International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Papaniya TD et al. Int J Reprod Contracept Obstet Gynecol. 2023 Jun;12(6):1844-1848
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20231566

Original Research Article

Comparison of ferric carboxymaltose and iron sucrose for treatment of iron deficiency anemia in pregnancy at tertiary care centre, Western India

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Received: 20 April 2023
Accepted: 11 May 2023

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ABSTRACT

Background: Iron deficiency anemia is the most common haematological health problem among pregnant women but can be prevented by effective measure. The study aimed to evaluate the efficacy and safety of intravenous ferric carboxymaltose (FCM) in comparison with intravenous Iron sucrose (IS) for treatment of iron deficiency anemia in pregnancy.
Methods: A prospective interventional comparative study was conducted from (June 2021-June 2022) at a tertiary care hospital. Pregnant women diagnosed with moderate to severe iron deficiency anaemia were screened for the study. One hundred patients were randomized to receive either intravenous FCM or IS. Treatment effectiveness was assessed by repeat Haemoglobin (Hb) and RBC indices measurement after 4 weeks of completion of therapy. Safety was assessed by analysis of adverse drug reactions during infusion and 2 hours after infusion.
Results: Mean rise in Hb at 4 weeks was significantly higher in FCM group (1.67±0.47 Vs 1.07±0.25; p<0.0001) as compared to IS group. There was also rise in other biochemical parameters like MCV and MCHC in both groups. Numbers of visits were significantly less in FCM group. No serious adverse events were noted in either group.
Conclusions: Intravenous ferric carboxymaltose is more effective and safer as compared to intravenous iron sucrose in the management of anemia during pregnancy. It has advantage to administer large dose in single sitting which reduce overall cost of therapy and hence will lead to better compliance in community setting.

Keywords: Iron deficiency anemia, Iron sucrose, Ferric carboxymaltose, Haemoglobin

INTRODUCTION

Iron deficiency is the most common nutritional deficiency in pregnancy and is a major contributory factor to maternal morbidity, mortality and higher perinatal mortality rate.[1,2] According to World Health Organization (WHO) report, about 32.4 million pregnant women suffering from anemia worldwide, of which 0.8 million women are severely anemic. Moreover, 50% cases of anemia attributable to iron deficiency anemia (IDA).[3] It is a global public health problem and is responsible for 40% of maternal deaths in developing countries out of which it is responsible for 25% of direct maternal deaths.[1]

WHO defines anemia as haemoglobin less than 11 gm%. Indian Council of Medical Research has categorised anemia during pregnancy as mild (haemoglobin: 10-10.9 gm%), moderate (haemoglobin: 7-9.9 gm%), severe (haemoglobin: 4-6.9 gm%) and very severe (haemoglobin: < 4 gm%).[4] The reasons for high incidence of anemia in India include low dietary intake of iron, poor bio-availability of iron, phytate-rich Indian diet, faulty food

habits, chronic blood loss during menses and high prevalence of infections like malaria and hookworm infestations.[5] Progression from iron deficiency to IDA in pregnancy is common, due to the increased demand for iron during pregnancy (about 1000mg), required to support maternal haemoglobin mass expansion as well as the growing foetus and placenta.[6] IDA can cause various complications during pregnancy like increase susceptibility towards infection, reduce physical and mental functions, increase need of blood transfusion during delivery, cardiovascular complications, intra uterine growth retardation, preterm delivery, and perinatal mortality and morbidity.[2,7]

The mainstay of treatment for iron deficiency anaemia is iron supplementation either oral or parenteral. The indications for parenteral iron treatment are intolerance to oral iron, non-compliance to oral iron and patients who need rapid restoration of iron stores in case of moderate to severe anemia, especially in the late second and third trimester. Parenteral therapy promises a better response in these patients and can obviate the need for blood transfusions in the antenatal and postpartum period.[8]

Iron sucrose (IS) and ferric carboxymaltose (FCM) are dextran free iron preparation for parenteral therapy. The most commonly used intra venous 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 200mg per day or 600 mg per week and requires multiple hospital visits and puts a heavy burden on hospital resources. IV FCM has a near neutral pH (5-7), physiological osmolarity and increased bioavailability, which makes it possible to administer high single doses over shorter time periods (up to 1000mg in a single dose infused in 15 minutes) than other parenteral preparations. It is dextran free; therefore, the risk of anaphylaxis or serious hypersensitivity reactions is very low, and a test dose is also not required.[9] Hence this study aimed to compare and evaluate the efficacy and safety of intravenous ferric carboxymaltose and iron sucrose in treatment of anemia during pregnancy.

METHODS

This prospective interventional comparative study was conducted during June 2021-June 2022 in Obstetrics and Gynaecology department at Tertiary care hospital (PDU Medical College and Hospital, Rajkot). Total 100 antenatal women of gestation week from 20-34 weeks and having iron deficiency anemia with haemoglobin (Hb) 7-10 gram % were enrolled with prior consent.

Exclusion criteria

H/O allergy to iron compound. Chronic kidney disease. anemia due to other cause, haematological disorder, asthma, hepatitis, gestation week <20 week and >34 week, delivered before 4 weeks.

A detailed clinical history (menstrual, obstetric), previous treatment history including iron therapy and information regarding chronic medical illness was taken. Complete general physical examination and obstetric examination was done. Routine antenatal investigations were done according to standard departmental protocol. Investigation related to anemia like haemogram, red cell indices (MCHC, MCV) were done. These enrolled women were divided randomly in to two groups of 50 each. One group of 50 received IS (Group I) while other 50 received FCM (Group II) after calculating total iron requirement. Routine deworming was done for all antenatal women by oral Albendazole tablet 400mg.

Total iron requirement was calculated as follow: 10

Total iron dose required (mg) = 2.4 × Body weight (kg) × (Target HEMOGLOBIN - Actual HEMOGLOBIN) + 500mg (storage iron).

Haemoglobin deficit was calculated by subtracting from 11 gm%.

Group I: received intra venous iron sucrose 200 mg (2 ampoules of 100 mg) in 100 ml 0.9% NS over 15-30 minutes on alternate days until the total dose was administered (not to exceed 600 mg per week). The first few ml was infused intravenously over a period of 15 mins, if there was no adverse reaction remaining amount was infused over 30 mins period.

Group II: received 1000 mg of ferric carboxymaltose in 200 ml of 0.9% NS as follow:

100 - 500 mg in 100ml NS - 15 mins duration

500 - 1000mg in 200ml NS - 30 mins duration,

Subsequent doses if needed were planned on 7th and 14th day.

Parenteral iron therapy was administered under doctor's supervision. The general condition of antenatal period, blood pressure and pulse rate were noted before infusion and every 5 mins during infusion. Fetal heart rate was monitored before and after infusion. During therapy any adverse drug reaction was noted. The women were then followed up after 4 weeks of completion of therapy. On follow up, examination for pallor was done again and Haemoglobin was measured again. Rise of Hb was noted and data analysed statistically by appropriate statistical method.

RESULTS

Most of the patients were belonging to 20-30 years age groups (Group I-94%; Group II-94%), were literate (Group I-96%; Group II-94%), and Multigravida (Group I-70%; Group II-58%) in both groups. Most of patients in both groups were booked (Group I-78%; Group II-60%),

taken ANC visits (Group I-92%; Group II-84%) and also most of them were taken haematinics (Group I-80%; Group II-86%) (Table 1).

Table 1: Baseline characteristics of study participants.

Variables		Group I (IS) no (%)	Group II (FCM) no (%)
Age	20-25	25 (50)	19 (38)
	26-30	22 (44)	28 (56)
	31-35	02 (4)	03 (6)
	>35	01 (2)	0
Residence	Rural	21 (42)	23 (46)
	Urban	29 (58)	27 (54)
Religion	Hindu	38 (76)	36 (72)
	Muslim	10 (20)	10 (20)
	Other	02 (4)	04 (8)
Education	Literate	48 (96)	47 (94)
	Illiterate	02 (4)	03 (6)
Occupation	Laborer	18 (36)	21 (42)
	Housewife	29 (58)	27 (54)
	Services	03 (6)	02 (4)
Parity	Primigravida	15 (30)	21 (42)
	Multigravida	35 (70)	29 (58)
Booked/ Unbooked	Booked	39 (78)	30 (60)
	Unbooked	11 (22)	20 (40)
ANC visit	Taken	46 (92)	42 (84)
	Not taken	04 (8)	08 (16)
Hematinics taken	Taken	40 (80)	43 (86)
	Not taken	10 (20)	07 (14)

Table 2: Rise in haematological parameters after treatment in both groups (paired t test).

Haematological parameters	Group I (IS) Mean±SD	Group II (FCM) Mean±SD
Haemoglobin		
Baseline	8.45±0.67	8.44±0.74
After 4 weeks	9.54±0.66	10.08±0.69
P value	<0.0001	<0.0001
MCV		
Baseline	70.41±11.29	71.11±9.3
4 weeks	73.06±13.24	74.53±11.63
P value	0.008	0.005
MCHC		
Baseline	31.74±1.45	32.05±1.43
4 weeks	32.55±2.26	33.16±1.38
P value	0.001	<0.001
MCH		
Baseline	23.29±4.49	22.69±3.44
4 weeks	26.32±3.47	25.89±3.06
P value	<0.001	<0.001

In Group I receiving IS, mean rise in Hb was 1.07±0.25 and in Group II receiving FCM, mean rise in Hb was 1.67±0.47 as compared to their baseline Hb. Mean rise in Hb in both groups was found statistically significant (p<0.0001). There was also rise MCV, MCHC and MCH in Group I after iron sucrose transfusion and in Group II after transfusion of FCM. Mean rise in MCV, MCHC and MCH in both groups after transfusion when compared to their baseline readings were also found statistically significant. Mild adverse reactions were observed in 10% patients in Group I (vomiting, rigors) and in 6% patients from Group II (vomiting, rigors). No major side effect was noted making the both drugs safe in pregnancy (Table 2).

Table 3: Efficacy of irons sucrose Vs FCM for rise in haemoglobin (Unpaired t test).

Haemoglobin	Group II (FCM) MeanSD	Group I (IS) Mean±SD	P value
Base line	8.44±0.74	8.45±0.67	<0.001
After 4 weeks	10.08±0.69	9.54±0.66	
Rise in haemoglobin level (Difference between baseline and after 4 weeks)	1.67±0.47	1.07±0.25	

At 4 weeks post treatment, the rise in mean Hb level was more in Group II (FCM) as compared to Group I (iron sucrose). Statistically the rise in mean Hb level was significant. Thus, FCM is better than iron sucrose in increasing hemoglobin level after 4 weeks of treatment (Table 3).

DISCUSSION

As per NFHS-5 data, the prevalence of anemia in India is 52.2% among pregnant women i.e. increased by 1.8 percentage points compared to NFHS-4 data. The prevalence of anaemia among pregnant women was the highest in Bihar among large states with 63.1%, followed by Gujarat (62%). Anemia during pregnancy is a major health concern globally and iron deficiency anemia which is preventable condition is associated with unfavourable consequences both for mother and perinatal mortality and morbidity. Timely intervention by parenteral iron therapy can reduce chances of morbidity and mortality during pregnancy and subsequently reduce burden over health sector by reducing complications during delivery due to anemia. Iron sucrose is drug of choice as parenteral iron therapy in moderate to severe iron deficiency anemia in pregnancy. However, limited maximum dose per sitting and frequent visits per week is a major disadvantage of it. FCM can be administered in large dose in single sitting with higher efficacy and safety. This study aimed to compare and evaluate the efficacy and safety of IV FCM and IS in anemia during pregnancy.

The demographic data like age were comparable among both groups. Majority of the patients were in the age group of 20-30 years (Group I-94%; Group II–94%). The findings of present study are correlated with the study conducted by Patel Alpesh et al at tertiary care hospital at Pravara institute of medical science, Loni, Maharashtra among 100 antenatal women, Deepali Janugade in Department of Obstetrics and Gynaecology, Krishna Institute of Medical Sciences, Karad, Maharashtra among 80 antenatal women, Khan and Gupta in the department of obstetrics and gynecology in Rohilkhand medical college and hospital, Bareilly among 110 antenatal women, found that most of the pregnant women were in 21–29 years of age.[11-13] Study by Sunil et al in Jammu among 100 women with anemia found mean age of FCM group was 26.46±3.58 years and mean age of Iron Sucrose group was 24.64±2.87 years.[14] Metgud MC et al, conducted a study in the Gynaecology department of a hospital in Karnataka, India where the mean age was 25.33±3.53 in FCM group vs. 24.85±4.18 years in Iron Sucrose group.[15] Joshi SD et al, conducted a similar prospective study on 100 antenatal patients in VIMS, Karnataka with the mean age group in the FCM group 22.56 years and 25.1 years in Iron Sucrose group, with the majority of patients belonging to the age group of 21-25 years of age.[16] The age group of 20-29 years is found to be more prone to anaemia probably because of increased demand, improper dietary habits, lack of health education and iron deficiency during the adolescence period.

We found that anemia was more common in urban area (due to faulty dietary habits) as compared to rural area (Group I-58%; Group II–54%). Similar findings were observed in a study by Mahaur B et al in Himachal Pradesh.[17]

In our study anemia was more common in Multigravida than in Primigravida (Group I-70%; Group II–58%). The findings were consistent with results obtained in study by, Patel Alpesh et al, Deepali Janugade, Khan S and Gupta S. A., Mahaur B et al and Beigh et al.[11-13,17,18] Sunil et al found that 44% of patients in FCM group and 38% in Iron Sucrose group were Primigravida, while 56% of patients in FCM group and 62% in Iron Sucrose group were multigravida.[14] In the study conducted by Metgud MC et al, 56.86% of females were multigravida in FCM group and 76.9% in the Iron sucrose group.[15] Higher incidence of anaemia in multigravida is because multiple pregnancies especially without proper spacing leads to consumption of iron stores without adequate time for replenishment.

In Group I who received iron sucrose had mean haemoglobin rise of 1.07±0.25 and in Group II who received ferric carboxymaltose had mean haemoglobin rise of 1.67±0.47. There was significant rise in Hb in both groups and it was statistically significant ($p<0.001$). There was a statistically significant rise in Hb in FCM group as compared to that of Iron Sucrose (1.67 vs 1.07). The results of the present study with regard to efficacy of FCM in comparison with Iron Sucrose have been consistent with the other studies conducted by Patel Alpesh et al, Deepali Janugade, Khan S and Gupta S. A., Sunil et al, Metgud MC et al, Mahaur B et al, and Beigh et al.[11-15,17,18] Breymann C et al. compared FCM with oral iron therapy for treatment of iron deficiency anemia in pregnancy. Hb levels improved at comparable rates in both groups. Patients in FCM group had significantly more women who achieved Hb > 110 g/L and within a shorter time frame. The authors concluded to consider FCM to be first-line treatment option for correction of IDA especially in the third trimester of pregnancy.[19] The study conducted by Ambily J et al and by Divyani et al, had shown significant rise of haemoglobin in women who received ferric carboxymaltose than women who received iron sucrose. Results were equivalent as this study.[20,21]

There was comparatively lesser side effects in FCM group as compared to Iron Sucrose group (6% vs 10%), all of them being mild in nature. The first study on the use of FCM for treatment of IDA in pregnancy was published by Christoph P et al. The study concluded comparable safety and tolerability of FCM to ISC and that FCM offers the advantage of a much higher iron dosage at a time reducing the need for repeated applications and increasing patients' comfort. The authors documented a comparable rise in Hb levels at the end of the study.[22]

CONCLUSION

Ferric carboxymaltose is safe as parenteral iron therapy during pregnancy and it is better in correction of iron deficiency anemia as well as replenishment of iron store than iron sucrose. FCM has the advantage of a large dose administration per sitting, lesser total number of required doses (convenient dosing), hence lesser number of hospital visits, less equipment required for infusion and also less discomfort caused to the patient due to multiple needle pricks. Significantly, FCM with shorter duration of treatment makes it patient friendly dosing which results in good compliance from patient side. Less resources also decreases burden on tertiary care hospital as well. It can be used as a first line drug in the management of iron deficiency anemia in pregnancy to decrease high incidence and burden of the disease on our society set up..

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Papaniya TD, Parmar MT, Solanki HM. A Comparison of ferric carboxymaltose and iron sucrose for treatment of iron deficiency anemia in pregnancy at tertiary care centre, Western India. Int J Reprod Contracept Obstet Gynecol 2023;12:1844-8.