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A study comparing efficacy and safety of ferric carboxymaltose versus iron sucrose in postpartum women with anemia.

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Abstract
Introduction:
Anemia is one of the major health issues worldwide. The WHO and ACOG define postpartum anemia as hemoglobin less than 10 gm. %. Studies evaluating the prevalence of postpartum anemia have found it to be very common (range, 22 to 29 percent; as high as 35 to 60 percent in some populations). In PPA oral iron preparations give satisfactory results in raising Hb levels but have side effects and poor compliance. Iron sucrose has been widely used for treating anemia and its efficacy and safety are well established but it requires multiple dosing. FCM can be administered in large doses over a short period of time with fewer side effects overcoming the limitations of the existing IV iron agents. Parenteral therapy with FCM, a non-dextran containing IV agent, is designed to administer large doses in a short time.
Aims and objectives:
To compare the efficacy and safety of intravenous FCM and iron sucrose in postpartum iron deficiency anemia.
Materials and methods:
In this prospective comparative study 150 postpartum women with iron deficiency anemia were divided into 2 equal groups and were given 1000 mg of FCM or Iron sucrose. An increase in Hb and serum ferritin was noted after 15 days.
Result:
An increase in Hb and serum ferritin was seen in both the groups (p value .0001 and .0001). For comparing FCM and Iron sucrose, an independent t test was applied and FCM was found better than iron sucrose. (P value .0001 and .0078)
Conclusion:
Ferric carboxymaltose is as effective as IS in correcting preoperative IDA among patients with postpartum anemia. The added benefits of FCM over IS included significant rapid correction of IDA, replenishment of iron stores, and reduced hospital visits with better patient compliance.
Keywords: *Ferric Carboxymaltose. Iron Sucrose. Postpartum Anemia. Efficacy.*

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I. Introduction

Anemia is one of the major health issues worldwide. Iron deficiency anemia is the most common type of nutritional deficiency affecting both developed and developing countries. An estimate by WHO attributes about 591,000 perinatal deaths and 115,000 maternal deaths globally to iron deficiency anemia directly or indirectly [**1**]

The WHO and ACOG define postpartum anemia as hemoglobin less than 10 gm. %. . An estimated 30% of reproductive age group women are anemic [**2, 3**]. Among pregnant women, the prevalence is even higher. The WHO estimates that over 40% of pregnant women globally have anemia **[3**]. Studies evaluating the prevalence of postpartum anemia have found it to be common (range, 22 to 29 percent; as high as 35 to 60 percent in some populations, such as those with instrumental delivery, manual removal of the placenta, or third- or fourth-degree vaginal tear) **[4, 5**]

To treat PPA oral iron preparations give satisfactory results in raising Hb levels but have side effects and poor compliance. Also, oral therapy is not sufficient for the treatment of moderate to severe anemia. Parenteral therapy promises a better response in these patients and can obviate the need for blood transfusions in the antenatal and postpartum period [**6**]

A number of settings are there in which IV iron is preferred over oral iron.

1. Poor adherence/gastrointestinal side effects
2. Prefer to replete iron stores in one or two visits rather than over the course of several months.
3. Conditions that interfere with oral absorption.

IV iron preparations have been used for treating iron deficiency anemia with a promising result and making it possible to avoid blood transfusion and side effects of oral preparation [**7**]. Iron sucrose has been widely used for treating anemia and its efficacy and safety are well established but it requires multiple dosing. FCM can be administered in large doses over a short period of time with fewer side effects overcoming the limitations of the existing IV iron agents [**8**].

II. Objectives:

To evaluate the efficacy and safety of FCM iron in improving hemoglobin levels in PPA and compare it with iron sucrose in treating post-partum anemia.

III. Materials And Methods

It was a prospective study over a period of one year from March 2019 to March 2020 in a district hospital of north India. Postpartum patients with Hb of less than 10 gm. % were included in the study. Patients with anemia other than iron deficiency anemia, patients with a history of allergy to IV iron, and patients who received blood transfusion recently were excluded from the study.

The adverse effects of drug administration in the two groups were recorded. A total of 75 patients were given 1000 mg of iron sucrose (Group A) and 75 patients were given 1000 mg of injection FCM. Iron sucrose was given by an infusion of 200 mg in 200 ml of normal saline over 20- 30 minutes every alternate day. A maximum of 600 mg is given per week. FCM is given by 1000 mg of FCM in 250ml of normal saline over 15 minutes. Complete hemogram and serum ferritin were repeated after 2 weeks from the last dose of injection of IS and FCM.

Statistical Analysis

Firstly, descriptive statistics were used to calculate the mean ± SD. To compare the means of parameters of both the groups, an independent Student t test was performed. A 95% limit and a 5% level of significance were adopted. Therefore, a P value of less than 0.05 was considered significant. Statistical analysis was performed using the SPSS software package (SPSS for Windows, version 22.0; SPSS, Inc., Chicago, IL, USA)

IV. Results And Observations

The present study included 150 postpartum women with iron deficiency anemia. The first consecutive 75 women (group A) were given iron sucrose and the next consecutive 75 women were given FCM (group B).women in the two groups were chosen in the way that they have a comparable demographic profile (table 1). These data like age, parity, mode of delivery, mean pre transfusion Hb levels, etc. were comparable in both the groups (P value >0.05). Mean post transfusion Hb in IS and FCM group was 9.81 and 10.73g/dl respectively, which is statistically significant (p value =0.0001) (table 2). Mean ferritin after transfusion with IS and FCM was 179.35 and 288.90ng/dl respectively which is also statistically significant (p value=0.0001) (table 2). The mean increase in Hb and serum ferritin in IS and FCM groups was 1.228, 2.63g% and 114.93 and 128.55ng/dl, respectively (table 3).

- On comparing both groups using the independent student t test, we found that increase in Hb concentration and serum ferritin level in the FCM group was found statistically significant over IS group(p value 0.001 and 0.0078 respectively) (Table 3).

Adverse reactions were minimal in both the groups (p value>0.005) (table 5). Pain and burning over the injection site were seen in one in each group. Rash and itching were seen in one woman of each group.3 women among IS group had nausea and vomiting and it was seen in 4 women of the FCM group. Dizziness was seen in 2 women of each group. However, no major adverse effect like hypotension, hypertension, or severe anaphylaxis was seen in any of the two groups.

Table 1 Demographic profile:

Parameters	Group A [IS]	Group B [FCM]	P value
Age	28.62 ± 5.68	27.52 ± 5.30	.2221
Parity	1.89 ± 0.81	2.12 ± 1.05	.1352
Postpartum Hemorrhage	2.64%	4%	
Mean Hb	8.57 ± 1.26	8.1 ± 0.91	.097
Mode of delivery[lscs]	26.2%	25.2%	
Mean ferritin	64.42 ± 33.21	63.4 ± 32.86	.85
Antenatal anemia	55%	53.3%	

Table 2 Comparison of mean Hb and ferritin pre- and post-transfusion with iron sucrose and ferric carboxymaltose injection:

	Pre- transfusion mean Hb (g %)	**Post-Transfusion mean Hb (g %)**	**P value**	**Pre- transfusion mean Ferritin (ng/dl)**	**Post- transfusion mean Ferritin (ng/dl)**	**P value**
Group A [IS]	8.57 ± 1.26	9.81 ± 0.64	0.0001	64.42 ± 33.2	179.35 ± 39.21	0.0001
Group B [FCM]	8.1 ± 0.91	10.73 ± 0.82	0.0001	63.4 ± 32.86	288.90 ± 30.2	0.0001

Table 3 Comparison of mean increase in Hb and ferritin after transfusion of IS and FCM:

Parameter	**Group A [IS]**	**Group B [FCM]**	**P value**
Mean difference in increase in Hb (g %)	1.228 ± .361	2.63 ± .543	.0001
Mean Difference in increase in Ferritin(ng/dl)	114.93 ± 28.2	128.55 ± 33.45	.0078

Table 4

	GPA	**GPB**	**P value**
Post transfusion mean Hb	9.81±.64	10.73±0.82	0.0001
Post transfusion mean ferritin	179.35±39.2	288.90±30.2	0.0001

Table 5 Adverse reactions in Iron sucrose and FCM groups:

	Iron Sucrose Group	**FCM Group**
Rashes and itching	1	0
Nausea, Vomiting	3	4
Rigors	0	0
Fever	0	0
Pain/Burning at injection site	1	1
Hypotension/Hyper Tension	0	0
Dizziness	2	2
Severe Anaphylactic Reaction	0	0

V. Discussion

Ferric carboxymaltose is a colloidal iron (III) hydroxide in complex with carboxymaltose, a carbohydrate polymer that releases iron necessary to the function of hemoglobin, myoglobin, and specific enzyme systems; allows transport of oxygen via hemoglobin. Ferric carboxymaltose is a non-dextran formulation that allows for iron uptake (into the reticuloendothelial system) without the release of free iron. An iron (III)-hydroxide core contained in a carbohydrate shell confers stability to the FCM complex, allowing a slow and controlled release of iron from within the cells of the reticuloendothelial system. [9, 10] this stability is also reported to limit the amount of labile (unbound) iron entering the circulation. Labile iron is toxic to cells [11-13]

FCM is non dextran complex that consists of a ferric hydroxide core stabilized by a carbohydrate shell. The design of the macromolecular ferric hydroxide carbohydrate complex permits guarded delivery of iron to the cells of the reticuloendothelial system and subsequent delivery to the iron binding proteins ferritin and transferrin with negligible risk of a large amount of iron being released into the serum [**14**]. Being a non-dextran molecule and having a very low immunogenic potential, it is not predisposed to a high risk of an anaphylactic reaction.

These properties allow the administration of large doses (15mg/kg, max 1000mg) infusion in a single and rapid session, without the requirement of a test dose and thus makes it suitable as the first choice for treatment of iron deficiency anemia.

In this study, we compared the efficacy and safety of FCM and IS. Both are effective in improving postpartum anemia and both have a good safety profile. On comparing both the groups using independent t test we found that increase in Hb concentration and serum ferritin in FCM group is found statistically significant over IS group (p value .0001 and .0001).our study also documented the safety of FCM .there were minimal side effects of this drug and that too were minor ones as burning sensation over the injection site, headache, itching, etc. No major side effects were seen.

The first study on the use of FCM for the treatment of IDA in pregnancy was published by Christoph P et al. [**15**]. The study concluded comparable safety and tolerability of FCM to ISC and that FCM offers the advantage of a much higher iron dosage at a time reducing the need for repeated applications and increasing patients' comfort. The authors documented a comparable rise in Hb levels at the end of the study. Froessler et al. reported use of FCM in the second and third trimester of pregnancy and found FCM infusion prior to delivery significantly increased Hb levels and improved iron store and documented its safety [**16]**

Husain et al. compared FCM with iron dextran (ID) in iron-deficiency anemia and showed FCM had greater efficacy with a favorable safety profile [**17**]. In the same study, the mean increase in serum ferritin was 543.2 and 319.7 ng/ml in FCM and ID groups, respectively.

More people treated with FCM had a sustained Hb increase of ≥ 10 g/L from baseline to study end than for those given iron sucrose (48.6% vs 41.0%, 95% CI 3.6% to 11.6%) [18]

Mean increases in serum ferritin and transferrin saturation were also significantly greater in the FCM group compared with the iron sucrose group. The mean total iron dose received over the treatment phase was 1464 ± 158 mg in the FCM group and 963 ± 138 mg in the iron sucrose group-[**18**]

The present study showed that FCM is more effective and more rapid in improving Hb concentration as well as increasing the serum ferritin concentration. FCM had increased patient compliance and satisfaction as it requires fewer visits and a short time to increase the Hb as compared to iron sucrose.

VI. Conclusion

Ferric carboxymaltose is as effective as IS in correcting preoperative IDA among patients with postpartum anemia. The added benefits of FCM over IS included significant rapid correction of IDA, replenishment of iron stores and reduced hospital visits with better patient compliance.

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