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Original Research Article

Efficacy and Safety of Intravenous Ferric Carboxy Maltose in Iron Deficiency Anaemia during Post-Partum Period after Pregnancy

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Abstract:

Objective: Ferric carboxymaltose (FCM), a polynuclear iron-hydroxide carboxymaltose complex is considered safe for treating postpartum anaemia due to high treatment adherence, enhanced iron storage normalisation, a low incidence of gastrointestinal side effects, and a short treatment duration. Therefore, this study aimed to test the efficacy of ferric carboxymaltose for the postnatal women having iron deficiency anaemia during postpartum period and pregnancy.

Methodology/Material: Total of 200 participants were randomly selected from Obstetrics and Gynaecology Unit. Group A received parenteral ferric carboxymaltose administration while in group B iron sucrose was administered. The highest permitted dose of ferric carboxymaltose each week was 15 mg/kg, not to exceed 1000 mg/dose, administered intravenously over a period of about 15 minutes. For comparison, iron sucrose mixture was given three times per week in a single dose. Using the repeated measures ANOVA/Freidman test, the haemoglobin levels in both treatment groups were compared at baseline and after 21 days.

Results: Overall ferric group shows 27.7% mean improvement while iron sucrose group had mean improvement of 25%. Regarding, mean corpuscular volume a significant mean improvement of 30% was reported in ferric group while 27% was reported in group B (p=0.0001).There were no severe adverse events that could have been fatal. Total of 5 women experienced localised side effects of ferric carboxymaltose including itchiness and irritation while another 9 experienced systemic side effects like giddiness, headache, and nausea.

Conclusion: In conclusion, iron carboxyl maltose injection significantly improved Hb and other parameters in an effective and safe way with less side effects than iron sucrose complex.

Keywords: Postnatal, Anemia, Iron deficiency.

Introduction

Anaemia is a condition in which an individual's RBC counts and/or haemoglobin concentration are below normal and inadequate to support their

bodily needs. According to the World Health Organisation (WHO), anaemia in pregnancy is defined as haemoglobin (Hb) levels that are less than 10.5 g/dl in the second trimester and less than 11 g/dl in the first and third trimesters.[1] According to the WHO, anaemia, and specifically iron deficiency anaemia (IDA) among pregnant women, is a serious problem with prevalence rates as high as 56% in developing countries and 14% in industrialised nations.[1][2] Additionally, postpartum anaemia has been associated to a number of side effects, including depression and anxiety, longer hospital stays, as well a impairedneonatal development. It is connected to wound infection and puerperal pyrexia.[3] Treatment for IDA during pregnancy has been carried out using a variety of clinical techniques. While blood transfusions are often reserved for severe instances, oral supplements are typically used as first-line therapy.[4] Though oral iron therapy has been the most frequently given, issues like trouble with the tablets' digestion or other adverse effects may make it impossible to utilise this therapy, especially in people with gastrointestinal illnesses.[5]

Anaphylactic responses could be brought on by parenteral medications like sorbitol and iron dextran. There have been studies linking iron sucrose complex to less side effects, low renal excretion, little tissue accumulation and toxicity, and good availability for erythropoiesis. It is common for viral infections and adverse responses to follow blood transfusions. Compared to oral iron, iron sucrose complex raises haemoglobin more quickly, but it is more expensive and requires hospitalisation.[6]

Ferric carboxymaltose (FCM), a polynuclear iron-hydroxide carboxymaltose complex that has been licenced for use in more than 70 countries to treat IDA, has attracted renewed interest.[6]Ferric carboxymaltose has two advantages: it can be administered in fewer doses or at higher doses for shorter periods of time.Iron stores are replenished as a result of the controlled release of iron into the reticuloendothelial system in the liver and spleen.[7] It was developed primarily to treat anaemia fast and with high doses. In contrast to other iron sources like ferric gluconate or the iron sucrose complex, ferric carboxymaltoseis more stable, which enables it to deliver iron slowly yet effectively.[8]

Due to stability of ferric carboxymaltose, high doses of iron can be administered in a shorter amount of time than with iron sucrose complex, where larger dosages and longer infusion periods are usually required to sufficiently refill the iron storage. Ferric carboxymaltose is also regarded as safe for treating postpartum anaemia due to high treatment adherence, enhanced iron storage normalisation, a low incidence of gastrointestinal side effects, and a short treatment duration.[2] Finding of a recent randomized controlled trial revealed that oral iron had a mean haemoglobin level change from baseline to the maximum value of 0.8 g/dl, iron sucrose complex had a mean change of 1.9 g/dl, any iron had a mean change of 2.0 g/dl, and FCM had a mean change of 2.2 g/dl.[3] Drug-related adverse effects were also the least frequently reported in the category of ferric carboxymaltose.

Even though the dosage of ferric carboxymaltose IV is rather large, another study found that it is equally safe when used to treat IDA postpartum as iron sucrose complex.[9]In controlling and restoring haemoglobin levels to normal after childbirth, ferric carboxymaltose and iron sucrose complex are equally efficient. After one application of FCM, benefits like a low incidence of local site reactivity and higher compliance have also been seen. According on a literature search, iron sucrose complex and ferric carboxymaltose are both equally effective. However, because ferric carboxymaltose is dextran-free and has a higher safety

profile, a test dosage is not necessary and up to 1000 mg can be given in a single dose over a 15-minute period. Therefore. we designed this study to compare the efficacy of ferric carboxymaltose for the postnatal women having iron deficiency anaemia during postpartum period and pregnancy.

Methodology:

During the timeframe, 200 cases visited the obstetrics department (100 in each group). Patients who had placenta previa in the past, had placental abruption during the index pregnancy, and had serum ferritin levels less than 15 ng/I were taken into consideration. Additionally, 24 to 48 hours after birth, cases with haemoglobin levels ranged from 6 to 10 g/dI were included. Patients with clotting disorders, hemolytic anaemia, non-iron deficiency anaemia, peripartum blood transfusion, intolerance to derivatives of iron, history of asthma, thromboembolism, eczema, and atopic allergy, as well as women with infection symptoms or indications of renal or hepatic dysfunction, were excluded from the study. A comprehensive assessment was done included a history, physical examination, and investigations ruled out other causes of anaemia. Using clinical tests, a complete blood count, and serum ferritin levels, the patient's initial iron status was assessed. Randomly, two groups of these women were divided. After enrolling, Group A got two 200 mg IV doses of iron sucrose complex on days 2 and 4.

The dose was calculated according to body weight and haemoglobin deficiency. Iron was administered in doses of 100–200 mg, which is the recommended quantity.Group A received parenteral ferric carboxymaltose administration while in group B iron sucrose was administered.The dosage of ferric carboxymaltose was given once a week until a maximum of 2500 mg was given or the person's calculated cumulative dose was reached. The highest permitted dose of ferric carboxymaltose each week was 15 mg/kg, not to exceed 1000 mg/dose, administered intravenously over a period of about 15 minutes. The iron sucrose mixture was given three times per week in a single dose. The iron sucrose complex was given over a period of two hours after being diluted in 250 cc of 0.9% NaCl to prevent any allergic reactions.[2] For 30 minutes, patients were monitored for symptoms such as anaphylaxis, urticaria, hypotension, headaches, chest pain, dyspnea, tachycardia, breathlessness, skin rash, facial flushing, metallic taste, etc. The medicine was discontinued after administering a total of 400 mg. Patients who were being treated with ferric carboxymaltose and iron sucrose complex were being observed at day 21.The data were entered and statistically analysed using SPSS 20. Using the repeated measures ANOVA/Freidman test, the haemoglobin levels in both treatment groups were compared at baseline and after 21 days. The therapy groups were compared for side effects using the chi-square and Fisher exact tests. It was deemed significant at a P value of 0.05.

Results

This study recruited 200 postnatal having iron deficiency anaemia during pregnancy and postpartum periods. The mean age of Ferric carboxymaltose group was 27.8 ± 4.38 in years with average BMI of 23.89 ± 14.1 kg/m^2.

Meanwhile in iron sucrose group the mean age was 26.98 ± 9.8 in years with average BMI of 26.47 ± 5.2kg/m^2. In group A the parity rate more than 2 was 78% while in group B it was reported as 56%. Group B had history of high abortion rate than Group B (30% vs 18% respectively) (Table 1).

Table 1: Demographic characteristics

Variables	Ferric carboxymaltose (N=100)	Iron sucrose complex (N=100)
Age	27.8 ±4.32	26.98 ±9.8
BMI kg/m^2	23.89 ±1.41	26.47 ±5.2
Parity		
>2	22 (22%)	44 (44%)
2 or more	78 (78%)	56 (56%)
Gravida		
<3	56 (56%)	60 (60%)
3 or more	44 (44%)	40 (40%)
History of Abortion		
Yes	30 (30%)	18 (18%)
No	70 (70%)	82 (82%)

At 48 hours average hemoglobin levels in group A and B was reported as 7.76 ± 1.43 and 8.89± 1.29 respectively with no significance while at day 21 it increased upto 13.39± 2.31 in group A and 12.46 ± 2.3 in group B. However, a statistical difference was found between both groups at day 21 (p<0.001). Mean corpuscular hemoglobin levels at 48 hours in ferric group was reported as 26.23 ± 6.3 and 26.03 ± 4.49 while at day 21 elevated MCV reported in both groups with statistical significance of 0.001. Overall ferric group shows 27.7% mean improvement while iron sucrose group had mean improvement of 25%. Regarding, mean corpuscular volume a significant mean improvement of 30% was reported in ferric group while 27% was reported in group B (p=0.0001) Table 2. There were no severe adverse events that could have been fatal.

Total of 14 women experienced localised side effects of ferric carboxymaltose including itchiness and irritation while another 19 experienced systemic side effects like giddiness, headache, and nausea.

Table 2: Mean changes in hemoglobin levels, MCV, MCVH levels at 48 hours and 21 day

	Ferric carboxymaltose	Iron sucrose complex	Student t test	p value
Hemoglobin (g/dl) level				
At 48 hours	7.76 ± 1.43	8.89 ± 12.46	8.67	0.05
At 21st day	13.39 ± 2.31	12.46 ± 2.3	-7.32	<0.0001
Levels of Mean corpuscular hemoglobin concentration (g/dl)				
At 48 hours	26.23± 6.3	26.03 ± 4.49	-7.95	0.39
At 21st day	33.88 ± 1.45	32.46 ± 1.35	-3.45	0.01
Level of mean corpuscular volume (fl)				
At 48 hours	63.89 ± 6.31	64.79 ± 6.02	2.76	0.07
At 21st day	81.38 ±	±	-2.2	0.0000
Mean corpuscular hemoglobin (g/dl) levels				
At 48 hours	22.68 ± 3.10	23.56± 2.77	1.63	0.12
At 21st day	30.98 ± 0.98	29.26 ± 0.96	-3.32	0.001

Discussion

Insufficient intake of iron in pregnancy and peripartumblood loss are primary causes of postpartum iron deficiency anemia. Iron deficiency is more likely to occur in women with poor socioeconomic

level and inadequate dietary intake. An obstacle in taking care of the baby might arise from iron deficiency, which also puts the mother's health at danger during a critical period for mother-infant bonding. Anaemia may also result in more blood transfusions and a longer hospital stay. The most useful measurement for treating anaemia due to iron deficiency is haemoglobin. This is due to the fact that varying ferritin levels can produce erroneous results. To lower postpartum morbidity and mortality, regular treatment for postpartum anaemia should include intravenous iron as a first line therapy.[10]

Ferric carboxyl maltose has undergone numerous trials to determine its efficacy and safety in the treatment of postpartum iron deficient anaemia. As opposed to parenteral and oral iron treatments, it has been shown to be more safe and effective. Very little gastrointestinal side effects are associated with ferric carboxyl maltose. More advantages include improved patient comfort, shorter turnaround times, and lower costs.[11][12] According to Rathod et al.,[13] mean Hb increased more in the ferric carboxyl maltose group than in the oral and iron sucrose complex groups over the course of two weeks, respectively. In their study both iron Sucrose Complex, and Ferric Carboxyl Maltose groups, reported similar patterns of serum ferritin. When compared to the other two groups, the FCM group reported considerably less adverse iron medication reactions. Therefore, they concluded that Ferric carboxyl maltose is superior to both oral iron and IV iron formulation for both Hb level serum ferritin.

The efficiency and safety of iron sucrose complex against ferric carboxyl maltose in treating postpartum iron deficient anaemia were examined in a comparative interventional prospective trials in 2018.[14][15] Multiple doses of 200 mg/day, totalling 1000 mg, were given to the subjects in the IV Iron Sucrose Complex group on days 0, 2, 4, 6, and 8.In the ferric carboxyl maltose group, 1000 mg of ferric carboxyl maltose IV was administered as a single dosage. On days 0 and 30, blood tests for haemoglobin and serum ferritin were repeated. The ferric carboxymaltose group had a considerably higher mean increase. According to the results of another trial[16], oral ferrous sulphate was less effective at treating postpartum iron deficiency anaemia while being less safe and well tolerated than ferric carboxyl maltose.

In the present study we observed that 100 patients who were receiving iron carboxymaltose had haemoglobin levels more than 12 g/dl at day 21, which was statistically significant. According to a prospective experiment comparing parenteral and oral forms of iron therapy, parenteral iron, particularly Ferric carboxyl maltose, was more effective in replenishing iron reserves and had the advantage of requiring fewer doses and having fewer adverse effects. In another randomized controlled trial, parenteral iron in treating postpartum iron deficient anaemia was evaluated for both safety and efficacy. On day 1 and, one group received 1000 mg of iron FCM, whereas the other received 300 mg of iron sulphate up to twice weekly. At 12 weeks, the Ferric carboxyl maltose group's mean Hb rise was significantly higher.

Present study explores a huge improvement in fatigue scores which was linked to ferric carboxyl maltose. However, neither group experienced any severe adverse effects. Similar to our study[17], another one showed that in India, the mean rise in haemoglobin (Hb) after patients received ferric carboxyl maltose versus iron sucrose complex was 9.690.49 g/dl and 12.220.43 mg/dl, respectively. At weeks 2 and 6, respectively, the increase in Hb measured by FCM was 9.80.43 g/dl and 12.22041 g/dl. At 2 and 6 weeks, serum ferritin levels in the IV FCM group were also greater than those in the Iron Sucrose

Complex group (p=0.049 and p=0.023, respectively). In Australia[18], a prospective open label, randomised controlled study with excellent findings supported the use of intravenous FCM in the therapy of post-operative anaemia.

Studies show that when FCM is administered to patients, there are less negative side effects. According to a different study, although having a dose that is five times higher, FCM is just as safe and effective as oral iron therapy or intravenous iron.[19][20] Hb can be quickly replaced after delivery using iron sucrose and ferric carboxyl maltose. FCM also has the benefits of patient satisfaction, less side effects, and a quick hospital stay. According to a study by Joshi et al.,[20] FCM is a routine treatment for postpartum IDA and has few side effects. According to Verma et al.,[21] iron deficiency anaemia in postpartum women is commonly treated with FCM since it is low cost, highly effective, well tolerated, and safe. Another recent study provides evidence for the better efficacy and low negative effects of using a single dosage of ferric carboxyl maltose during the postpartum period.[23]

Conclusion:

In conclusion, iron carboxyl maltose injection significantly improved Hb and other parameters in an effective and safe way with less side effects than iron sucrose complex. Therefore, more studies including a larger sample size are required in order to promote the use of IV FCM for treating post-partum anaemia in territory hospitals of country.

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