Section: OBS & Gynae

Original Research Article

COMPARATIVE STUDY OF FERRIC CARBOXY-MALTOSE V/S IRON-SUCROSE IN IRON DEFICIENCY ANEMIA DURING PREGNANCY IN A TERTIARY CARE HOSPITAL OF KUMAON REGION

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Abstract

Background: The study was done to compare efficacy and safety of ferric carboxy maltose versus iron sucrose in iron deficiency anaemia during pregnancy. **Materials and Methods:** 100 antenatal women with moderate iron deficiency anemia were selected and were randomized into two groups in a 1:1 ratio. Group A: consisted of 50 antenatal women who received iron sucrose. Group B: consisted of 50 antenatal women who received Ferric carboxymaltose at Obstetrics and Gynaecology Department, Dr. SushilaTiwari hospital, Haldwani during study period Jan2021-Sept2022. Haemoglobin estimation, MCV, MCHC, MCV, Serum Iron, Serum Ferritin were described using frequency, percentages, mean, standard deviation using Microsoft Excel software. **Result:** The mean haemoglobin in Group A was 7.85 ± 0.50 gm% prior to transfusion of iron sucrose, which increased to 10.55 ± 0.52 and 10.94 ± 0.54 gm% at 2 and 4 weeks respectively.The mean haemoglobin in Group B was 8.06 ± 0.29 gm% prior to transfusion of ferric carboxymaltose, which increased to 11.48 ± 0.56 gm% and 11.84 ± 0.58 gm% at 2 and 4 weeks respectively. **Conclusion:** The findings of our study showed significant increase in hemoglobin level in both the group but the rise was more among those who received injection. FCM than injection iron sucrose. Because of high efficacy and safety of ferric carboxymaltose, it should be used as an alternative first line drug in the management of Iron deficiency anaemia in pregnancy to decrease the incidence and burden of the disease in Indian population.

INTRODUCTION

Anemia is defined as decreased oxygen carrying capacity of blood. Anaemia is one of the major health issues worldwide and is one of the major illness in developing countries like India leading to increased maternal mortality and morbidity. Of the half of the global maternal deaths due to anaemia occur in South Asian countries with India alone contributing to about 80% of it.[1,2]

Anemia is a major contributor to maternal and foetal morbidity and mortality, particularly in less developed ccountries. The functional classification of anaemia has three major categories. These are marrow production defects (hypoproliferation), red cell maturation defects (ineffective erythropoiesis) and decreased red cell survival (blood loss/haemolysis). The majority of hypoproliferative anemias are due to mild to moderate iron deficiency or inflammation.[3,4]

Most common type is the nutritional anaemia – Iron deficiency anaemia. Menstruation and pregnancy put women at a higher risk for anemia.[5]

Iron deficiency anemia in pregnant women is mainly due to increased demand or due to poor absorption. Iron needs increase exponentially during pregnancy to meet the increased demands of the foeto-placental unit, to expand maternal erythrocyte mass, and to compensate for blood loss at delivery.[6,7]

WHO defines anemia as haemoglobin less than 11 gm% in first trimester, less than 10.5 in second and third trimester and less than 10 postpartum.[8]

Various Modes of Treatment are

Oral iron
Parenteral iron
Blood transfusion

Due to poor compliance to oral iron and gastrointestinal side effects and because of inherent risks following blood transfusions, parenteral iron

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has gained more importance to treat iron deficiency anemia in clinical practice.
Among them second generation intravenous iron sucrose is most commonly used.
Upcoming is the third generation ferric carboxymaltose.
Iron sucrose got approved by FDA in Nov 2000. Its administered as intravenous bolus injection over 5-10 minutes or as an infusion in 200ml normal saline over 15-20 mins without any prior testing dose and maximum daily dosage of 200mg, not more than thrice a week. Its common side effects include metallic taste, nausea, dizziness and local irritation.
Ferric carboxymaltose is a novel non-dextran with type I complex administered rapidly 500mg in 100ml Normal saline over 6 mins and 1000-1500 mg in 250ml normal saline over 15 mins as intravenous infusion. Its advantage is that a larger amount of iron dose can be given in single sitting. It has faster and controlled delivery. It raises Hb and replenishes iron stores in shorter duration of time with minimal toxicity and anaphylaxis. It has a wider therapeutic index, better compliance and tolerance.[9,10]

MATERIALS AND METHODS

A hospital based prospective study was conducted among 100 antenatal women with moderate iron deficiency anaemia. Assuming the prevalence of anemia to be 25% and margin of error 10%.The sample size calculated along with loss to follow up was 100.
100 antenatal women with moderate iron deficiency anemia were selected and were randomized into two groups in a 1:1 ratio.
Group A: consisted of 50 antenatal women who received iron sucrose.
Group B: consisted of 50 antenatal women who received Ferric carboxymaltose.

Inclusion Criteria

- Pregnant women with moderate iron deficiency anemia between 16-36 weeks of period of gestation.
- Pateints who are willing for the study.

Exclusion Criteria

- Patients who are not willing for the study.
- H/O allergy to iron compounds
- Chronic kidney disease
- Anemia due to other causes(including antepartum haemorrhage)
- Hematological disorders
- H/O recent blood transfusion

Methodology

Antenatal women with moderate Iron deficiency anaemia were selected.
Upon selection, a detailed clinical history (menstrual, obstetric), previous treatment history including parentral iron therapy or blood transfusion, compliance with oral iron and chronic medical illness was taken.
Routine antenatal investigations were done according to the standard departmental protocol.
In these antenatal women Haemoglobin estimation, Hematocrit, blood indices such as MCV, MCH, MCHC, peripheral blood smear, serum iron and serum ferritin examination were done .
Required iron dose was calculated for each patient using the formula below:

Ganzoni Equation

2.4× Body weight in Kg ×(Target HB- Actual HB) + 500gm(Body weight = pre- pregnancy body weight)
Patients in the FCM group were administered i.v. FCM. Maximum dose per sitting was 1000 mg. Patients in iron sucrose group were administered i.v. iron sucrose.
The general condition of the patient, blood pressure and pulse rate were noted before infusion and every five minutes during infusion and fetal heart rate monitoring was done before and after infusion.
Haemoglobin estimation, Hematocrit , blood indices such as MCV, MCH, MCHC, peripheral blood smear, serum iron and serum ferritin were repeated after 2 weeks and 4 weeks of Iron-sucrose and FCM administration.
Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Results on continuous measurements were presented on Mean ± SD (Min-Max) & categorical as Frequency (Percentage). Inferential statistics like Chi-square test/Fischer Exact test, Independent t test was applied. The significance of level adopted was 5%.

RESULTS

The mean haemoglobin in Group A was 7.85 ± 0.50 gm% prior to transfusion of iron sucrose, which increased to 10.55 ± 0.52 and 10.94 ± 0.54 gm% at 2 and 4 weeks respectively. A statistically significant increase in mean Hb was seen in Group A ($p<0.05$).
The mean haemoglobin in Group B was 8.06 ± 0.29 gm% prior to transfusion of ferric carboxymaltose, which increased to 11.48 ± 0.56 gm% and 11.84 ± 0.58 gm% at 2 and 4 weeks respectively. A statistically significant increase in mean Hb was seen in Group B ($p<0.05$).
The comparison of mean haemoglobin between Group A and Group B was also found to be statistically significant at 2 weeks and 4 weeks ($p<0.05$).

Table 1: Distribution of Study Participants Based on Haemoglobin Estimation

Mean Hb (Gm %)	Group A	Group B
Pre-Transfusion	7.85 ± 0.50	8.06 ± 0.29

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After 2 Weeks	10.55 ± 0.52	11.48 ± 0.56
After 4 Weeks	10.94 ± 0.54	11.84 ± 0.58

Table 2: Distribution of Study Participants Based on MCV

Mean MCV (fl)	Group A	Group B
Pre-Transfusion	75.30 ± 3.47	75.24 ± 3.98
After 2 Weeks	85.38 ± 3.64	85.03 ± 4.09
After 4 Weeks	87.12 ± 3.60	86.77 ± 4.03

The comparison of mean MCV between Group A and Group B was not found to be statistically significant at 2 weeks and 4 weeks ($p>0.05$).

Table 3: Distribution of Study Participants Based on MCH

Mean MCH (pg)	Group A	Group B
Pre-Transfusion	22.12 ± 2.95	22.34 ± 2.87
After 2 Weeks	26.35 ± 1.14	26.75 ± 0.98
After 4 Weeks	28.49 ± 0.94	28.62 ± 0.96

The comparison of mean MCH between Group A and Group B was not found to be statistically significant at 2 weeks and 4 weeks ($p>0.05$).

Table 4: Distribution of Study Participants Based on MCHC

Mean MCHC (g/dl)	Group A	Group B
Pre-Transfusion	28.28 ± 0.95	28.00 ± 1.06
After 2 Weeks	31.38 ± 0.79	31.59 ± 0.86
After 4 Weeks	33.06 ± 0.77	33.07 ± 0.76

The comparison of mean MCHC between Group A and Group B was not found to be statistically significant at 2 weeks and 4 weeks ($p>0.05$).

Table 5: Distribution Based on Doses Administered

Doses	Group A	Group B
1-4	48	50
>4	2	0
Total	50	50

In Group A, 48 cases required 1-4 doses and 2 cases required more than 4 doses of iron sucrose. In Group B, 50 cases required 1-4 doses of ferric carboxymaltose.

Table 6: Distribution Based on Adverse Effects

Adverse Effects	Group A	Group B
Local	2	0
Systemic	O	0
None	48	50

Group A (iron sucrose) showed 2 case with local reactions (pain with swelling at site of injection and localised urticarial reaction with tingling around site of injection respectively) and no systemic adverse effect. No adverse effects were noted in Group B (ferric carboxymaltose).

Table 7: Distribution of Study Participants Based on Serum Iron

Mean Serum Iron (µg/Dl)	Group A	Group B
Pre-Transfusion	28.50 ± 1.23	29.06 ± 1.06
After 2 Weeks	182.06 ± 10.77	193.59 ± 12.86
After 4 Weeks	168.06 ± 9.32	172.07 ± 11.76

The mean serum iron in Group A was 28.50 ± 1.23 µg/dl prior to transfusion of iron sucrose, which reached to 182.06 ± 10.77 and 168.06 ± 9.32 µg/dl at 2 and 4 weeks respectively. A statistically significant change was noted in mean serum iron in Group A ($p<0.05$). The mean serum iron in Group B was 29.06 ± 1.06 µg/dl prior to transfusion of ferric carboxymaltose, which reached to 193.59 ± 12.86 and 172.07 ± 11.76 µg/dl at 2 and 4 weeks respectively. A statistically significant change was noted in mean serum iron in Group B ($p<0.05$).

Table 8: Distribution of Study Participants Based on Serum Ferritin

Mean Serum Ferritin (µg/L)	Group A	Group B
Pre-Transfusion	7.49 ± 4.23	8.16 ± 5.06

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After 2 Weeks	270.06 ± 14.73	325.00 ± 12.86
After 4 Weeks	205.30 ± 15.32	273.50 ± 16.76

The mean serum ferritin in Group A was 7.49 ± 4.23 µg/L prior to transfusion of iron sucrose, which reached to 270.06 ± 14.73 and 205.30 ± 15.32 µg/L at 2 and 4 weeks respectively. A statistically significant change was noted in mean serum ferritin in Group A ($p<0.05$). The mean serum ferritin in Group B was 8.16 ± 5.06 µg/L prior to transfusion of ferric carboxymaltose, which reached to 325.00 ± 12.86 and 273.50 ± 16.76 µg/L at 2 and 4 weeks respectively. A statistically significant change was noted in mean serum ferritin in Group B ($p<0.05$).

DISCUSSION

The present study was a hospital based prospective study conducted on 100 antenatal women with mild to moderate iron deficiency anemia to compare the efficacy and safety, cost effectiveness, and ease of administration of transfusing Ferric carboxymaltose versus Iron sucrose. The participants were divided into two groups, Group A received iron sucrose and Group B received ferric carboxymaltose.[11,12]

This study showed that iron sucrose as well as ferric carboxymaltose can be used in the pregnant patients with iron deficiency anaemia of pregnancy to correct deficit in the haemoglobin and for restitution of iron stores. Both modalities had increase in the haemoglobin level after 2 weeks and 4 weeks.[13]

The mean haemoglobin in Group A was 7.85 ± 0.50 gm% prior to transfusion of iron sucrose, which increased to 10.55 ± 0.52 and 10.94 ± 0.54 gm% at 2 and 4 weeks respectively. The mean haemoglobin in Group B was 8.06 ± 0.29 gm% prior to transfusion of ferric carboxymaltose, which increased to 11.48 ± 0.56 gm% and 11.84 ± 0.58 gm% at 2 and 4 weeks respectively.[14]

The mean MCV in Group A was 75.30 ± 3.47 fl prior to transfusion of iron sucrose, which increased to 85.38 ± 3.64 and 87.12 ± 3.60 fl at 2 and 4 weeks respectively. The mean MCV in Group B was 75.24 ± 3.98 fl prior to transfusion of ferric carboxymaltose, which increased to 85.03 ± 4.09 and 86.77 ± 4.03 fl at 2 and 4 weeks respectively.[15]

In the present study, Group A (iron sucrose) showed 2 case of local reaction. No systemic adverse effect was observed. No adverse effects either local or systemic were noted in Group B (ferric carboxymaltose).[15]

We observed that in Group A, 48 cases required 1-4 doses and 2 cases required >4 doses of iron sucrose. In Group B, all 50 cases required only 1-4 doses of ferric carboxymaltose. Ferric carboxymaltose reduces the need for repeated intravenous catherization and multiple visits to hospital thus increasing patients' comfort.[16]

Our study did not include travel costs and the number of working days lost due to travel which would have been more in iron sucrose group as the number of visits was significantly higher in iron sucrose group.[17]

All the observed adverse events were mild and quickly reversible.

One of the drawback of this study was that, there was small sample size in both treatment groups. A few confounding variables were mised out. Larger sample sizes are necessary to compare safety and efficacy of intravenous ferric carboxymaltose over iron sucrose therapy in Indian setup.[19]

Overall, this study concluded that Ferric carboxymaltose was safer and more efficient, more affordable in treatment of iron deficiency anaemia in pregnant women as compared to iron sucrose with lesser adverse effect and better patient compliance.

CONCLUSION

The findings of our study showed significant increase in hemoglobin level in both the group but the rise was more among those who received injection FCM than injection iron sucrose.

This study also established that FCM is safer than Iron sucrose.

Treatment with FCM resulted in rapid replenishment of iron stores in pregnant women with significantly higher rise of hemoglobin and with lesser adverse effects.

The convenient dosing with lesser number of total doses resulting in lesser number of hospital visits and hence lowering of total cost involved in transportation, fewer equipment required for infusion and reduction in discomfort caused to the patient due to multiple needle pricks resulted in good patient compliance.

Because of high efficacy and safety of ferric carboxymaltose, it should be used as an alternative first line drug in the management of Iron deficiency anaemia in pregnancy to decrease the incidence and burden of the disease in Indian population.

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