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### Iron Carboxymaltose: A Safe and Effective Molecule to Combat Anemia in Pregnancy

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#### KEYWORDS

Iron  
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#### A B S T R A C T

A large group of pregnant females attend antenatal clinics at 28-32 wks of pregnancy when they already become anaemic. Most of the pregnant women do not consume oral iron (56%) because of side effects, only 10% women consume correctly. The present prospective study is consistent with other studies that ferric carboxy maltose administration in the second and third trimester of pregnancy is likely to be safe and effective the mean haemoglobin level achieved in the intravenous iron ferric carboxy maltose was significantly higher than iron sucrose group the simple FCM dosing regime was associated with greater patient compliance compared with iron sucrose .

#### Introduction

Anemia is one of the world's leading cause of disability and thus one of the most serious global public health problems. Anemia affects nearly half of the pregnant woman in the world. Globally anaemia affects 1.62 billion people which correspond to 24.8% of the population. Prevalence of anaemia is highest in south Asian countries in the world. It is estimated that half of the global maternal deaths due to anaemia occur in south Asian countries.

India alone contributes 50% of global maternal deaths due to anemia(1). It is estimated that in India 50% of population suffering from anemia. About 20-40% of maternal deaths in India are due to anemia and one in every 2 Indian women (56%) suffers from some form of anaemia(2). In Indian 41.8% pregnant women are affected from anaemia which is the underlying cause of maternal mortality and prenatal mortality (3).

The low dietary intake of iron and folic acid coupled with poor bioavailability of iron is the major factor responsible for very high prevalence of anaemia in the India(4, 5). Iron deficiency anemia is a common nutritional deficiency amongst women of childbearing age. Pregnant women with IDA are associated with significant prenatal morbidity and mortality. Women with IDA are at increased risk of preterm birth, fetal growth restriction, intra uterine fetal death and low apgar score and infections. According to WHO, anemia in pregnancy is defined when the hemoglobin concentration in peripheral blood is less than 11 gm /dl. Hemoglobin level 9-11 gm/dl is mild, 7-9 gm/dl is moderate and less than 7 gm/dl is severe anaemia (6).

A large group of pregnant females attend antenatal clinics at 28-32 wks of pregnancy when they already become anaemic. Most of the pregnant women do not consume oral iron (56%) because of side effects, only 10% women consume correctly. Iron deficiency anemia is preventable and treatable, our aim is to replenish the iron stores during antenatal period and during labour and enhances the hemoglobin level to produce the positive effect of the health of mother and infant.

Oral iron is the best treatment of choice for the majority of patients with iron deficiency anemia in pregnancy. However oral supplementation has some disadvantages like poor absorption, poor compliance and significant side effects of gastrointestinal tract(7).

Parenteral iron helps in restoring iron stores faster and more effectively than oral iron. Intravenous iron preparations offer an alternative approach in pregnant women with moderate to severe anaemia which are having intolerance of oral iron preparation.

The incidence of anaphylaxis and other adverse reaction with i.v iron sucrose is markedly lowered with ferric carboxymaltose injection. Also reduces the multiple dose infusion by giving intravenous ferric carboxymaltose. FCM has a neutral pH (5.0-7.0) and physiological osmolarity, which makes it possible to administer its higher single dose over short time periods than other parenteral preparations(8). Because it does not contain dextran, chances of anaphylaxis is very low, so test dose is not required.

There is very limited clinical studies regarding the use of FCM during pregnancy. So our aim of study is to use of injection ferric carboxymaltose in the treatment of pregnancy with anaemia and to improve the quality of life and to withstand the stress of labour.

### **Materials and Methods**

This comparative study was conducted in the department of obstetrics and Gynaecology, S.N Medical College, Agra over a period of 1 Year from July 2014 to July 2015.

Total 100 antenatal women with Iron deficiency anemia attending the outpatient department between the 28-34 wks of gestation age were included in our study. Cases were randomly distributed into two groups consisting of 50 cases each.

Women in Group A received intravenous ferric carboxymaltose 1000mg single dose in 250ml of 0.9% normal saline over 15 minutes. In group B 50 women received intravenous iron sucrose in 5 doses of 200mg diluted in 100ml of 0.9% normal saline and infused over 20 min on alternate days up to 5 days. Women having history of allergic reactions to previous parenteral iron

therapy, megaloblastic anemia, aplastic anemia, thalassaemia, sickle cell anaemia, H/o asthma, allergy, patient with anaemia due to chronic illness like liver disease, renal disease and infections were excluded from the study.

Total dose calculation for iron deficit is given below:

**Total iron dose required (mg)=2.4 x Bodyweight (in Kg) x (Target Hb- Actual Hb in gm/dl) + 500mg.**

The factor 2.4 is derived from the blood volume which is 7% of body weight and iron content of Hb, which is 0.34% ( $0.07 \times 0.0034 \times 100 = 2.4 \text{mg}$ ) (Conversion from gm/dl to mg).

## **Results and Discussion**

In the present study cases selected in both the groups were comparable in terms of age, parity and socioeconomic status. Total 100 antenatal women between 28-34 wks of gestation were included in the study, 50 cases in each group. Mean age of antenatal women included in our study was 25.2 yrs, mean parity was 2 or more and mean gravidity was 4+\_3 as (table 1). Majority of the cases belonged to lower middle class(class 4) according to Modified B.J.Prasad classification in both groups. Cases were randomly given injection ferric carboxymaltose and iron sucrose. Antenatal women in Group A (FCM group) were given injection ferric Carboxymaltose and in Group B (iron sucrose group) injection sucrose was given after informed consent.

In our study in group A, 41 women had moderate anemia and 9 had severe anaemia and in group B, 43 women had moderate anemia and 7 women were severely anaemic. In both groups combined 84%

women had moderate anemia and 16% had severe anemia. Most of the women presented with anaemia at mean haemoglobin 8. Blood parameters was done before infusion and repeated 4 wks after infusion.

In group A preinfusion mean hemoglobin in was 9.02 gm/dl, and after infusion mean hemoglobin was 11.48 gm/dl. The increase of mean hemoglobin was 2.48 gm/dl, 4 wks after infusion of ferric carboxymaltose (Table II). In group B pre infusion mean hemoglobin was 9.06 gm/dl and 4wks after infusion mean hemoglobin was 11.40 gm/dl. The increase of mean hemoglobin concentration 4wks after the infusion was 2.34 gm/dl (Table II). Table IV depicted that postinfusion increase in hemoglobin concentration was slightly more in Group A. It was 11.48 in Group A and 11.40 in Group B. It is slightly more (0.14gm/dl) in Group A. Both group significantly showed improvement in other blood parameters after Infusion. All adverse reactions are presented in Table V. No serious adverse effects were recorded in any of the women receiving infusion. Pain at injection site was more in Group B in 4 women while in Group A only 2 women complained of pain at injection site (Table V). 1 women in Group A & 4 women in Group B required medication for nausea and vomiting (Table V).

In India many women with Iron deficiency anemia present late in pregnancy or at this gestation age (in third trimester) it is difficult to achieve the desired hemoglobin level with oral supplementation in moderate and severe anemia. To overcome this problem IV iron preparations (e.g iron dextran, iron sucrose, ferric carboxymaltose) are given. Now a days iron dextran is not used because of side effects, iron sucrose has to be given multiple injections to achieve desired haemoglobin. FCM is easy

to administer by giving a single dose injection in comparison to multiple small dose injections of iron sucrose. Ferric carboxymaltose infusion significantly increased hemoglobin level and other blood parameters. The incidence of adverse effects was also lowered in group A. No risk of adverse drug effects on higher iron dose of FCM in comparison to multiple small doses of Iron sucrose. FCM can be used on outpatient basis and women monitored for 1hr post procedure to ensure maximum safety observation and monitoring. FCM is well tolerated in pregnancy with fewer side effects. Single dose administration reduces the frequency of hospital visit. FCM represents a novel iron preparation that overcomes limitations of existing i.v preparations, is effective in correction of Hb deficit and rapidly replenishes the iron stores.<sup>(9)</sup>

To date no prospective Controlled clinical study has been performed using ferric carboxymaltose in pregnant women. A recent Cochrane review concluded that large good quality trials, assessing clinical outcomes (including side effects) as well as the effects of treatment by severity of anemia are required.<sup>(10)</sup> In this study FCM & Iron sucrose both increase the haemoglobin level and other blood parameters significantly. Very few studies are available regarding the use of intravenous ferric carboxymaltose in pregnancy. So we need large good quality trials to assess clinical outcomes including the adverse effects as well as the effect of treatment by severity of anaemia are required<sup>(10)</sup>. As unavailability of studies, observations may help regarding safety efficacy and potential health benefits and risk. Two recent retrospective observational studies comparing ferric carboxymaltose to different iron preparations highlighted the safety and efficacy of FCM. Gionnoulis et al. reported increase of haemoglobin by 4-6

gm/dl in 4 wks in patient receiving iron sucrose, whereas in our study increase in haemoglobin 4 wks after iron sucrose is 2.10 gm/dl<sup>(11)</sup>. In our study increase in mean haemoglobin is 2.48gm% after 4 weeks in patient with FCM and 2.10gm% in patient with Iron sucrose. Rise in haemoglobin was associated with increase of all other parameters significantly. Our results validate several randomized, controlled, multicenter trials in pregnancy and post partum patients where FCM was considered to be very effective in the treatment of anaemia. Adverse effects were 16% in group A and 20% in group B. In group A pain at injection site(0%), breathlessness(4%), transient hypotension(4%), headache(2%), skin rash in(2%), urticaria(2%), nausea & vomiting in(2%). Pain at injection site was common adverse effect in patient with group B (8%), followed by transient hypotension(6%), nausea & vomiting reported in(1%). All the patients had uneventful recovery after receiving treatment.

In a prospective study by Frossler et al<sup>(12)</sup> intravenous ferric carboxymaltose infusion significantly increased haemoglobin level ( $p < 0.01$ ) above baseline levels in all women. Increase in haemoglobin and serum ferritin level 3 & 6 weeks after infusion and upto 8 weeks post infusion. Van Wynk et. Al<sup>(13)</sup> reported increase in mean haemoglobin 2gm% in 7 days and 3 gm% in 3-4 weeks in patient receiving FCM during postpartum period. Other baseline parameters were also significantly higher in FCM group as compared to Iron sucrose group.

In our study on postpartum women it was found that mean hemoglobin level and the rate of increase in hemoglobin level was significantly higher in patients receiving intravenous iron carboxymaltose during postpartum period.<sup>14</sup>

**Table.1** Demographic Profile of Women Given Iron Preparations

S. N.	V a r i a b l e s	M e a n ± S D
1	A g e ( y e a r s )	2 5 . 2 ± 6 . 8
2	G r a v i d a	4 ± 3
3	Parity	2 ± 2
4	Gestational age(wks)	3 3
5	Haemoglobin level (Pre infusion)	8

**Table.2** Comparison of Blood Parameters before and after Drug Intervention in Group A (Fcm Group)

S. N.	Blood Parameters	G r o u p		P-value	z - v a l u e
		F C M B e f o r e (Mean ± SD)	A f t e r (Mean ± SD)		
1	Haemoglobin (gm%)	9 . 0 2 ± 0 . 8	1 1 . 4 8 ± 0 . 6	0 . 0 0 1	1 7 . 4 8
2	RBC (mCells/cmm)	3 . 5 0 ± 0 . 4	4 . 0 1 ± 0 . 4	0 . 0 0 1	6 . 3 7
3	P C V	2 8 . 9 2 ± 3 . 4	3 3 . 7 6 ± 3 . 0	0 . 0 0 1	7 . 5 4
4	M C V ( f l / d l )	7 8 . 6 3 ± 9 . 6	8 2 . 1 0 ± 7 . 2	0 . 0 4	2 . 0 4
5	M C H C ( g m / d l )	3 0 . 0 9 ± 3 . 5	3 3 . 1 8 ± 3 . 2	0 . 0 0 1	4 . 6 0
6	M C H ( p g / d l )	2 6 . 7 5 ± 3 . 9	2 8 . 8 0 ± 4 . 1	0 . 0 1	2 . 5 6
7	T C	6 6 5 3 . 7 2 ± 2 7 9 . 6	5 2 8 9 . 6 0 ± 2 5 7 . 4	0 . 0 0 1	2 5 . 3 8
8	Platelet Count	2 4 2 . 1 6 ± 8 2 . 6	2 2 8 . 8 7 ± 6 9 . 2	0 . 3 8	0 . 8 7

**Table.3** Comparison of Blood Parameters before and after Infusion in Group B (Iron Sucrose Group)

S. N.	Blood Parameters	B e f o r e (Mean ± SD)	A f t e r (Mean ± SD)	z-value	P-value
1	Haemoglobin (gm%)	9 . 0 6 ± 0 . 7	1 1 . 4 0 ± 0 . 8	1 5 . 5 6	0 . 0 0 1
2	RBC (mCells/Cmm)	3 . 6 9 ± 0 . 3	3 . 7 9 ± 0 . 4	1 . 4 1	0 . 1 6
3	P C V	2 8 . 1 2 ± 2 . 1	3 2 . 4 0 ± 2 . 7	8 . 8 1	0 . 0 0 1
4	M C V ( f l / d l )	8 2 . 6 9 ± 2 . 2	8 4 . 4 8 ± 2 . 3	3 . 7 8	0 . 0 0 1
5	M C H C ( g m / d l )	3 3 . 0 2 ± 1 . 8	3 2 . 9 4 ± 1 . 5	0 . 2 4	0 . 8 0
6	M C H ( p g / d l )	3 1 . 2 8 ± 1 . 6	3 2 . 0 4 ± 1 . 6	2 . 3 7	0 . 0 1
7	T C	5 8 9 0 . 6 4 ± 3 3 . 6	5 6 5 1 . 2 0 ± 2 0 6 . 7	8 . 0 8	0 . 0 0 1
8	Platelet Count	2 9 6 . 0 4 ± 8 4 . 9	2 5 9 . 1 8 ± 9 3 . 6	2 . 0 6	0 . 0 4

**Table.4** Comparison of Blood Parameters B/W Two Group after Infusion

S.N.	Blood Parameters	FCM Group	Iron sucrose group	z-value	P-value
		Before (Mean ± SD)	After (Mean ± SD)		
1	Haemoglobin (gm%)	11.48 ± 0.6	11.40 ± 0.8	0 . 5 7	0 . 5 6
2	RBC (mcells/cmm)	4.01 ± 0.4	3.79 ± 0.4	2 . 7 5	0 . 0 0 7
3	P C V	33.76 ± 3.0	32.40 ± 2.7	2 . 2 1	0 . 0 2
4	M C V ( f l / d l )	82.10 ± 7.2	84.48 ± 2.3	2 . 2 2	0 . 0 2
5	M C H C ( g m / d l )	33.18 ± 3.2	32.94 ± 1.5	0 . 4 0	0 . 6 8
6	M C H ( p g / d l )	28.80 ± 4.1	32.04 ± 1.6	5 . 2 0	0 . 0 0 1
7	T C	5289.60 ± 257.4	5651.20 ± 206.7	7 . 7 1	0 . 0 0 1
8	Platelet Count	228.87 ± 69.2	259.18 ± 93.6	1 . 8	0 . 6 2

**Table.5** Adverse Drug Reactions

S.N.	Local Reactions	FCM Group	Iron Sucrose Group
1	Injection site Pain	0	4
2	Breathlessness	2	2
3	Palpitation	0	0
4	Sweating	0	1
5	Wheezing	0	0
6	Transient hypotension	2	3
7	Headache	0	0
8	Nausea Vomiting	1	1
9	Skin rash		
10	Urticaria	1	0

Thus FCM is easy to administer by giving single dose injections as comparison to multiple small dose injection of iron sucrose. No risk of of adverse effect on higher IV dose of FCM in comparison to multiple small injection of iron sucrose. FCM can be used on outpatient basis and women monitored for one hour post procedure to ensure maximum safety observation and monitoring.FCM is well tolerated in pregnancy with fewer side effects. Single dose administrate reduces the frequency of hospital visit.

To date no perspective, controlled clinical study has been performed using ferric carboxymaltose in pregnant women . A recent cochrane review concluded that large

good quality trials, assessing clinical outcome (including side effects) as well as the effects of treatment by severity of anaemia are required.

### Conclusion

To date from the prospective study is consistent with other studies that ferric carboxy maltose administration in the second and third trimester of pregnancy is likely to be safe and effective the mean haemoglobin level achieved in the intravenous iron ferric carboxy maltose was significantly higher than iron sucrose group the simple FCM dosing regime was associated with greater patient compliance compared with iron sucrose. Large single

dose of delivery of FCM is promising treatment modality in pregnant women with anaemia over other iron preparations in which multiple doses are required thus FCM reduces the burden on patients and health care systems to have multiple hospital visits and reduces the need of blood transfusion.

## References

- Bernd Froessler, Joshua Collingwood, Nicolette A Hodyl, Gustaaf Dekker. Intravenous ferric carboxymaltose for anaemia in pregnancy. *BMC pregnancy and Childbirth* 2014; 14(115).
- Bodnar LM, Siega-Riz AM, Miller WC, Cogswell ME, McDonald T. Who should be screened for postpartum anemia? An evaluation of current recommendations. *Am J Epidemiol* 2002; 156(903-12).
- Erin McLean, Ines Egli and Mary Cogswell. WHO global database on anemia . 2008.
- Giannoulis C, Daniilidis A, Tantanasis T, Dinas K, Tzafettas J. Intravenous administration of iron sucrose for treating anemia in postpartum women. *Hippocratia. PMC free article* 2009; 13(38-40).
- M Ezzati, AD Lopus, A Dogers, HS Vander, C Murray. Selected major risk factors and global and regional burden of disease. *Lancet* 2002 Nov 2; 360 (9343)(1347-1360): 18.
- Micronutrient Profile of Indian Population. Indian Council of Medical Research, New Delhi. 2004.
- Micronutrient Profile of Indian Population. Indian Council of Medical Research, New Delhi. 2004.
- National Family Health Survey. [.http://www.nfhsindia.org/pdf/India.pdf](http://www.nfhsindia.org/pdf/India.pdf), 2005-2006.
- National Nutrition Monitoring Bureau. NNMB Micronutrient Survey. *National Institute of Nutrition Hyderabad* 2002 .
- Pfenniger A, Schuller C, Christoph P, Surbek D. Safety and efficacy of high dose intravenous iron carboxymaltose vs. iron sucrose for treatment of postpartum anemia. *J perinat Med* 2012 April-2; 40(4).
- Public summary Document- Ferric Carboxymaltose, solution for I.V use, 500 mg in 10 ml, Ferinject. Australian Government Department of Health. November-2013.
- Revez L, Gyte Gillian ML, Cuervo Luis G, Casasbuenas A. Treatment for iron-deficiency anaemia in pregnancy. In *Cochrane Database of systematic Reviews. John Wiley & Sons, Ltd* 2011; (10).
- Ruchika Garg, Saroj Singh, Shikha Singh, Renu Rajvanshi; A Comparative Study to Evaluate the Efficacy and Safety of Single Dose Intravenous Iron Carboxymaltose vs Multidose Iron Sucrose in Postpartum Cases of Severe Iron Deficiency Anemia; *Journal of SAFOG 01/2015; 7(2):18-21*
- Van Wynk DB, Martens MG, Seid MH, Baker JB, Masngoine A. Intravenous ferric carboxymaltose compared with oral iron in the treatment of postpartum anaemia, A randomized controlled trial. *Obst Gynaecol* 2007; 110(267-78).

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