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Original Research Article

Efficacy And Safety of Intravenous FCM and Iron Sucrose (IS) in Post-partum Iron-Deficiency Anaemia: A Comparative Study

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Abstract

Aim: A comparative study of efficacy, safety and compliance of intravenous ferric carboxymaltose versus iron sucrose in the treatment of iron deficiency anaemia of pregnancy.

Methods: This comparative study was carried out in the Department of Obstetrics and Gynaecology, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India. Women less than 10 days after delivery with hemoglobin between ≥6 g/dl and ≤11 gm/dl requiring iron supplementation were enrolled. Total 200 women were categorized into two groups 100 each. Detailed history and clinical examination were done. Diagnosis was confirmed by peripheral blood smear, CBC and serum ferritin. All women were dewormed.

Results: Mean pre-treatment Hb was 8.1±0.77 and 8.11±0.61 in iron sucrose and ferric carboxy maltose group respectively. There was statistically significant rise (P <0.001) of Hb in FCM group 4.88 g/dl compared to iron sucrose group 3.82 g/dl. Mean rise of serum ferritin was 72.07±26.23 and 96.39±44.84 in iron sucrose and ferric carboxy maltose group. No serious adverse events were reported in either the FCM group or iron sucrose group. However, minor adverse effects like urticaria, injection site reactions, nausea hypotension occurred in 7 (7%) iron sucrose group and chest discomfort was noted in 2, nausea in 1, (3%) of FCM group.

Conclusion: Properties like ultra-short duration of treatment, fewer adverse reactions and better compliance makes FCM the first-line drug in the management of postpartum iron deficiency anemia.

Keywords: iron deficiency anemia, pregnancy, ferric carboxymaltose , iron sucrose

Introduction

Iron is an essential element for the functioning of all types of cells in the body. It plays a vital role in cell cycle regulation, electron transport in the respiratory chain, DNA synthesis and other metabolic reaction. The functioning of the oxygen binding molecules such as haemoglobin largely depends on the availability of iron. Anaemia is a condition in which the number of red blood cells or their oxygen carrying capacity is

insufficient to meet physiologic needs.[1-3] It is one of the commonest medical disorder among pregnant women in India. Iron deficiency anaemia is accompanied by depleted iron stores and signs of a compromised supply of iron to the tissues.[1] There is physiological variation in haemoglobin levels during pregnancy; at the beginning of a pregnancy, there is a normal reduction in haemoglobin level followed by a slight rise towards the end of pregnancy due to increased haemoconcentration. The initial reduction has been explained to result from increased red cell mass and demands of the fetus which exceeds iron intake with consequent reduction in iron stores of the woman's body.[2]

Anaemia is the most common nutritional deficiency disorder in the world. World Health Organization (WHO) has estimated that prevalence of anaemia in developed and developing countries in pregnant women is 14% and 51%. Its alarming to know that the prevalence in India is as high as 65 to 75%.[4]

Prevalence of anaemia in South Asian countries is highest compared to the countries. WHO estimates that even among the South Asian countries, India has the highest prevalence of anaemia. What is even more important is the fact that almost 50% of the global maternal deaths due to anaemia occur in South Asian countries.[5]

It is apparent that India's contribution to the prevalence of anaemia in pregnancy and maternal deaths due to anaemia is higher than warranted by the size of its population.[3] On hand estimates also suggest that the magnitude of reduction in the prevalence of anaemia during nineties in India is lower than that in neighboring South East Asian countries. In view of the high prevalence of anaemia in the country, five major surveys National Family Health Survey (NFHS) 2 and 3.[6,7] District Level Household Survey 2 (DLHS),[8] Indian Council of Medical Research (ICMR) Micronutrient Survey[9] and Micronutrient Survey conducted by National Nutrition Monitoring Bureau (NNMB)[10] were undertaken to find the prevalence of anaemia in the country. The results of these surveys showed that over 70% of pregnant women and adolescent girls in the country were anaemic. Anaemia gets aggravated by increased requirements during adolescence and during pregnancy.[8] Assuming that the absorption of iron is 8% in pregnant women, their normal dietary intake will meet only 30-45% of the requirement.[4]

There are two known factors which play a role in the development of iron deficiency anaemia (IDA) in pregnancy; the first is the woman's iron stores at the beginning of conception and the second is the amount of iron absorbed during gestation. Women in developing countries are not commonly affected by anaemia in pregnancy is an indication that preexisting iron stores are often insufficient and physiological adaptations to pregnancy is lacking to meet the increased requirements.[11]

Anaemia in pregnancy is associated with unfavorable consequences both for the mother and the foetus. Studies have shown that the adverse consequences of maternal anaemia may affect not only the neonate and infant but also increase the risk of non communicable diseases when the child grows into an adult and the risk of low birth weight in the next generation. The detection of anaemia and its effective management is available, affordable and it is possible to effectively implement these even in the rural setting. Not to mention the fact that these are very cost effective interventions.[4]

There are various promising forms of treatment for iron deficiency anaemia. Oral iron is the most preferred route of administration for mild anaemia. Treatment with iron preparations is used routinely in pregnancy. However, oral iron

supplementation often leads to adverse side effects, such as constipation, abdominal pain and other gastrointestinal symptoms. Because of these unwarranted gastrointestinal effects the compliance to iron treatment is highly variable.

Intravenous iron preparations show good potential, especially in cases of severe anaemia. They provide a greater and more rapid iron supply than oral iron therapy without the gastrointestinal side effects of oral preparations and make it possible to avoid blood transfusion which is associated with risks.[12] To date, many studies have focused on the use of i.v, iron and its side effects and safety in pregnant women. Iron sucrose has been used for years for i.v. treatment of iron deficiency in pregnant women after the first trimester.

However, its use is limited by the low maximum dosage due to local and systemic side effects in higher doses. In order to avoid these adverse effects the drug has to be administered in multiple infusions of lower doses less than 200 mg per day. Hence it increases the number of days of admission in the hospital and it becomes an extra burden on the hospital resources.

The search for an ideal parentral iron preparation has led to the introduction of ferric carboxymaltose. It comprises a macromolecular iron-hydoxide complex of polynuclear iron hydroxide tightly bound in a carbohydrate shell. This new complex has a molecular weight of 150,000 Daltons. This design allows for a controlled delivery of iron within the cells of reticulo-endothelial system and hence subsequent delivery to the iron binding proteins, with a minimal risk of release of large amounts of ionic iron in the serum. This iron preparation can be used intravenously in high doses with up to 1000 mg infused in l5 min with low risk of side effects. Its use is approved in the second and third trimesters of pregnancy.[13]

Material and methods

This comparative study was carried out in the Department of obstetrics and gynaecology, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India for 6 months

Inclusion and exclusion criteria

Women less than 10 days after delivery with hemoglobin between ≥6 g/dl and ≤11 gm/dl requiring iron supplementation were enrolled. Women with significant vaginal bleeding in the 24 hours prior, non- iron deficiency anemia, current treatment for asthma, recent treatment with IV iron or red blood cell transfusions (within 120 days) or erythropoietin within 3 months prior to screening, bleeding disorders and hemoglobinopathies, severe CVS disease or failure were excluded.

Methodology

Total 200 women were categorized into two groups 100 each. Detailed history and clinical examination was done. Diagnosis was confirmed by peripheral blood smear, CBC and serum ferritin. All women were dewormed. Women who had dimorphic anemia were given folic acid and B12 tablets along with iron supplementation. Alternate subjects were allocated into two groups. Group A, subjects were given I.V. iron sucrose in multiple doses, 200 mg/day on day 0, 2, 4, 6, 8 total of 1000 mg. (iron Sucrose 200 mg diluted in 100ml of 0.9% normal saline and given over 20 to 30 min.) Group B, subjects were given I.V. ferric carboxymaltose1000 mg single dose (Carboxymaltose 1000 mg diluted in 100ml of 0.9% NS given in 20 to 30 min). Both groups Hb% and serum ferritin are done on 0 and day 30 of last dose of parenteral iron. Side effects like headache, myalgia, arthralgia, nausea, vomiting, epigastric discomfort and anaphylactoid reactions were looked for during the procedure. The patients were observed for one hour after infusion. They were called after one month for fallow up, clinical

examination done and investigations were repeated.

Data analysis

Data analysis was done using SPSS software version 25.0. Percentage, mean, standard deviations were used to describe the data variables. Chi-square tests and student t test were used to compare the outcome variables among the two treatment group. A p-value of <0.05 was considered to be statistically significant.

Results

Of the 200 patients who were treated for postpartum anemia, 100 from iron sucrose group and 100 from ferric carboxy maltose group completed the protocol. Those who completed protocol and came for fallow up were included for statistical analysis and others were excluded from study and analysis.

Table 1: Age wise distribution of the study subjects among the two groups

Age group (years)	Iron sucrose group		Ferric carboxy maltose group		P-value
Below 23	75	75%	71	71%	0.65
23-30	17	17%	22	22%	
Above 30	8	8%	7	7%	
Mean±SD	24.66 ±3.12		25.02 ± 2.64		0.55

No clinically significant difference were observed between the FCM and iron sucrose group for any demographic characteristic i.e. in terms of age distribution, socioeconomic status, booking status in either group (Table 1). 70 to 78 % of women in either group had some visits to the healthcare provider and were advised regarding anemia correction during antenatal period, 22 to 27 percentage were unbooked in both the group. Postpartum anemia was more common in multiparous women in this study, 72 to 77% in both the groups. Hb levels increased from base line in both the treatment group at 30 days (Table 2). Mean pre- treatment Hb was 8.1±0.77 and 8.11±0.61 in iron sucrose and ferric carboxy maltose group respectively. There was statistically significant rise (P <0.001) of Hb in FCM group 4.88 g/dl compare to iron sucrose group 3.82 g/dl (Table 2).

Mean rise of serum ferritin was 72.07±26.23 and 96.39±44.84 in iron sucrose and ferric carboxy maltose group (Table 3).

Table 2: Comparison of hemoglobin levels among the two groups

Hb levels	Iron sucrose group	Ferrics carboxy maltose group	P-value
	Mean±SD	Mean±SD	
Pre treatment	8.1±0.77	8.11±0.61	0.39
Post treatment	12.08±1.17	12.70±1.04	<0.001
Hb difference	3.82 ± 1.22	4.88 ± 0.86	<0.001

Table 3: Comparison of serum ferritin levels among the two groups

Serum ferritin levels	Iron sucrose group	Ferric carboxy maltose group	P-value
	Mean±SD	Mean±SD	
Pre-treatment	16.23±7.37	15.82±6.04	0.73

Post-treatment	87.37±27.66	111.22±44.29	0
S. Ferritin difference	72.07±26.23	96.39±44.84	0

Table 4: Distribution of the study subjects based on adverse effects among the two groups

Adverse effects	Iron sucrose group		Ferric carboxy maltose group		P-value
Yes	7	7%	3	3%	0.25
No	93	93%	97	97%	

No serious adverse events were reported in either the FCM group or iron sucrose group. However, minor adverse effects like urticaria, injection site reactions, nausea hypotension occurred in 7 (7%) iron sucrose group and chest discomfort was noted in 2, nausea in 1, (3%) of FCM group (Table 4).

Discussion

Postpartum anaemia arises frequently and imposes a substantial disease burden during the critical period of maternal-infant interactions. Anemic women have a longer average length of hospital stay, are more likely to receive a blood transfusion and incur higher hospitalization costs, Hence, postpartum IDA require attention and high quality care.[14]

Traditional treatments, i.e. oral iron therapy and blood transfusion, involve significant drawbacks. In addition, inflammatory reaction secondary to surgically assisted deliveries leads to sequestration of iron in macrophages and decrease of intestinal absorption, so that administered iron is not available for erythropoesis.[15] To overcome this problem I.V. iron preparations were used.[16] Due to limitations of older parenteral iron preparation, search of novel drug resulted in iron sucrose and latest is FCM.

In this study FCM and Iron sucrose were used as per the protocol mentioned and both were effective in treating postpartum anemia minimizing adverse events. There was significant rise of Hb in FCM group compared to Iron sucrose. 4.88 g/dl and 3.82 g/dl espectively P <0.001 after one month.

Studies compared oral iron and FCM, oral iron and iron sucrose and found that both iron sucrose and FCM were independently more effective and safe than oral preparations. [17] In a randomized trial to assess safety and efficacy of intravenous FCM in the treatment of postpartum IDA, 227 women were assigned to IV FCM with 1000 mg maximum dose (up to 3 weekly doses) versus 117 women who received oral ferrous sulphate 100 mg twice daily. Intravenous FCM was as effective as oral ferrous sulphate with no statistically significant differences between groups at any point despite the shorter treatment period and a lower total dose of iron (mean 1.3 g IV iron versus 16.8 g oral iron). In the similar line, rise in Hb of 2.54 g/dl in this study was achieved with mean FCM dose of 1.06gm.[17]

In a multicenter randomized, controlled study, 13 women with PPA were given FCM 1000 mg/wk max 2.5g and 325 mg of ferrous sulphate tablets three times a day for 6wks and found shorter period to achieve Hb of 12 g/dl with sustained level at 42 days compare to ferrous sulphate. Patients with Hb levels ≤8 g/dL showed greatest difference in the responder rate between FCM and ferrous sulphate group (78.9% vs. 43.5%; p=0.0286).[18]

Retrospective study was conducted to assess the efficacy and safety of FCM and found effective.[19] In a prospective trial FCM was better tolerated than iron sucrose in postpartum anemia with superior efficiency.[20] A retrospective study compared the safety and efficacy of intravenous (IV) high dose FCM with iron sucrose (IS) for the treatment of postpartum anaemia in 210 inpatient women in postpartum period who received IV high dose FCM (15 mg/kg; maximum 1000 mg) or IS (2×200 mg), respectively. Rapid administration of IV FCM was as safe as IS in the management of PPA despite five times of higher dosage. FCM was as effective as IS in changing Hb levels from the baseline. There was no difference in the mean daily Hb increase between the groups. Women with severe anemia showed the most effective responsiveness. The single application of FCM shows advantages of lower incidence of side effects at the injection site, a shorter treatment period, and better patient compliance.[14]

In this study, both FCM and Iron sucrose were given the same dosage but single and multiple dosage respectively. In both the group there was significant rise of Hb and Ferritin after one month of the therapy which was comparable with the other studies. Like others severe anemia showed the most effective response in both the groups.[21]

Conclusion

Properties like ultra-short duration of treatment, fewer adverse reactions and better compliance makes FCM the first-line drug in the management of postpartum iron deficiency anemia.

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