

A STUDY ON SAFETY AND EFFICACY OF FCM IN COMPARISON WITH IRON SUCROSE IN IRON DEFICIENCY ANAEMIA IN ANTENATAL WOMEN IN A RURAL TERTIARY CARE HOSPITAL

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Abstract

Background: To evaluate the efficacy and safety of IV FCM in comparison with IV iron sucrose for the treatment of Iron deficiency anemia in pregnancy in a rural tertiary care hospital. **Materials and Methods:** This prospective interventional comparative study was conducted in the Department of Obstetrics and Gynecology at Bhaskar medical college, Yenkapally, Moinabad , RR dist, Telangana over a period of 2 years from October 2020 - Sept 2022. 60 pregnant patients with hemoglobin in the range 6gm/dl – 9.9 gm/dl between 14 to 34 weeks gestation were selected randomly. Patients were divided into two groups of 30 each. Group A is Iron Sucrose (IS) group; were treated with intravenous iron sucrose in multiple doses on alternate days. Group B is Ferric Carboxy maltose (FCM) group; were treated with intravenous FCM 1000mg. In both groups hemoglobin was assessed before and after (3 weeks; 6 weeks) parenteral therapy. **Results:** There was significant rise of hemoglobin > 2 gm/dl in both the groups. The single dose regime of FCM group was having very good compliance as compared to Iron sucrose group. **Conclusion:** Intravenous Ferric carboxy maltose has similar efficacy and safety as Intravenous Iron sucrose in the management of anemia during pregnancy. Our conclusion is parenteral iron should be considered for the antenatal women presenting with moderate to severe iron deficiency anemia in late second and third trimesters.

INTRODUCTION

Anemia is a common health problem worldwide during pregnancy with a prevalence of 41.8%.^[1]The most common cause of anemia in pregnancy is iron deficiency.^[2]The prevalence of iron deficiency anemia is 18.5% in developed countries and 35% - 75% in developing countries.^[3] Almost 53.7% of Indian pregnant women are anemic as reported in NHFS 5 survey.^[4] High incidence of anemia in India are because of low dietary intake of iron, poor bio-availability of iron, faulty food habits, phytate rich Indian diet , malabsorption, poor iron stores at birth, chronic blood loss during menses and high prevalence of infections like malaria and hookworm infestations.^[5,6]

If iron deficiency anemia remains untreated during pregnancy , it can lead to maternal morbidity and mortality.^[7] Iron deficiency anemia has been shown to be associated with an increased risk of premature birth, low birth weight baby, preeclampsia, placental

abruption and increased peripartum blood loss as well as cardiac failure and related death.^[8]

WHO defined anemia in pregnancy as hemoglobin levels < 11gm% and hematocrit < 33%, 9. According to WHO, anemia in pregnancy is classified as; mild anemia Hb-9-10.^[9] gm%, moderate anemia Hb -7 -8.9 gm% and severe anemia Hb < 7 gm%. CDC takes a cutoff point of 11 gm% in first and third trimesters and 10.5 gm% in second trimester to define anemia in pregnancy.^[10] ICMR (Indian medical Council and research) has categorized anemia during pregnancy as - Mild anemia - Hb -10 - 10.9gm%, Moderate anemia -Hb - 7 - 9. 9 gm%, Severe anemia - Hb - 4-6.9 gm%, very severe anemia- Hb- < 4gm%.^[11] Using 11 gm/dl as a cut off for the definition of anemia is probably too high for Indian women and hence FOGSI (The Federation of Obstetric and Gynecological Societies of India) has suggested a cut off of hemoglobin of 10 gm/dl for Indian women.^[12]

Therapy for iron deficiency includes mainly dietary modifications, oral iron supplementation and in selected cases parenteral iron and blood transfusions.^[12] Oral iron therapy is main stay in treating iron deficiency anemia in pregnancy, however tolerability is a major limiting factor.^[13] Oral iron substitution has shown to be insufficient for the treatment of moderate to severe iron deficiency anemia in second and third trimesters and often associated with noncompliance due to gastrointestinal side effects like nausea, diarrhea, bloating, heart burn, constipation and dark stools. Therefore guidelines recommend that physicians consider IV iron administration in pregnant women in case of iron deficiency anemia with intolerance to oral iron, insufficient hemoglobin increase after oral iron.^[14]

Ministry of Health and Family Welfare, Government of India released operational guidelines of an intensified national iron plus initiative (I-NIPI), Anemia Mukh Bharat. This guideline provides protocols for management of anemia during pregnancy.^[13] As per the guidelines, parental iron (IV Iron sucrose or Ferric Carboxy maltose) may be considered as the first line of management in pregnant women with mild (10-10.9 g/dL) or moderate anemia (7-9.9 g/dL) detected late in pregnancy or in whom compliance to oral iron is likely to be low. Also, IS or FCM is considered as a second-line treatment in case no improvement is observed with the oral iron supplement. In severe anemia (5.0-6.9 g/dl), IS or FCM is recommended as first-line treatment.^[13]

The most commonly used intravenous iron preparation is iron sucrose. It does not require test dose and it is safe. The only disadvantage is limited dose can be given at one time. The maximum permissible dose is 200 mg per day or 600 mg per week. FCM is the latest intravenous IV formulation which can be used at higher doses and allows rapid administration. Because it is free of dextran and its derivatives, FCM does not cross react with dextran antibodies and never needed the administration of a test dose. FCM molecule is a novel iron complex, which consist of ferric hydroxide core chelated in a carbohydrate shell and this complex is taken up by macrophages as a whole, avoiding iron toxicity and oxidative stress.

MATERIALS AND METHODS

This prospective interventional comparative study was conducted in the Department of Obstetrics and Gynecology at Bhaskar medical college, Yenkapally, Moinabad, RR dist, Telangana. This was done over a period of two years (October 2020-September 2022) after approval from hospital ethical committee. The antenatal women attending the Department of OBG were the source of our sample. 60 antenatal women between the gestational age of 14 -34 weeks and hemoglobin levels between 6

gm%- 9.9 gm % were recruited for the study. Women were categorized as mild, moderate, and severe anemia according to WHO.

Inclusion Criteria

All antenatal women who are having hemoglobin of 6-9.9 gm/dl between 14 to 34 weeks of gestational age

Exclusion Criteria

Hypersensitive reaction to any iron preparation
Patients with uncontrolled hypertension
Patients with impaired liver function
Patients with impaired renal function
Patients with heart disease
Patients with hemoglobinopathies

Written informed consent was taken from all the subjects. Detailed clinical history (menstrual, obstetric), previous treatment history, including iron therapy, compliance with oral iron and chronic medical illness was obtained. Demographic data like age, education, socioeconomic status, height, weight was recorded. Complete general, physical, systemic examination and obstetric examination was carried out.

Routine antenatal investigations were done according to standard departmental protocol. Investigations related to anemia like haemogram, peripheral blood smear, red cell indices (MCHC, MCV, MCH), Hb electrophoresis, serum ferritin levels, serum iron, total iron binding capacity, transferrin saturation, complete urine analysis along with culture and sensitivity, stool examination for ova, cyst and occult blood, smear for malarial parasite and serum proteins were done.

After the confirmation of iron deficiency anemia, total Iron requirement was calculated using Ganzoni's formula. Total iron dose required (mg) = $2.4 \times \text{pre pregnancy body weight(kg)} \times (\text{Target Hb(14 gm/dl)} - \text{Actual Hb}) + 500\text{mg}$ (storage iron). 2.4 is a correction factor that takes into account the patient's blood volume, estimated at 7 % of body weight and hemoglobin iron content, which is 0.34 %. Iron deficit was calculated and rounded up to nearest multiple of 100 for each individual.

These women were randomly divided into two groups, Group A: Iron sucrose; Group B: FCM. Routine deworming of all antenatal women was done by oral Albendazole tablet 400 mg. After taking informed written consent from each subject, general condition of the women, pulse rate, blood pressure were noted before starting the infusion and every five minutes during the infusion. Fetal heart rate was monitored before and after the infusion. Any minor and major adverse events were noted and the patient was observed for two hours after the completion of infusion.

Group A (Iron sucrose) subjects were called on alternate days for infusions. After completing the infusion they were observed for 2 hours and discharged. Group B (FCM group) subjects were discharged after one day later and called after a week if she needs second dose. These women were

followed and reassessed with Hb estimation after three weeks and six weeks after the infusion.

RESULTS

After considering inclusion and exclusion criteria, 60 pregnant women who were eligible were included in the study. After taking consent they were randomized into two groups of 30 each (group A Iron Sucrose; group B FCM). All 60 patients completed the treatment and were included in analysis.

Age distribution shows that 77% in group A and 93% in group B were between 20 to 30 years of age, whereas 20% in group A and nil patients in group B were less than 20 years of age and 3% in group A and 7% in group B were above 35 years of age in this study, 85% of the

women in both groups were between 20 to 30 years of age.

All the women in both the groups were literate, 85% in both groups were educated up to 10 th standard. Regarding social economic status, 70% in both the groups belong to middle class and 30% belong to lower class. Regarding built and nourishment, 80% of the women in both the groups were moderately built and 90% of the women in both the groups were moderately nourished.

Regarding gestational age, 23% in group A and 27% in group B were between 14 to 20 weeks of gestation, 50% in group A and 20% in group B were between 20 to 28 weeks of gestation and 23% in group A and 50% in group B were between 28 to 34 weeks of gestation.

Regarding parity, 57% in group A and 48% in group B were primi gravidae where is 43% in group A and 52% in group B were multi gravidae.

Table 1: Hematological parameters vs study groups

| | Group | N | Mean | Std. Deviation | P Value |
|----------------------|--------------|----|-------|----------------|---------|
| Hb (gm/dl) | Iron Sucrose | 30 | 8.31 | 0.60 | 0.616 |
| | FCM | 30 | 8.21 | 0.90 | Not.Sig |
| HCT(%) | Iron Sucrose | 30 | 26.09 | 1.32 | 0.18 |
| | FCM | 30 | 25.36 | 2.66 | Not.Sig |
| MCV(fl) | Iron Sucrose | 30 | 68.25 | 6.83 | 0.079 |
| | FCM | 30 | 64.58 | 8.94 | Not.Sig |
| MCH (pg) | Iron Sucrose | 30 | 21.78 | 3.33 | 0.66 |
| | FCM | 30 | 22.19 | 3.83 | Not.Sig |
| MCHC(gm/dl) | Iron Sucrose | 30 | 30.65 | 1.78 | 0.096 |
| | FCM | 30 | 31.73 | 3.03 | Not.Sig |
| MI(mentzer's index) | Iron Sucrose | 30 | 18.07 | 2.81 | 0.417 |
| | FCM | 30 | 17.51 | 2.42 | Not.Sig |
| RDW | Iron Sucrose | 30 | 17.73 | 1.91 | 0.603 |
| | FCM | 30 | 18.03 | 2.54 | Not.Sig |
| S.Ferritin (ng/ml) | Iron Sucrose | 30 | 8.20 | 3.71 | 0.205 |
| | FCM | 30 | 10.29 | 8.11 | Not.Sig |
| S.Iron (mcg/dl) | Iron Sucrose | 30 | 22.87 | 6.56 | 0.13 |
| | FCM | 30 | 30.26 | 25.49 | Not.Sig |

13% in group A and 10% in group B were having hemoglobin of more than 11 g/dl, 74% in group A and 57% in group B were having hemoglobin percent of 10 to 11 g/dl, whereas 13% in group A and 33% in group B were having hemoglobin levels less than 10 gm/dl. Majority of the women were having Hb values between 10 to 11 g/dl in the first antenatal visit.

Mean hemoglobin in group A was 8.3 gm/dl, and it was 8.2 gm/dL in group B before the correction of anemia. Mean ferritin value was 8.2 ng/ml in group A and group B it was 10.29 ng/ml; serum iron in group A was 22.86 mcg/dl and in group B it was 30.25 mcg/dl.

Distribution according to severity, 17% in group A and 20% in group B were having mild anemia; 80% in group A and 70% in group B were having moderate anemia and 3% in group A and 7% in group B were having severe anemia. Majority of the women were in the category of moderate anemia that is hemoglobin between 7 to 9 g/dl.

Table 2: Severity of Anemia Vs Study groups

| gm/dl | Iron sucrose group | | FCM group | | P Value |
|---------|--------------------|---------|-----------|---------|-----------------|
| | Frequency | Percent | Frequency | Percent | |
| 9 to 10 | 5 | 17 | 6 | 20 | 0.772 |
| 7 to 9 | 24 | 80 | 22 | 73 | Not Significant |
| < 7 | 1 | 3 | 2 | 7 | |

Number of doses required and number of visits to the hospital: In group A, 6-8 doses of Iron Sucrose were required whereas in group B ,1-2 doses of FCM were required for each patient. In the present study, the number of doses required to correct anemia was significantly less with FCM thereby reducing the number of hospital visits for repeated infusions.

In this study, there were no adverse reactions with Iron sucrose group whereas with FCM group, minor adverse reactions were noted in 10% which were managed symptomatically. No major adverse reactions were noted in both the groups.

For group A who received Iron Sucrose the treatment cost for 1000 mg in five divided doses was Rs.4000 where as in group B who received FCM total cost per 1000 mg in single dose was Rs.4200. Though the cost of FCM is slightly higher than Iron Sucrose, the safety and efficacy are comparable to Iron Sucrose. Compliance is better with FCM because of reduced number of visits to hospital.

Statistical Analysis

Data collected was entered in the Microsoft excel spread sheet and later transferred into Statistical Package for Social Sciences (SPSS Inc., Chicago., IL, version 24.0 trial version) for analysis. Parametric data was represented in means and Standard deviations and non- parametric data was expressed in proportions. Statistical tests like chi square, independent sample t test and paired sample t test were used. P Value less than 0.05 is considered statistically significant.

DISCUSSION

Anemia during pregnancy is a major health concern affecting half the pregnant woman. Iron deficiency is one of the most important causes of maternal and neonatal morbidity in both developed and developing countries. It is also important indirect cause of maternal death. Hence diagnosis of iron deficiency anaemia is important and all pregnant women should have anemia corrected before delivery.

The aim of the study was to compare the safety and efficacy of FCM with iron sucrose in pregnant women with iron deficiency anaemia in rural population in a tertiary care hospital.

The study was conducted on 60 antenatal women and were randomly categorised into

Iron sucrose and FCM groups. Majority of the study population (85%) were between the age group of 18 to 25 years of age. This may be because of early marriage in rural population. 85% of the women have primary education, 70% of the woman belong to middle class. In spite of good literacy rate and moderate income they were anemic , this might be because of low dietary iron ,poor absorption , phytates in the diet or helminthiasis.

The average gestational age at the time of anemia diagnosis was 26 weeks (average) with a minimum of 14 weeks and a maximum of 34 weeks. This shows that iron deficiency anemia occurs in late

second trimester due to haemodilution and increased iron requirement from second trimester onwards.

Overall 53% of the women were primi gravidae in both the groups and the prevalence of anemia was slightly higher in primi gravidae in the present study. In 65 % of the women haemoglobin at the initial visit was between 10 to 11 gm/dl. This might be because of low iron stores in these women before the conception.

Total number of doses given in iron sucrose group were more as compared to FCM group thus requiring multiple visits to hospital. The single administration of FCM shows advantage of shorter treatment period, less number of visits which reduces the transport cost and also reduces discomfort due to multiple needle punctures. Patients compliance was better with FCM in view of few days of admission, reduced frequency of venous access and reduced hospital stay.

Registered adverse events seen in the FCM group were mild and quickly reversible. There were no treatment related serious adverse events. None of the adverse events required further medical intervention.

Both groups had significant increase in hemoglobin levels at three weeks and six weeks. After parental iron transfusion. The rise in hemoglobin was slightly higher in FCM than Iron Sucrose, but the rise was not statistically significant.

Table 3: Hb changes at different time intervals vs Study groups

| | Group | Mean (Hb %) | SD | P Value |
|-------------------------------|--------|-------------|------|---------|
| Hb (gm/dl) before transfusion | Orofer | 8.31 | 0.60 | 0.616 |
| | FCM | 8.21 | 0.90 | Not.Sig |
| Hb(gm/dl)-3wks | Orofer | 10.55 | 0.35 | 0.302 |
| | FCM | 10.70 | 0.71 | Not.Sig |
| Hb(gm/dl)-12wks | Orofer | 11.98 | 0.50 | 0.07 |
| | FCM | 12.29 | 0.69 | Not.Sig |

From this study, we observed that FCM is as safe and effective as iron sucrose in the management of iron deficiency anemia despite five times of higher dosage. Both drugs are effective and offer a comparable improvement in anemia.

Limitations

Limitation of this study was small sample size in both the groups. Large trials are required to compare the safety and efficacy of FCM over iron sucrose in Indian pregnant women.

CONCLUSION

The findings of our study showed significant increase in hemoglobin levels in both the groups after the parenteral infusion. FCM is a intravenous iron preparation which is safe to give in pregnancy. It is not inferior to iron sucrose complex and is well tolerated in pregnancy.

FCM has the advantage of a large dose administration per sitting, lesser number of required doses and lesser number of hospital visits and total cost involved into transportation, equipment required for infusion and the discomfort caused to the patient due to multiple needle pricks.

Our conclusion is parenteral iron should be considered for the antenatal women presenting with moderate to severe iron deficiency anemia in late second and third trimesters.

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