritin level of 84.8±17.4 mg/L, while Group IS only reached 27.4±5.3 mg/L, again indicating a highly significant difference with a p-value of less than 0.0001. These results suggest that the FCM treatment was more effective in improving both hemoglobin and serum ferritin levels compared to the IS approach over the specified time periods (Table 2).

**Table 1. Baseline Characteristics.**

| | Group FCM (N=50) | Group IS (N=50) | P-value |
|---|---|---|---|
| Age | 57.5±7.8 | 58.3±8.1 | 0.61 |
| Male Gender (%) | 23 (46%) | 22 (44%) | 0.84 |
| BMI (Kg/m$^2$) | 24.3±3.5 | 24.9±4.3 | 0.44 |
| Hypertension (%) | 29 (58%) | 27 (54%) | 0.68 |
| Diabetes (%) | 16 (32%) | 17 (34%) | 0.83 |

| | | | |
|---|---|---|---|
| Dialysis Duration (months) | 23.5±12.4 | 25.7±11.9 | 0.37 |
| Pre-dialysis Urea (mg/dL) | 24.1±6.3 | 23.8±6.7 | 0.81 |
| Pre-dialysis Creatinine (µg/dL) | 708 ± 145 | 743 ± 165 | 0.26 |

**Table 2. Comparison of Study Outcomes.**

| | **Group FCM (N=50)** | **Group IS (N=50)** | **P-value** |
|---|---|---|---|
| Hemoglobin (g/dL) | | | |
| Baseline | 7.45±0.8 | 7.38±0.9 | 0.68 |
| After 4 weeks | 9.9±1.2 | 9.4±1.3 | 0.04 |
| After 3 months | 11.1±1.4 | 9.9±1.2 | <0.0001 |
| Serum Ferritin (mg/L) | | | |
| Baseline | 21.4±3.5 | 22.8±4.1 | 0.06 |
| After 4 weeks | 56.3±15.3 | 25.3±5.5 | <0.0001 |
| After 3 months | 84.8±17.4 | 27.4±5.3 | <0.0001 |

**DISCUSSION:**

Individuals undergoing hemodialysis often struggle to regulate their iron levels due to the continuous loss of blood—and consequently iron—during each dialysis session. Initial hemoglobin measurements suggest that, despite the common use of erythropoiesis-stimulating agents (ESAs), typically administered in lower doses, factors such as diminished iron stores and underlying inflammation play a significant role in the inadequate response to ESA treatment (Covic and Mircescu, 2010).

Hemodialysis (HD) triggers a state of inflammation that contributes to elevated serum hepcidin levels (Wojtaszek et al., 2020). Hepcidin plays a crucial role in inhibiting both the absorption of iron in the duodenum and the release of iron stored in the liver and macrophages. This disruption hampers the recycling of iron, leading to a decreased supply of this essential mineral for the production of red blood cells (Saboor et al., 2021). Consequently, this situation worsens the pre-existing anemia associated with chronic illness, which is characterized by functional iron deficiency in patients undergoing HD. Additionally, oral iron supplements are often ineffective in restoring iron levels. This is due to their poor absorption, tolerance issues, and the resulting low rates of patient adherence to the treatment regimen (Maslovsky, 2005). To ensure optimal iron levels, it is highly advisable for patients with chronic kidney disease (CKD) undergoing hemodialysis (HD) to receive iron supplements through intravenous administration instead of oral forms (Cases et al., 2021; Musio, 2020).

Concerns have been raised by healthcare professionals about the safety of older formulations of parenteral iron. These concerns mainly focus on the risk that excess iron could lead to the production of reactive oxygen species, which may exacerbate oxidative damage to tissues in patients with chronic inflammatory diseases. Additionally, there are risks associated with rapid administration of large doses of intravenous iron, which can result in vasoactive reactions. Another significant issue is the potential for anaphylactic reactions, which can occasionally be fatal, particularly in patients who have pre-existing anti-dextran antibodies in response to intravenous iron dextran (Ku et al., 2023; Salim et al., 2019).

The novel iron compound ferumoxytol can be administered through rapid intravenous injections, with a recommended regimen of two doses of 510 mg given 3 to 8 days apart. Unlike ferric carboxymaltose (FCM), ferumoxytol includes dextran derivatives in its formulation. Phase III clinical trials have demonstrated notable increases in hemoglobin (Hb) levels when compared to oral iron treatments, particularly in patients with chronic kidney disease (CKD) who are undergoing hemodialysis and those not requiring dialysis (Provenzano et al., 2009; Zuo et al., 2022).

In the present study, we compared the outcomes of FCM and IS for the treatment of IDA in CKD patients on hemodialysis. We found that FCM was associated with a significantly higher increase in Hb

and ferritin levels than IS therapy. Similar to our results, Papaniya et al. also found FCM to be superior to IS therapy, the authors reported mean Hb levels of 10.08±0.69 g/dL in FCM group and 9.54±0.66 g/dL in IS group (Papaniya et al., 2023).

A randomized, active-controlled, multicenter trial conducted in 2014 evaluated the effectiveness of ferric carboxy maltose compared to iron sucrose for managing iron deficiency anemia in 2,561 patients with compromised renal function. The participants had hemoglobin levels at or below 11.5 g/dL and chronic kidney disease (CKD), characterized by a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 $m^2$ or a GFR above 90 mL/min/1.73 $m^2$ with either confirmed kidney damage or an increased risk for cardiovascular issues. Ferric carboxy maltose was administered at a dosage of 15 mg of iron per kilogram of body weight, up to a maximum cumulative dose of 750 mg, given on days 0 and 7, allowing a total potential dosage of 1,500 mg. In contrast, iron sucrose was given according to FDA guidelines, consisting of five infusions of 200 mg each on days 0, 7, and 14, with an additional dose provided between days 0 and 7, and another between days 7 and 14, reaching a total of 1,000 mg cumulatively. The study followed the participants for eight weeks, during which the average hemoglobin increase was more significant in the group receiving ferric carboxy maltose compared to the iron sucrose group, yielding results of 1.13 g/dL versus 0.92 g/dL, respectively. This produced a mean difference of 0.21 g/dL, with a 95% confidence interval ranging from 0.13 to 0.28 (Onken et al., 2014).

Hofman et al., in their study on switching the IS to FCM in patients on hemodialysis, reported that switching to FCM is associated with a significant increase in Hb levels compared to IS therapy, a reduction in the dose of ESAs, and lower doses of FCM (Hofman et al., 2018).

Alzahrani et al. conducted a cost comparative analysis of FCM and IS for treating IDA. The authors reported that FCM is associated with fewer injections and lower treatment costs than IS (Alzahrani et al., 2023).

However, a study by Macdougall et al. reported that both IS and FCM are equally effective for treating IDA in hemodialysis patients, with a mean increase in Hb of 0.5 g/dL in the FCM group and 0.4 g/dL in the IS group at the 5-week follow-up. The safety profiles of these two drugs were also similar (Macdougall et al., 2019). The shorter follow-up period in this study could be the reason for this. In our study, we found that an increase in Hb and serum ferritin levels was more evident at 3 months follow-up than at 4 weeks follow-up.

## CONCLUSION:

In hemodialysis patients, intravenous ferric carboxymaltose (FCM) is more effective than intravenous iron sucrose (IS) in treating iron deficiency anemia. This research supports the use of FCM as an innovative option for treating IDA. It provides patients with a highly effective iron supplement that is also characterized by a favorable safety record.

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