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Original Research Article

Role of ferric carboxymaltose in battle with anemia among north Indian pregnant women

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ABSTRACT

Background: Anemia among pregnant women is a serious global health concern. Anemia is a major hematological, nutritional deficiency but still a manageable health problem among the pregnant women and very common in developing countries like India in under privileged population. Increased morbidity and mortality is seen in pregnant women and their foetuses suffering from anemia. Aim of this study was to study safety and efficacy of injection ferric carboxymaltose in pregnant women with iron deficiency anemia.
Methods: This is a Prospective interventional comparative randomized study carried among antenatal women in the Department of Obstetrics and Gynaecology, S. N. Medical College, Agra from (May 2021-October 2022), comprised of 200 pregnant women divided into two groups. Group A-100 antenatal women were transfused with iron sucrose (IS), Group B-100 antenatal women were transfused with ferric carboxymaltose (FCM).
Results: In FCM group after 3 weeks of post transfusion hemoglobin level was 10.5±0.44 and in iron sucrose group it was 9.9±0.59 (p=0.0001). 6 week post transfusion hemoglobin level in FCM group was 11.37±0.62 and in iron sucrose group it was 10.45±0.59 (p=0.0001). Average rise in hemoglobin in FCM group after 3 week post transfusion was 2.9±0.02 and after 6 week it was 3.77±0.16. In iron sucrose group at 3 week it was 2.1±0.06 and at 6 week it was 2.65±0.04. The average rise in hemoglobin level was greater among patients of FCM compared to Iron sucrose group.
Conclusions: Ferric carboxymaltose was safe and more effective in treatment of iron deficiency anaemia in pregnant women as compared to iron sucrose with lesser side effect and better patient compliance.

Keywords: Ferric carboxymaltose, Iron deficiency anemia, Iron sucrose, Mean cell haemoglobin, Mean cell hemoglobin concentration, Mean cell volume, Total iron binding capacity

INTRODUCTION

Anemia the Greek word (anhaima) meaning "without blood" is the deficiency of red blood cell and or hemoglobin which result in a reduced oxygen carrying capacity of blood causing tissue hypoxia. Anemia affects 1.62 billion individuals worldwide and is more prevalent in Africa (57.1%) and Southeast Asia (48.2%). Estimated global anemia prevalence in pregnant and nonpregnant women is 41.8 and 30.2%, respectively.[1] Analysis of data from the National Family Health Survey 5 (NFHS5) in India observed anemia in 52.2% of pregnant and 57.2% of nonpregnant women.[2] The prevalence pertaining to anemia in pregnancy is 33-89% and incidence being 42% (WHO, 2015).[3,4] 40% maternal deaths in developing countries are due to anemia among which 25% are directly associated with anemia.[4] Anemia during pregnancy adversely affects both mother (headache, fatigue, weakness, depression, preeclampsia, placenta previa, and cesarean delivery) and fetus (intrauterine growth restriction, low Apgar scores, low birth weight, and neonatal and perinatal death).[5,6]

Anemia among pregnant women is a serious global health problem. As per World health organization (WHO) report, about 32.4 million pregnant women were suffering from anemia worldwide, of which 0.8 million women were severely anemic. Moreover, 50% cases of anemia are attritutable to iron deficiency anemia.[7]

According to WHO about 591,000 peri-natal deaths and 115,000 maternal deaths globally are because of iron deficiency anemia directly or indirectly.[8] According to WHO, anemia in pregnancy has been defined as hemoglobin (Hb) levels <11 gm% and hematocrit <33%.[9]

ICMR (Indian medical council and research) has categorized anemia during pregnancy as - mild- Hb -10-10.9 gm%, moderate- Hb-7 -9.9 gm%, severe- Hb-4-6.9 gm%, very severe-Hb <4 gm%.[10]

In pregnant women, oral iron is often used for prevention of iron deficiency and is recommended as first line treatment for pregnant women with iron deficiency anemia [11]. Nearly 70% of women have gastrointestinal (GI) intolerance (nausea, constipation, diarrhea, indigestion, and metallic taste) with oral iron that affects compliance. [12] Thus, intravenous (IV) iron formulations such as iron sucrose and FCM may be preferred which can be administered from the second trimester onward.[13] Parenteral iron are more effective in replenishing iron stores than oral iron. Intravenous preparations of iron formulation provide an alternative approach in pregnant women with moderate to severe anaemia who have an intolerance of oral iron.

METHODS

This was prospective interventional comparative randomized study. Total 200 antenatal women between 16-34 weeks period of gestation with moderate to severe anemia were randomly selected from antenatal outpatient department and labour room in the Department of Obstetrics and Gynaecology, S. N. Medical College, Agra from May 2021-October 2022. Before conducting the study the clearance of institutional ethical committee was taken.

A detailed written informed consent was obtained from the participant and her relatives. The study was randomly divided into 2 groups:

Group 1: 100 pregnant women received intravenous iron sucrose. 200 mg elemental iron diluted in 100 ml 0.9% normal Saline over 15 to 20 min and repeated on alternate days as required maximum 3 dose per week can be given. 200mg on alternate day, maximum- 600 mg/week.

Group 2: 100 pregnant women received intravenous ferric carboxymaltose. Maximum single dose of 1000 mg diluted in 200 ml of 0.9% normal Saline given over 15 minutes and not more than once a week (1000 mg/week).

Inclusion criteria

Inclusion criteria were the H/O allergy to iron compound, chronic kidney disease, anemia due to other causes (vitamin B6, B12 deficiency), hematological disorder, bronchial asthma, hepatitis, heart disease, pancytopenia (bone marrow depression, H/O recent blood transfusion.

Following parameters were investigated: hemoglobin, peripheral smear, mean corpuscular volume, MCH, MCHC, TIBC, transferrin saturation (%), and serum ferritin.

Following are the monitoring parameters: Blood pressure, pulse rate, temperature, uterine contraction, FHS, allergic reactions, nausea, vomiting.

During and 1hour after infusion each patient was monitored in the ward for any adverse reactions. After completion of the regimen patients were discharged and each patient was followed up at 3rd and 6th week after completion of therapy.

In women with severe anemia refractory to conventional treatment Hb electrophoresis is performed to rule out hemoglobinopathy. A simple tool to identify beta-thalassemia trait is the Mentzer index. Mentzer index is the ratio of mean corpuscular volume to red blood cell count (MCV/RBC count).[14]

RESULTS

The present study comprised of 200 antenatal women between the gestation period of 16-34 weeks with hemoglobin level between 6-9.9 gm/dl, serum ferritin levels <30mcg. Out of which 100 women were in the intravenous Iron sucrose (IS) group (Group A) and 100 women were in the intravenous ferric carboxymaltose (FCM) group (Group B) (Table 1 and 2).

Table 1: Comparison of different variables in Group A and Group B.

Variable	Group A (IS)	Group B (FCM)	p-value
Age (in years)	25.12±4.40	26.17±3.12	0.171
Gestational age (weeks)	24.08±4.02	25.38±3.83	0.101
Pre-treatment Hb (gm/dl)	7.8±0.53	7.6±0.46	0.004
Pre-treatment S. ferritin (ng/dl)	14±5.3	15±6.63	0.240
Pre-treatment MCV	80.1±2.07	78.9±4.46	0.02

In our study the trend of hemoglobin increase in FCM group is faster and greater. The hemoglobin increase is about 10.45g at 6 weeks in iron sucrose group from baseline value of 7.8g where as in FCM group Hb increase

is about 11.37g from baseline value of 7.6g. There was significant (p=0.0001) difference in Hb level between both the groups at 3 and 6 weeks after i/v iron therapy (Table 3).

Table 2: Mean hematological parameters at the start of therapy and 6 weeks after therapy.

Parameter	Group A (IS)		Group B (FCM)		p-value
	Initially	At 6 weeks	Initially	At 6 weeks	
S.Iron (mcg/dl)	27.6	147	31	163	0.93
TIBC (mcg/dl)	492	347	531	355.9	0.85
MCH (%)	24	28.2	24.4	29.3	0.83
MCHC (pg)	28.7	31.5	30	33.2	0.55
Transferrin saturation (%)	11.5	36	12	38.5	0.94

Table 3: Correlation of Hb before and after therapy in both the groups.

Hemoglobin	Group A (IS)	Group B (FCM)	t-value	p-value
Pre-treatment Hb	7.8±0.53	7.6±0.46	2.84	0.004
Hb 3 weeks	9.9±0.59	10.5±0.44	8.15	0.0001
Hb 6 weeks	10.45±0.59	11.37±0.62	10.74	0.0001

MCV increases about 85.46 (fl) from baseline of 80.1(fl) in iron sucrose group whereas in FCM it increases to about 88.18 (fl) from 78.94 (fl). So there is significant improvement in blood indices following FCM injection. There was significant (p=0.0001) rise in MCV level between both the groups at 3 and 6 weeks after i/v iron therapy (Table 4).

Table 4: Correlation of mean rise in mean corpuscular volume (MCV) before and after therapy in both the groups.

MCV	Group A (IS)	Group B (FCM)	t-value	p-value
Pre-transfusion MCV	80.1±2.07	78.9±4.46	2.23	0.02
Post transfusion MCV at 3 weeks	84.22±2.4	86.2±2.09	6.22	0.0001
Post transfusion MCV at 6 weeks	85.4±2.19	88.18±1.40	10.69	0.0001

In our study S. ferritin increases to 77 from baseline 14 in iron sucrose group and FCM increases to 102 from 15. There was significant (p=0.0001) rise in S. ferritin level between both the groups at post treatment 3 and 6 weeks (Table 5).

Table 5: Correlation of serum ferritin before and after therapy in both the groups.

S. ferritin	Group A (IS)	Group B (FCM)	t-value	p-value
Pre-transfusion S. ferritin	14±5.3	15±6.63	1.17	0.24
At 3 weeks post S. ferritin	38±5.9	79.11±10.3	34.63	0.0001
S. ferritin 6 weeks	77±8.84	102±7.8	21.20	0.0001

Table 6: Comparison of side effect among both the groups.

Adverse drug reaction	Group A (IS) (%)	Group B (FCM) (%)
Injection site pain	3 (3)	3 (3)
Fever/chills	4 (4)	2 (2)
Nausea, vomiting	3 (3)	3 (3)
Abdominal pain	0	0
Headache	1 (1)	1 (1)
Rash, itching	2 (2)	1 (1)
Hypersensitivity reaction including anaphylactoid reaction	0	0
Diarrhea, constipation	0	0

Continued.

Adverse drug reaction	Group A (IS) (%)	Group B (FCM) (%)
Palpitation	0	0
Total	13 (13)	10 (10)

No serious side effects were reported in any group. Mild adverse effects like nausea, vomiting, diarrhea etc. were observed in 13 (13%) patients in group A and 10 (10%) patients in group B (Table 6).

DISCUSSION

In our study pre-treatment mean hemoglobin was 7.8 gm/dl, at 3 weeks Hb was 9.9gm/dl and at 6 weeks Hb was 10.45gm/dl in group A while pre-treatment mean hemoglobin was 7.6 gm/dl, at 3 weeks Hb was 10.5gm/dl and at 6 weeks Hb was 11.37gm/dl in group B. In the study by Khatun et al post treatment hemoglobin in group A at 3 week was 9.39±0.72 and in group B was 9.87±0.77. At 6 weeks in group A hemoglobin was 10.78±0.61and in group B hemoglobin was 11.51±0.76.[15]

In our study the mean rise of Hb from pretreatment to post treatment 3 week was 2.1±0.06 and post treatment 6 week was 2.65±0.04 in group A and the mean rise of Hb from pretreatment to post treatment 3 week was 2.9±0.02 and post treatment 6 week was 3.77±0.16 in group B. In study by VanWyck et al reported increase of hemoglobin by 2 gm/dl in 1st week and 4 gm/dl by 2-4 weeks of therapy in those receiving FCM.[16]

In our study pre-treatment serum ferritin level was 14±5.3, at 3 weeks serum ferritin level was 14±5.3 and at 6 weeks serum ferritin level was 77±8.84 in group A and pre-treatment serum ferritin level was 15±6.63, at 3 weeks serum ferritin level was 79.11±10.3 and at 6 weeks serum ferritin level was 102±7.8 in group B. In a study by Kumari et al showed that levels of serum ferritin was increased from 77.91 ng/dl to 182.86 ng/dl in iron sucrose group and from 78.05 ng/dl to 195.39 ng/dl in FCM group patients.[17]

In study by Urvashi et al, in group A (FCM) haemoglobin level rise is 3.95 g/dl and in group B it is 3.32 g/dl at 4 weeks of initial therapy. In group A, 100 % cases achieved target haemoglobin at 12 weeks after therapy while in group B 98% cases achieved target haemoglobin at 12 weeks after therapy. In group A, 12% cases have grade 1 adverse reaction while in group B 20% cases have adverse reaction.[18]

Ferric carboxymaltose for the treatment of anemia during Antenatal and Postpartum period: expert opinion by PC Mahapatra, Sanjay Gupte.[19] FCM should be used within 12-32 weeks of pregnancy and in postpartum period after 24 hours of delivery. Within 6 weeks of FCM treatment, there was rise in Hb by nearly 3-4 gm/dl with a significant rise in ferritin and replenishment of iron stores.

In our study the mean rise of serum ferritin level from pretreatment to post treatment 3 week was 61±0.29 and post treatment 6 week was 63±3.54. In group A and the mean rise of serum ferritin level from pretreatment to post treatment 3 week was 64.11±3.67 and post treatment 6 week was 87±1.17 in group B.

CONCLUSION

In our study a significant rise in haemoglobin and ferritin levels were found in both the groups. However the rise was found to be more in the women receiving parenteral FCM than parenteral iron sucrose. Iron stores were rapidly replenished in pregnant women who were treated with FCM. There was a significant increase in Hb and ferritin levels over a period of 6 weeks with fewer side effects. Good compliance was shown by the patient as there were lesser total number of required doses. Thus, ferric carboxymaltose was found to be safer and more effective in treating iron deficiency anemia in pregnant females when compared to iron sucrose.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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