International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Patel AR et al. Int J Reprod Contracept Obstet Gynecol. 2020 Jun;9(6):2437-2441
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20202325

Original Research Article

A comparative study of ferric carboxymaltose and iron sucrose as a parenteral iron treatment in iron deficiency anaemia during pregnancy

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Received: 17 March 2020
Accepted: 22 April 2020

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ABSTRACT

Background: Iron deficiency anemia during pregnancy is a serious global concern specially in developing country, which is preventable with effective measures. In women who cannot tolerate oral iron or have moderate to severe anemia, parenteral iron in the form of iron sucrose or ferric carboxymaltose can be very much useful. This study aimed to compare efficacy and safety of iron sucrose and ferric carboxymaltose in iron deficiency anemia during pregnancy.
Methods: This prospective interventional comparative study was conducted during May 2016 to April 2018 at tertiary care hospital and total 100 antenatal women from 28 to 34 weeks of gestation having moderate to severe anemia were included in this study and all women were divided in to 2 groups randomly and were given either iron sucrose or ferric carboxymaltose according to iron requirement. Rise in haemoglobin and serum ferritin were noted and data analysed statistically.
Results: The mean rise of haemoglobin with iron sucrose was 1.8 gm% and with ferric carboxymaltose was 2.6 gm%. The mean rise of serum ferritin with iron sucrose was 82.4 ng/ml and with ferric carboxymaltose was 100.9 ng/ml. Other than minimal local reaction one woman had developed severe anaphylactic reaction after receiving iron sucrose.
Conclusions: Intravenous ferric carboxymaltose is better and safe molecule than iron sucrose and it has advantage of ability to administer large dose in single sitting which reduce overall cost of therapy. Hence ferric carboxymaltose is a drug of choice as parenteral iron therapy in iron deficiency anemia during second trimester of pregnancy.

Keywords: Ferric carboxymaltose, Haemoglobin, Iron sucrose, Parenteral iron therapy

INTRODUCTION

Anemia is one of the common medical conditions affecting pregnancy and responsible for maternal and perinatal mortality and morbidity. Among anemia Iron deficiency anemia is commonest cause in both developed and developing countries. Worldwide it affects 41.8% of population and in India it ranges from, 23.6% to 61.4%.[1,2] IDA is responsible for 40% of maternal death in developing counties out of which it is responsible for 25% of direct maternal death.[2] The reason for high prevalence in India includes low dietary intake of iron, phytate rich Indian diet, faulty food habits, and high prevalence of infection like malaria and hookworm infestation.[3] This condition aggravated in pregnancy due to physiological changes and increase demand by growing fetus.[4] WHO defines anemia as haemoglobin less than 11 gm%. ICMR 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%).[5]

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]

Prophylactic oral iron supplement is recommended during pregnancy to meet physiological need during pregnancy. Major problem with oral iron is noncompliance due to bloating, nausea, vomiting and constipation. The main indication for parenteral iron treatment is moderate to severe anemia specially during late second and third trimester. Parenteral iron can avoid need of blood transfusion in antenatal or postnatal period.[6]

Iron sucrose and ferric carboxymaltose are dextran free iron preparation for parenteral therapy. Iron sucrose is most commonly used iron preparation during pregnancy. It has negligible safety issues and no test dose required. The only disadvantage is limited dose per sitting and it need multiple doses and frequent visits which also increase total cost of therapy. Ferric carboxymaltose is latest iv iron preparation which is dextran free type-1 iron complex. It has neutral pH, physiological osmolarity and increased bioavailability, which make it possible to administer high single dose over shorter period. It does not react with dextran antibodies and does not need test dose.[7] So authors have conducted this study with aim to compare efficacy and safety of intra venous iron sucrose and ferric carboxymaltose in anemia during pregnancy.

METHODS

This prospective interventional comparative study was conducted during May 2016 to April 2018 at tertiary care hospital at Pravara institute of medical science, Loni, Maharashtra. Total 100 antenatal women were enrolled with prior consent.

Inclusion criteria

- Antenatal woman between 28 to 34 weeks of gestation with Haemoglobin between 6 gm% to 9.9 gm % and s. Ferritin < 30 ng/ml.

Exclusion criteria

- Anemia due to causes other than IDA
- Hypersensitivity reaction to any iron preparation
- History of bleeding tendencies
- Thalassemia or haemochromatosis
- Medical disorders like chronic renal failure, cardiovascular disorder, tuberculosis, hepatitis B, hepatitis C or HIV infection.

Detailed history was taken and on clinical examination pallor of mucosa noted and investigations like complete blood count, peripheral smear, and level of serum ferritin are noted. These enrolled women were divided randomly in to two groups of 50 each. And each group has received parenteral iron according to iron deficit and replacement of iron storage.

Total iron requirement

Formula: (2.4×body weight (in kg) × haemoglobin deficit) + 500 mg (iron stores). Haemoglobin deficit was calculated by subtracting from 11 gm%.

Group A received Intra venous iron sucrose 200 mg (2 ampules of 100 mg) in 100 ml 0.9% NS over 30 minutes on day 0, 2, 4, 6 and 8 (total 1000 mg).

Group B received 1000 mg of ferric carboxymaltose in 200 ml 0.9% NS over 30 minutes.

Parenteral iron therapy was administered under doctor's supervision. During therapy any adverse drug reaction was noted. The women were then followed up after 3 weeks of completion of therapy. On follow up examination for pallor was done again and Haemoglobin and serum ferritin were measured again. Rise of haemoglobin and serum ferritin was noted and data analysed statistically by appropriate statistical method.

RESULTS

Table 1 shows that in this study majority of women (49%) belongs to age group 24-32 whereas 34% women belong to age group 18-24 and 17% belong to >32 years of age group. Out of total 100 women 31% were primigravida, 46% were second gravida and 23% women were multigravida.

Majority of patient (61%) were from lower socioeconomic class and 30% women were from middle and only 9% were from higher socioeconomic class. Majority women were 63% were illiterate and from rural area (78%).

Table 1: Demographic data of both groups.

		Group A (n=50)	Group B (n=50)	Total (100)
Age	18-24	16	18	34
	24-32	26	23	49
	>32	8	9	17
Parity	1	17	14	31
	2	21	25	46
	>2	12	11	23
Economy class	Higher	4	5	9
	Middle	14	16	30
	Lower	32	29	61
Literacy	Educated	21	16	37
	Illiterate	29	34	63
Residence	Rural	40	38	78
	Urban	10	12	22

Table 2: Distribution according to severity of anemia.

Severity of anemia	No. of women	
	Group A	Group B
Moderate (7-9.9)	45	43
Severe (4-6.9)	5	7

Table 2 shows that majority of women were having moderate anemia 68%, and 20% were mild and 12% were having severe anemia.

Table 3 shows mean rise of haemoglobin in Group A was 1.8 gm% where as in Group B mean rise of haemoglobin was 2.6. Mean rise of serum ferritin was 82.4 in Group A whereas 100.9 in Group B.

Table 4 shows that in Group A who received iron sucrose, 4 women had mild local reaction and 1 patient had severe anaphylactic reaction with respiratory problem which was managed effectively. In Group B who received ferric carboxymaltose 3 women had mild local reactions.

Table 3: Comparison of data before and after treatment.

Parameters	Iron sucrose			Ferric carboxymaltose			p value
	Pre-treatmen	Post-treatment	Difference	Pre-treatment	Post-treatment	Difference	
Haemoglobin (mean)	8.6	10.4	1.8	8.8	11.4	2.6	<0.001
Ferritin (mean)	17	99.4	82.4	17.5	118.4	100.9	<0.001

Table 4 Adverse reaction.

Adverse reaction	Iron sucrose	Ferric carboxymaltose
Mild local reaction	4	3
Mild systemic reaction	0	0
Severe anaphylactic	1	0
Total	5	3

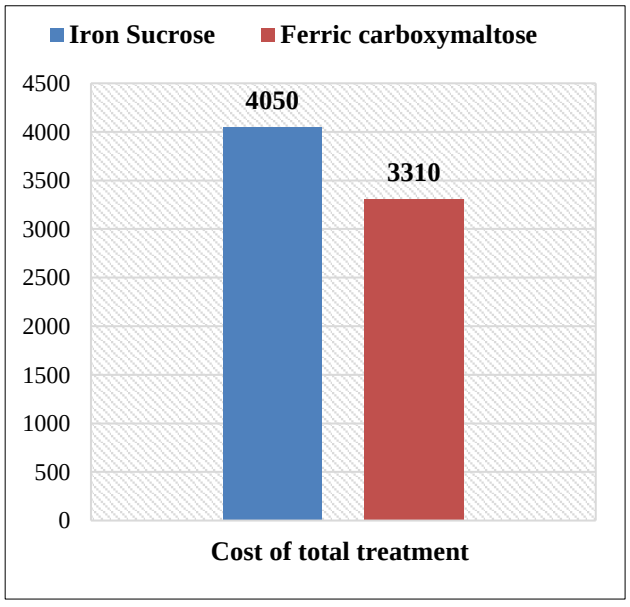

Figure 1: Comparison of cost of treatment in both groups.

Figure 1 shows that in Group A who received iron sucrose, treatment cost for 1000 mg in 5 divided doses was 4050 Rs whereas in Group B who received Ferric carboxymaltose, total cost for 1000 mg in single dose was 3310 Rs.

DISCUSSION

Anemia during pregnancy is a major health concern globally and iron deficiency anemia which is preventable condition affects almost 50% of it. Parenteral iron therapy can reduce chances of morbidity and mortality during pregnancy and timely intervention by it can subsequently reduce burden over health sector by reducing complications during delivery due to anemia.

Iron sucrose is standard choice of drug as parenteral iron therapy in moderate to severe iron deficiency anemia in pregnancy. However, limited maximum dose per sitting and per week is a major disadvantage of it, as it needs frequent visits to deliver required iron dose. ferric carboxymaltose can be administered in large dose in single sitting with higher efficacy and safety.

In this study majority of women were of 24-32 years age group (49%) and incidence of iron deficiency anemia (moderate to severe) is more in multigravida (69%) than primigravida (31%). It is well known fact that iron deficiency anemia is more prevalent on low socioeconomic class and community with poor literacy, due to nutritional deficiencies, phytate rich diet, frequent infections like malaria, intestinal worms, less interval between to pregnancies. In this study also authors have same findings of more prevalence in poor socioeconomic class, women with ill-literacy and residing at rural community.

In this study authors have noted haemoglobin and serum ferritin level before and after 3 weeks of completion of

parenteral iron therapy. In Group A who received iron sucrose had mean haemoglobin rise of 1.8 gm% and in Group B who received ferric carboxymaltose had mean haemoglobin rise of 2.6 gm%. In Group A who received iron sucrose had serum ferritin rise of 82.4 ng/ml and in Group B who received ferric carboxymaltose had serum ferritin rise of 100.9 ng/ml. This study has shown significant ($p<0.001$) rise of both haemoglobin and serum ferritin in both the group but rise is more in group B who had received ferric carboxymaltose.

The study published by Christoph P et al, concluded comparable safety and tolerability of ferric carboxymaltose to iron sucrose and documented a comparable rise in haemoglobin levels at the end of the study. The current study, in contrast, showed significantly higher haemoglobin levels in ferric carboxymaltose group as compared to iron sucrose group after 3 weeks.[8] The study conducted by Ambily J et al, and by Divyani et al, had shown significant rise of haemoglobin and serum ferritin in women who received ferric carboxymaltose than women who received iron sucrose. Results were equivalent as this study.[9,10]

In 2019 study conducted by Sabina K et al, has shown that after parenteral iron therapy serum ferritin increase significantly in both iron sucrose and ferric carboxymaltose treatment but rise is significantly more in group who had receive ferric carboxymaltose, which is similar finding as this study.[11] In this study in Group A authors have found minimal local reaction in 4 women and 1 woman had severe reaction whereas from Group B had 3 women had mild local reaction. In an observational review study conducted by Qassim A et al, author has reported adverse drug reaction with iron sucrose 6.7% and with ferric carboxymaltose 5% which is insignificant and no iron preparation is superior to each other.[12]

In this study per 1000 mg of iron as a parenteral iron Group A had cost of 4050 Rs, whereas Group B had total treatment cost 740 Rs cheaper than Group A. In this calculation authors had not added transportation cost and other burden due to frequent visits.

In addition to cheaper and less frequent visits required for parenteral iron therapy, this study showed higher rise of Haemoglobin and serum ferritin with ferric carboxymaltose with lesser side effects. And it is very useful in pregnant women presenting with moderate to severe anemia specially 28 to 34 weeks of gestation.

CONCLUSION

This study shows that 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. Compared to iron sucrose, ferric carboxymaltose has advantage of large dose administration per sitting, early rise of haemoglobin, lesser total number of doses required and less side effects, which make treatment safe, short, and cost effective. Patient's compliance is more in ferric carboxymaltose treatment as it requires less frequent visits which reduce transport cost and it reduces discomfort due to multiple needle puncture. Here authors conclude by this study that ferric carboxymaltose is recommended as a parenteral iron therapy in iron deficiency anemia during second and third trimester of pregnancy.

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: Patel AR, Patel VS, Patel PR. A comparative study of ferric carboxymaltose and iron sucrose as a parenteral iron treatment in iron deficiency anaemia during pregnancy. Int J Reprod Contracept Obstet Gynecol 2020;9:2437-41.