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Original Research Article

Comparison of iron-sucrose with ferric carboxymaltose for treatment of postpartum iron deficiency anaemia

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ABSTRACT

Background: Anaemia is a major public health problem worldwide. Haemoglobin (Hb) cut-off in anaemia should be taken as 11 gm/dl in the first and third trimester and 10.5 gm/dl in the second trimester, and a post-partum Hb of 10.0 gm/dl. The aim of the study is to compare the efficacy of iron-sucrose versus ferric carboxymaltose (FCM) in the treatment of postpartum anaemia.
Methods: A prospective randomized interventional study of 132 post-partum females was conducted at a tertiary care hospital, over a 6-month period. Post-partum females delivered via normal vaginal delivery or caesarean section with Hb levels of above 7 gm/dl and below 9.9 gm/dl were randomized into 2 groups. Iron deficit calculated, in mg, according to Ganzoni's formula. One group received intravenous FCM – 500 mg in 250 ml normal saline (NS) over 30 minutes and the other received intravenous iron sucrose - each ampoule containing 200 mg in 100 ml NS over 30 minutes up to a maximum dose of 1000 mg. Follow up done after 15 days, 4 weeks and 6 weeks. The data was tabulated and compared using statistical analysis.
Results: At a 4 and 6 weeks follow up, the mean rise in hemoglobin (Hb) of group A (1.4 g/dl) was significantly greater than that of group B (0.89 g/dl).
Conclusions: The study concludes that thought efficacy of drugs is similar, injection FCM shows a prompt rise in Hb, allows a higher dose to be dispensed in a single seating and is more significant in improving quality of life over a period of time even though it has a marginally higher cost.

Keywords: Anaemia, Iron-sucrose, Ferric carboxymaltose, Injectable iron therapy

INTRODUCTION

Anaemia is a major public health problem worldwide. According to the World Health Organization (WHO) report of 2016, prevalence of anaemia in pregnancy is 40.1%, ranging from 10-12% in the developed world to up to 87.2% in some regions of India.[1,2] The National Family Health Survey 2015-2016 (NFHS-4) shows a marginal fall in the prevalence of anaemia in pregnant women from 58% (NFHS-3) to a current rate of 50%.[3,4] WHO defines as anaemia in pregnancy as a haemoglobin (Hb) level below 11 gm/dl.[1] The centre for disease control and prevention (CDC), recommends that Hb cut-off in anaemia should be taken as 11 gm/dl in the first and third trimester and 10.5 gm/dl in the second trimester, and a post-partum Hb of 10.0 gm/dl.[5,6]

Approximately 80% of anaemia in pregnancy results due to iron deficiency. This occurs primarily due to poor iron stores and low iron content of an average diet. A pregnant woman needs approximately 900-1000 mg of iron throughout pregnancy considering the balance between iron losses and absorption during gestational period. This amounts to a requirement of 0.8 mg/day, 4-5 mg/day and over 6 mg/day of iron required in the first, second and third trimester, respectively.[2]

Oral and parenteral iron therapy has the same rate of response in the rise of Hb. Parenteral iron therapy for anaemia in pregnancy is recommended when there is intolerance to oral iron, poor response to oral iron therapy, non-compliance, inflammatory bowel disease. Intravenous administration is now preferred to intramuscular iron since it can be given in fewer sittings and newer molecules have a better safety profile than the intramuscular iron preparations. Iron dextran is a first-generation iron preparation for intravenous administration. A total of 1000 mg can be administered in one sitting. However, due to risk of fatal anaphylactic reactions it is withdrawn from standard therapy.

Iron-sucrose (ISC) is considered a second-generation intravenous preparation. It's primary mechanism of action is the rise of serum ferritin levels. There are no reported fatal complications or deaths and hence does not require a test dose. It requires multiple small dose infusions. It is administered as a 200-300 mg/day dose, which can be repeated every 3-4 days. A total of 600 mg/week can be administered. The dose is diluted in 0.9% normal saline (NS). A dose of 200 mg can be given over 30 minutes in 100 ml NS, whilst a dose of 300 mg must be given over 90 minutes. On completion, the patient must be observed for 30 minutes, and a 50 ml flush of normal saline must be ensured.

Ferric carboxymaltose (FCM) is a third-generation preparation like ferumoxytol and iron isomaltose. These are faster acting iron preparations, not requiring a test dose due to no serious anaphylaxis reported. A maximum single dose of 1000 mg or 20 mg/kg, whichever is lesser, is approved for treatment of anaemia. The remainder of the calculated dose can be administered after 1 week. The dose is diluted in 100 ml NS and is infused immediately over a period of minimum 15 minutes. This is followed by a flush of 50 ml NS. FCM is well tolerated and has a comparable safety profile to ISC, with an advantage of larger single dose administration in one sitting, hence reducing repeated transfusions.

METHODS

Prospective randomized interventional study in department of obstetrics and gynaecology, MGM Women's and Children Hospital, Kalamboli, Navi Mumbai over 6-month period. A total number of 132 post-partum females delivered via normal vaginal delivery or caesarean section. Sampling was done by simple random method and group allocation was randomized. Post-partum females delivered via normal vaginal delivery or caesarean section with Hb levels >7 gm/dl or ≤9.9 gm/dl.

Inclusion criteria

Patients with informed consent, willing to follow up, age group of 18-35 years, post-partum females delivered via normal vaginal delivery or caesarean section, Hb less than 7 gm/dl and greater ≤9.9 gm/dl were included in the study.

Exclusion criteria

Patients not willing to give consent, Hb ≤7 gm/dl, having known allergy to FCM and ISC, history of blood transfusion in current pregnancy, thalassemia, coagulation disorders, thrombocytopenia (≤1.5 lakh), medical disorders, renal, hepatic, cardiac disorders, and patients aged >35 years were excluded from the study.

Methodology

Written informed consent to be taken from all patients. Complete history and general physical examination of all participants on admission noted. Routine blood investigations on admission noted. Patient demographic data including age, parity, mode of delivery noted. Hb levels 48 hours post-partum recorded. A total of 132 post-partum females were randomized into 2 groups.

According to Ganzoni's formula, dosage (in mg) for iron deficit is calculated by the formula given.

$$Dosage = [2.4 \times \{(Pre-pregnancy\ body\ weight\ in\ kg) \times (target\ Hb - actual\ Hb\ in\ gm/dl)\}] + 500\ mg\ for\ iron\ stores$$

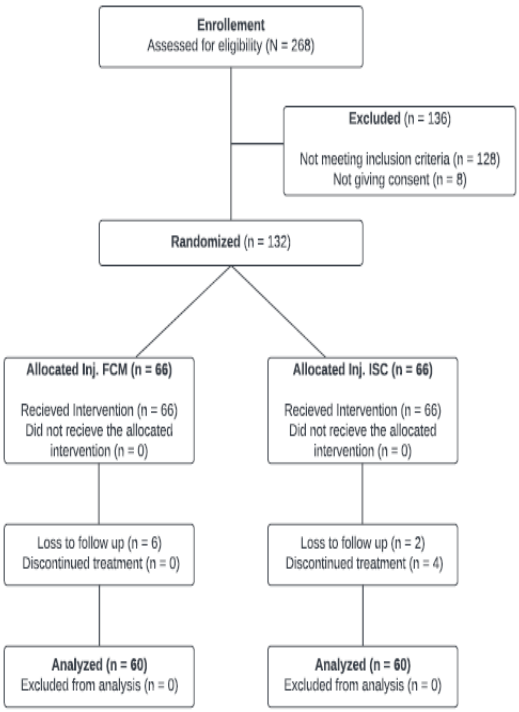

Figure 1: Methodology.

In group A, 66 post-partum females delivered via normal vaginal delivery or caesarean section with Hb levels of Hb levels of greater than 7 gm/dl but less than 9.9 gm/dl who

received intravenous FCM – 500 mg in 250 ml NS over 30 minutes. In group B, 66 post-partum females delivered via normal vaginal delivery or caesarean section with Hb levels of greater than 7 gm/dl but less than 9.9 gm/dl who received intravenous ISC- each ampoule containing 200 mg in 100 ml NS over 30 minutes.

Patients were followed up after 15 days, 4 weeks and 6 weeks to record the rise in Hb level. Data was recorded and tabulated.

Outcome measures

Primary outcome

Rise in Hb from baseline after 15 days, 4 weeks and 6 weeks.

Secondary outcomes

Change in RBC indices, and improvement in fatigue scores – linear analogue scale (LASA) score.

Data analysis method

Data will be entered using secondary data in Microsoft excel and analysed via independent and paired-t test.

RESULTS

Patients in both groups were followed up with repeat Hb estimation at 15 days as well as 4 weeks after administration of iron therapy. At 15 days post treatment, there was no significant difference in rise in Hb between group A and group B (Table 1). At 4 weeks the mean rise in Hb was marginally significant between group A (0.7 gm/dl) compares to group B (0.31 gm/dl). However, at 6 weeks follow up, the mean rise in Hb of group A (1.4 gm/dl) was significantly greater than that of group B (0.89 gm/dl) (Table 1 and Figure 2).

The total cost of injection FCM was ₹3,255/-, while, injection ISC was ₹3,765/- for a standardized maximum 1000 mg dose. In the study, the number of doses of injection ISC given to most patients was 3, amounting to marginally lower price for injection ISC therapy. However, the above values do not take in account the intangible costs, such as travel expenses, loss of working days and inconvenience faced by individual (Table 2).

Incidence of adverse effects was greater in group A (16.7%) as compared to group B (10%), with skin rashes being the most common reaction in both groups, closely followed by itching. Serious side effects such as anaphylaxis were seen in only 1.7% of patients treated with FCM and not seen in a single patient treated with ISC (Figure 3).

Fatiguability and poor well-being are known symptoms of anaemia that can be improved by treatment. The present study used a LASA to measure improvements in fatigue scores and a 10-point numeric scale to assess the feeling of well-being and is an important measure of quality of life.

LASA scores was almost insignificant at 15 days between the two groups but were significantly higher in group A at the end of 4 weeks (Figure 4).

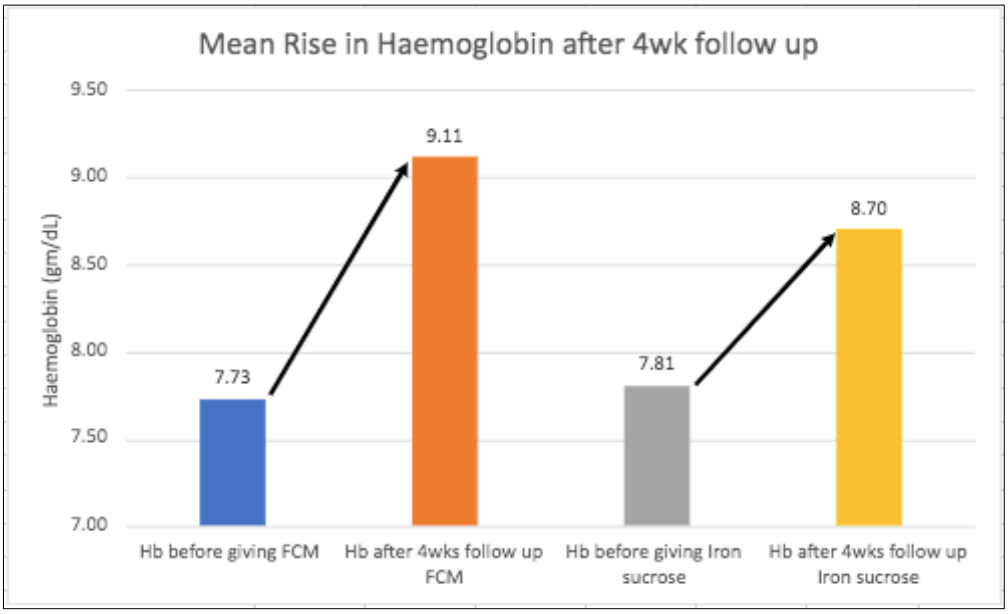

Figure 2: Mean rise in haemoglobin levels.

Table 1: Haemoglobin levels.

Variables	Mean	SD	T value	P value
Before starting treatment				
Group A	7.73	0.46	-0.9666	0.3357
Group B	7.81	0.48		
15 days after treatment				
Group A	8.01	0.48	-0.1698	0.8651
Group B	7.99	0.49		
4 weeks after treatment				
Group A	8.40	0.5	0.42	0.0001
Group B	8.12	0.49		
6 weeks after treatment				
Group A	9.113	0.639	4.05	0.000091
Group B	8.702	0.488		

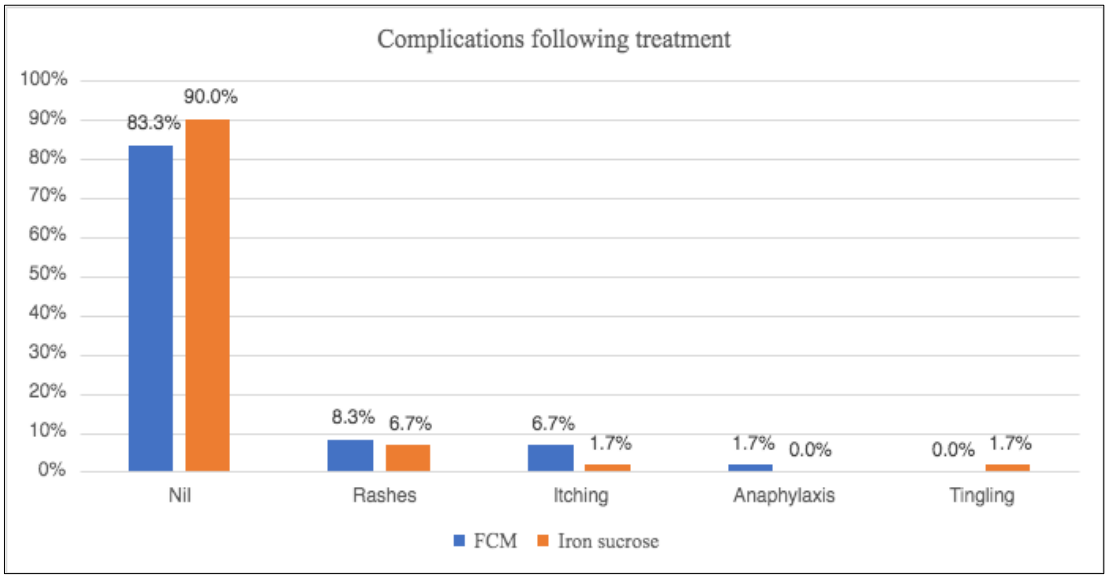

Figure 3: Complications following treatment.

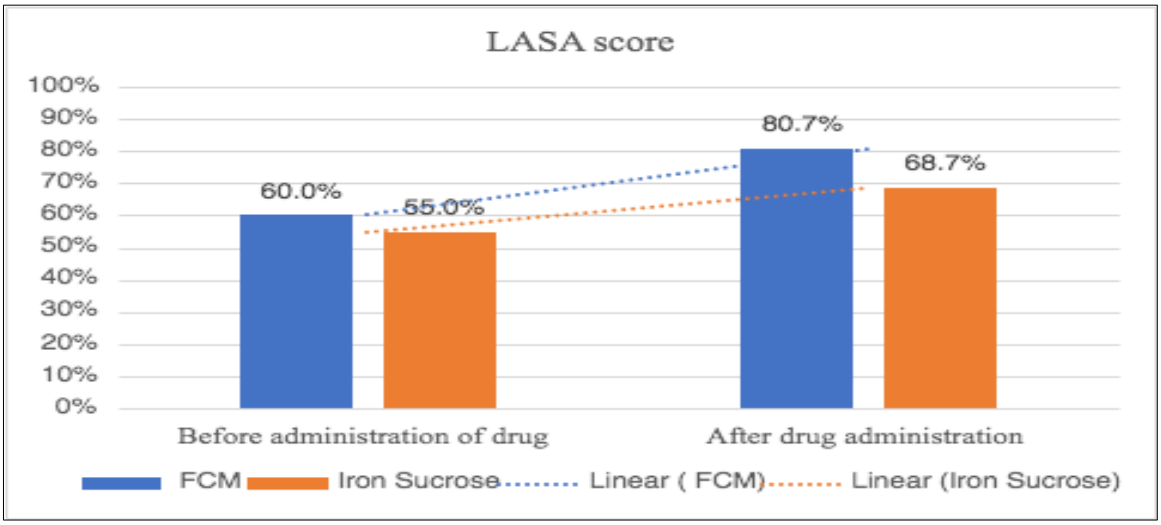

Figure 4: LASA score following treatment.

Table 2: Cost analysis of 1000 mg dose of drug.

Parameters	Inj. FCM	Inj. ISC
Drug	₹3,040/-	₹350/- (per 200 mg)
IV set	₹141/-	₹141/-
Scalp vein no.22	₹24/-	₹24/-
100 ml NS	NA	₹18/-
250 ml NS	₹30/-	- N.A -
10 cc syringe	₹20/-	₹20/-
Hospital charges (per day)	No extra duration of stay	₹200/-
Total	₹3,255/-	₹753 (×5)
Total for 1000 mg	₹3,255/-	₹3,765/-

DISCUSSION

In this study, individuals having a Hb below 7 gm/dl, with significant pallor or tachycardia were given blood transfusion.

The study differentiates the two intravenous iron preparations for the correction of iron deficiency anaemia in pregnancy. Injection FCM was found non-inferior to injection ISC in correction of anaemia. Rather, injection FCM had a significantly higher and rapid Hb rise as compared to injection ISC group and with significantly less sittings for the dose. ISC has been the standard of care for parenteral iron therapy for treatment of anaemia in pregnancy. However, the main pitfall with ISC is limited maximum permissible dose per week thus need of multiple visits to deliver the required iron dose, while FCM can be administered in a larger amount at a time.

A randomized control trial of treatment of moderate and severe iron deficiency anaemia with FCM and iron-sucrose showed a significantly greater rise in the FCM group – 2.9 gm/dl versus 2.2 gm/dl; p value <0.01 after 12 weeks.[7] Breymann et al conducted a similar study and showed that Hb levels improved at comparable rates in both groups which corresponds to our study. Patients in FCM group had significantly more women who achieved Hb rise within a shorter time frame.[8]

A study by Christoph et al concluded comparable safety and tolerability of FCM to ISC and that FCM offers the upper hand of a higher iron dosage at a time reducing the need for repeated administration and increasing patients' compliance.[9]

The total cost of drug was analysed in both the groups in the present study and showed significantly higher cost in FCM group. But this analysis did not include number of working days lost which would have been more in ISC group as the overall cost of therapy with ISC would have been higher due to the need of multiple IV sets and scalp vein required with each administration to receive the complete dosage and travel cost if the patient takes the dose as outpatient therapy.[7]

CONCLUSION

This study proves that it is more suitable to give injection FCM to combat postpartum iron deficiency anaemia, despite the fact that it has similar efficacy to injection ISC. FCM allows a higher dose to be dispensed in a single seating, has a significant rise in Hb and greater improvement of quality of life over injection ISC. Moreover, the convenience with FCM administration improves the patient compliance and treatment satisfaction even though it has a marginally higher cost.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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