A Comparative Study of Injection Ferric Carboxymaltose and Iron Sucrose in Anaemia Complicating Pregnancy

Shabina Khan[1], Shivika Gupta[2]

ABSTRACT

Introduction: Anemia during pregnancy is most commonly caused by iron deficiency anemia. It can cause severe consequences for both the mother and developing fetus. Study aimed to compare the safety and efficacy of intravenous ferric carboxy maltose (FCM) vs iron sucrose in anaemia in pregnancy.

Material and Methods: This is prospective observational study; all women treated with FCM and iron sucrose for anemia during pregnancy between May 2017 and April 2018 at our Hospital were included. Total 110 women were selected. Each study group contained 55 women receiving FCM which was group A and 55 in group B receiving Injection Iron Sucrose between 30 and 36 weeks of pregnancy. Treatment effectiveness was assessed by repeat Hemoglobin and Serum Ferritin level measurement after 2 weeks of completion of therapy. Safety was assessed by analysis of adverse drug reactions during infusion and 2 hours after infusion.

Results: Intravenous ferric carboxymaltose infusion significantly increased Hemoglobin values compared to Intravenous ferrous sucrose. None of the women developed serious adverse reaction in FCM group.

Conclusion: Ferric carboxymaltose can be used safely in Iron deficiency anemia complicating pregnancy.

Keywords: Anemia, Ferric Carboxymaltose, Hemoglobin, Iron Sucrose, Serum Ferritin

INTRODUCTION

Iron deficiency anemia is most common medical condition during pregnancy in developing countries. The prevalence of anemia in pregnant women is high, affecting 41.8% of all pregnant women. The prevalence of anemia in pregnancy is much more in developing counties.[1]

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. The prevalence of Iron deficiency anemia (IDA) in pregnancy in India ranges from 23.6%- 61.4%. [2] Besides mortality it also causes increased perinatal mortality and morbidity but remains a major preventable cause of unfavorable perinatal and maternal outcome.

World Health Organization (WHO) defines Anemia as hemoglobin (Hb) less than 11g/dl during pregnancy. 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 hemoglobin mass expansion as well as the growing fetus and placenta.[3] Anaemia is also physiological due to hemodilution

Iron deficiency (IDA) in pregnancy can cause various kinds of gestational complications, as we as increased maternal and infant morbidity and mortality[4,5] Maternal consequences include cardiovascular symptoms, reduced physical, mental and immune function and peripartum iron reserves[6,7] Diet alone cannot supply such high amounts of iron, because of poor bioavailability [8]. All this makes iron supplementation, a necessity in all pregnant women.

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. Current intravenous iron formulations include ferric gluconate, iron sucrose, iron polymaltose and recently ferric carboxymaltose[9]. They have similar structure, but differ by the size of the core and the surrounding carbohydrate. Iron sucrose and ferric carboxymaltose are dextran free intravenous alternatives. Iron sucrose has been widely used due to its higher bio-availability for erythropoiesis than iron dextran and offers a good safety profile[10]. But it cannot be given in higher doses and requires frequent doses for administration.

Ferric carboxy maltose is a novel iron complex which consist of an iron-hydroxide core chelated in a carbohydrate shell and this complex is taken up as a whole by macrophages, leading to very low levels of non transferrin bound iron, avoiding iron toxicity and oxidative stress [11]. (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) Because it is free of dextran and its derivatives, FCM does not cross react with dextran antibodies[12,13] and does not need the administration of a test dose. It does not pre-dispose to anaphylactic reactions since it has a low immunogenic potential. Study aimed to compare the safety and efficacy of intravenous ferric carboxy maltose (FCM) vs iron sucrose in anaemia in pregnancy.

[1]Associate Professor, Department of Obstetrics and Gynaecology, RMCH, Bareilly, [2]Resident, Department of Obstetrics and Gynaecology, RMCH, Bareilly, India

Corresponding author: Dr Shivika Gupta, Room no 66, G Block, Rohilkhand Medical College, Bareilly, India

How to cite this article: Shabina Khan, Shivika Gupta. A comparative study of injection ferric carboxymaltose and iron sucrose in anaemia complicating pregnancy. International Journal of Contemporary Medical Research 2019;6(8):H6-H9.

DOI: http://dx.doi.org/10.21276/ijcmr.2019.6.8.20

MATERIAL AND METHODS

The study was conducted in the department of obstetrics and gynecology in Rohilkhand medical college and hospital, Bareilly during year may 2017-april 2018. Total 110 women from 30-36 weeks were selected and placed random in to groups, one group of 55 received iron sucrose while other 55 received ferric carboxymaltose.

Inclusion criteria

55 antenatal patients with gestational age more than 30 weeks and moderate anemia with Hb 7-9.9gm and S.ferritin levels <30mcg were included in the study.

Exclusion criteria

- Hypersensitivity reaction to any iron preparation
- History of blood transfusion
- History of bleeding tendencies
- History of iron overload disorders
- Thalassaemia's or haemochromatosis or medical disorders like chronic renal failure, cardiovascular disorder, tuberclosis, hepatitis B/C or HIV infection were excluded from study.

These patients were evaluated for CBC, PBF and S.ferritin levels. The dose of intravenous iron was calculated by the following formulas; Total iron Requirement: 2.4 x body weight (in kg) x hb deficit+500mg (iron stores). Hemoglobin deficit was calculated by subtracting from 11gm%.

All women were dewormed. Women who had dimorphic anemia were given 500ug folic acid and B12 tablets daily.

Group A, subjects were given IV iron sucrose in multiple doses, 200mg/day on day 0,2,4,6,8 total of 100mg (iron sucrose 200mg diluted in 100ml of 0.9%noraml saline and given over 20 to 30min). Group B, subjects were given IV ferric carboxy maltose 1000mg single dose (carboxymaltose 100mg diluted in 100ml of 0.9%NS given in 20 to 30mins).

In both groups Hb% and serum ferritin were done on day 0 and 30 of last dose of parentral iron. Side effects like headache, nausea, myalgia, arthalgia, nausea, vomiting, epigastric discomfort and anaphylactic reactions were looked for during the procedure. The patients were observed for one hour after infusion, they were called after one month for follow up and then clinical examination was done and investigations were repeated for comparison.

Age (years)	Group A No (%)	Group B No (%)
15-19	02 (3.6)	01 (1.8)
20-24	25(45)	19 (34)
25-29	24(43)	24 (43)
30-34	3(5.4)	11(20)
35-39	1(1.8)	0
Total	55	55
Mean ± SD (years)	24.56 ± 3.53	25.58 ± 3.70
Statistical inference	t= 1.4792, p= 0.142 (not significant)	

Table-1: Distribution of patients according to age

Gravidity	Group A No (%)	Group B No (%)
Primigravida	25 (45)	22(40)
Multigravida	30 (54.5)	33(60)
Total	55	55
Statistical inference, chi -square value – 0.15, p –value = 0.698 (not significant)		

Table-2: Gravidity of patients

Pre- treatment Hb (gm/dl)	Group A No (%)	Group B No (%)
7-7.9	12(21)	16(29)
8-8.9	25(45)	25(45)
9-9.9	18(32.7)	14(25)
Total	55	55
Statistical inference, chi -square value – 1.07, p –value = 0.899 (not significant)		

Table-3: Pre- treatment haemoglobin (gm/dl) of the patients

Pre- treatment serum ferritin (mcg/l)	Group A No (%)	Group B No (%)
0-9.9	16	16
10-19.9	27	27
20-29.9	12	12
Total	55	55
Statistical inference, chi square value – 0.00, p –value = 1.000 (not significant)		

Table-4: Pretreatment serum ferritin (mcg/l) of the patients

RESULTS

A total of 110 antenatal women were included in study. Most of which were aged between 20-29 years. Majority of them were multigravida in both groups (table-1,2).

Most patients in Group A (45%) and in Group B (45%) had their pre-treatment hb in range of 8-8.9 g/dl (table-3).

	Hemoglobin (gm/dl)		Statistical inference (unpaired t Test)
	Group A Mean ± S.D	Group B Mean ± S.D	
Rise in haemoglobin (gm/dl) at 2 weeks post treatment	1.06 ± 0.47	1.79 ± 0.47	t= 11.21 P < 0.001 Highly significant

Table-5: Rise in mean Haemoglobin (gm/dl) level at 2 weeks post treatment

Variable	Group A Mean ± S.D	Group B Mean ± S.D	Statistical Inference (unpaired t test)
Rise in serum ferritin (mcg/dl) at 2 weeks post treatment	84.78 ± 10.53	123.80 ± 16.03	t= 15.08 P < 0.001 Highly significant

Table-6: Rise in mean serum ferritin (mcg/L) at 2 weeks post treatment

Adverse drug reactions	Group A No (%)	Group B No (%)
Diarrhoea	6(12)	2(4)
Nausea	2(4)	1(2)
Constipation	6(12)	3(6)
Abdominal pain	2(4)	0
Injection site reactions	4(8)	1(2)
Headache	6(12)	3(6)
Dysguesia	2(4)	0
Skin discoloration	2(4)	6(12)
Vomiting	3(6)	1(2)
Hypersenstivity reaction	0	0
Hypertension	0	0
Hot flushing	0	0
Hypotension	0	0
Total	26(52)	17(34)
Chi square value – 3.3048; p = 0.69; not significant		

Table-7: Adverse drug reactions

Variable	Group A Mean ± S.D	Group B Mean ± S.D	p-value
Baseline hb (gm%)	8.40 ± 0.64	8.45 ± 0.64	P = 0.682(not significant)
Hb rise at 4 weeks (gm%)	1.06 ± 0.11	1.79 ± 0.47	P < 0.001(highly significant)
Baseline serum ferritin (mcg/l)	14.74 ± 5.82	14.09 ± 6.05	P = 0.567(not significant)
Serum ferritin rise at 4 weeks (mcg/l)	84.78 ± 10.53	123.80 ± 16.03	P < 0.001(highly significant)
Adverse drug reactions(%)	52	34	P < 0.001(highly significant)

Table-8: Comparison of two groups a/c to the results obtained

Patients with serum ferritin less than 30 mcg/dl were selected, majority of patients in both groups had their pre treatment serum ferritin in range of 10-19.9 mcg/l (table-4).

At 2 weeks post treatment, the rise in mean Hb level was more in Group B (FCM) as compared to Group B (iron sucrose). Statistically the rise was highly significant (table-5).

At 2 weeks post treatment, the rise in mean serum ferritin was 84.78 ± 10.53 in Group A (iron sucrose), whereas it was 123.80 ± 16.03 in Group B (FCM), which is statically highly significant (table-6).

No serious side effects were reported in any group. Mild adverse effects like nausea, vomiting, diarrhea, constipation etc were observed in 52% patients in Group A, and 34% patients in Group B (table-7,8).

DISCUSSION

The aim of the study was to compare the safety and efficacy of ferric carboxymaltose with iron sucrose in antenatal women with iron deficiency anaemia. Iron deficiency anaemia is on of the most important causes of maternal and neonatal morbidity in both developed and developing countries. So, diagnosis for IDA id important and all pregnant women should be corrected of anaemia before delivery. IDA is also an important indirect cause of maternal death.

Our results are in line with a no of randomized control studies, which have shown the safety and efficacy of ferric carboxy maltose. The demographic data like age were comparable among both groups. Baseline Hb and ferritin levels in both groups were clinically insignificant. The prevalence IDA in primi was 40-45% while in multi was 60%. The reason for the high prevalence in multi could be frequent pregnancies. Lack of spacing between two births, leading to depletion of iron stores. There was a statistically significant rise in Hb in FCM group as compared to that of Iron Sucrose (1.79 vs 1.06 g/dl). Serum ferritin also was significantly higher in the FCM group (123.80 vs 84.78 mcg/L) with comparatively lesser side effects (34% vs 52%), all of them being mild in nature. The results of the present study with regard to efficacy and safety of FCM in comparison with Iron Sucrose have been consistent with the other studies conducted by Garg R et al[14], Joshi SD et al[15] and Maheshwari B et al.[16] In a study by Van Wyck et al[17] the hb rise >3 g/dl in patients treated with FCM over 4 weeks, whereas in our study the mean rise was 1.79 g/dl. In a study by Giannoulis et al[18] the increase in hb was 4-6 g/dl in 4 weeks in patients treated with iron sucrose, whereas in our study the Hb levels showed increase by 1.09 g/d over 4 weeks. Breymann et al[19] reported the increase in ferritin levels from 39.9 to 150 mcg/l in 4 weeks, in our study we observed in FCM group, mean ferritin level increased from 14.09 to 137.80 mcg/l in 4 weeks. Adverse reactions do occur with iron sucrose, GI side effects being most common. None of the patients in our study required prolonged hospitalization, they had an uneventful recovery. David et al[20], Evstatiev et al[21] and Iftikar et al[22] proved that FCM was well tolerated and had better compliance than other preparations. The result of our study were consistent with the above trials

CONCLUSION

From our study we concluded that FCM appears to be safe and efficient for correction of IDA in third trimester of pregnancy with lesser adverse effects and better patient compliance. In this study we also found, correction of IDA

by single large dose of FCM is significant.

REFERENCES

1. Milman N. Anemia- still a major health problem in many parts of the world. Annals of hematology 2011; 90:369-377
2. FOGSI General Clinical Practice Recommendations Management of Iron deficiency anemia in pregnancy 2016
3. Froessler B, Collingwood J, Hodyl NA, Dekker G. Intravenous ferric carboxymaltose for anemia in pregnancy. BMC Pregnancy Childbirth. 2014;14:115
4. Milnam N:Prepartum anemia: prevention and treatment. Annals of hematology 2008, 87:949-959.
5. Scholl TO, Hediger ML:Anemia and iron deficiency anemia:compilation of data on pregnancy outcome. The American journal of clinical nutrition 1994,59(2 suppl):492S-500Sdiscussion 500S-501S
6. Ekiz C, A gaoglu LKarkasZ, Gurel N, Yalcin I; The effect of iron deficiency anemia on the function of immune system. The hematology journal: the official journal of the European Hematology Association 2005; 5:579-583.
7. Haas JD, Brownie Tt:Iron deifiency and reduced work capacity: a critical review of the research to determine a casual relationship. The jopurnal of nutrition 2001, 131: 676S-688S;discussion 688S-690S.
8. Dev SM, Sharma AN. Food security in India: performance, challenges and policies. Oxfam India Working Papers Series 2010;4:1-42
9. Auerbach M,Adamson J. How we diagnose and treat iron deficiency anaemia. Am J Hematol 2016;9:31-9.
10. Gautham KSK. Intravenous iron sucrose. World J Anaemia. 2017;1:20-2
11. S. Neiser, M. Wilhelm, K. SCHWArtz, F. Funk, P. Geisser, and S. Burckhardt, " Assessment of dextran antigenicity of intravenous iron products by an immunodiffusion assay", Portuguese Journal of Nephrology and Hypertension 2011;25:219-224.
12. P. Geisser, "The pharmacology and safety profile of ferric carboxymaltose (Ferinject): structure/ reactivity relationships of iron preparations", Portuguese Journal of Nephrology and Hypertension 2009;23:11-16.
13. P. Geisser. The pharmacology and safety profile of ferric carboxymaltose (Ferinject): structure/ reactivity relationships of iron preparations. Portuguese Journal of Nephrology and Hypertension 2009;23:11-16.
14. Garg R, Nigam A, Agrawal P, Nigam A, Agrawal R. Iron Carboxymaltose: A Safe and Effective Molecule to Combat Anaemia in Pregnancy. Int J Curr Res Aca Rev 2016;4:124-30.
15. Joshi SD, Chikkagowdra S, Kumar V. Comparative study of efficacy and safety of intravenous ferric carboxymaltose versus iron sucrose in treatment of postpartum iron deficiency anaemia. Int J Reprod Contracept Obstet Gynecol. 2016;5:2566-70.
16. Maheshwari B, Mahtab V, Tyagi S, Tyagi P. Evaluation of efficacy, safety and cost effectiveness of oral iron and injectable iron sucrose and ferric carboxy maltose in pregnant women in 2nd and 3rd trimester in anaemia. Ind J Obstet Gynecol Res. 2017;4:96-100.
17. Van WDB, Martens MG, Seid MH, Baker JB, Mangione A. Intravenous ferric carboxymaltose compared with oral iron in the management of postpartum iron deficiency anaemia; a randomized controlled trial. Obstet Gynecol 2008;110:267-78
18. Giannoulis C, Daniilidis A, Tantanasis T, Dinas K, Tzafettas J.I ntravenous ferric carboxymaltose compared with oral iron in the treatment of postpartum anaemia. Hippokratia 2009;13:38-40
19. Breymann C, Gliga F, Bejenariu C, Strizhova N. Comparative efficacy and safety of intravenous ferric carboxymaltose in the treatment of postpartum anaemia. Int J Gynaecol Obstet 2008;101:67-73
20. David BB, Lawrence TG. Experience with intravenous FCM in patients with iron deficiency anaemia.Ther Adv Hematol. 2014;5:48-60.
21. Evstatiev, Marteau, Iqbal T, Khalif IL, Stein J, Bokemeyer B. FERGI Study Group: A randomized controlled trial on ferric carboxy maltose for iron deficiency anaemia in inflammatory bowel disease. Gastroenterology. 2011;141:846-53.
22. Iftikhar H, Jessica B, Angelia B, Todd A, Andy H, David BB. Direct comparison of the safety and efficacy of ferric carboxymaltose versus iron dextran in patients with IDA. Anaemia. 2013; Article ID 169107.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 12-07-2019; **Accepted:** 04-08-2019; **Published:** 14-08-2019