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Research Article

Comparative study of efficacy and safety of intravenous ferric carboxy maltose versus iron sucrose in treatment of postpartum iron deficiency anemia

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ABSTRACT

Background: Iron deficiency is the commonest treatable cause of postpartum anemia. Parenteral iron therapy results faster and higher replenishment of iron stores and correction of Hb levels with better compliance. The study was to compare the safety and efficacy of ferric carboxy maltose (FCM) with iron sucrose to treat iron deficiency anemia in the post-partum.

Methods: 200 women of postpartum iron deficiency anemia were allocated into two groups. Iron sucrose group, subjects were given I.V. iron sucrose in multiple doses, 200 mg/day on day 0,2,4,6,8 total of 1000 mg. FCM group , subjects were given I.V. ferric carboxymaltose 1000 mg single dose. Both groups Hb%, and serum ferritin were done on 0 and day 30 of last dose of parenteral iron. Side effects, compliance were noted.

Results: There was statistically significant rise (P <0.001) of Hb in FCM group 4.68 g/dl compare to iron sucrose group 3.92 g/dl. Mean rise of serum ferritin was 71.07±27.23 and 95.39±45.84 in iron sucrose and ferric carboxy maltose group. No serious adverse events were reported in either the FCM group or Iron sucrose group.

Conclusions: 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: Ferric carboxy maltose, Iron sucrose, Postpartum anemia, Iron deficiency, Intravenous iron therapy

INTRODUCTION

Postpartum anemia is a common problem throughout the world.[1] The prevalence of postpartum anemia is 27% and a postpartum hemoglobin (Hb) level of less than 8 g/dl is observed in 10% of women.[2,3] Anemia may result from inadequate dietary intake, parasitic infection or malaria, and may be exacerbated by the physiological effects of pregnancy and blood loss at the time of birth.[4] Postpartum anemia has been associated with postpartum depression, stress, anxiety, cognitive impairment.[5,6] Poor mother-infant interactions and delayed infant development.[7]

Oral iron therapy is currently the treatment of choice for the majority of patients with iron deficiency anemia but it has disadvantages like poor absorption, poor compliance and gastro-intestinal (GI) side effects. Parenteral iron helps in restoring iron stores faster and more effectively than oral iron intravenous (IV) iron sucrose is safe, effective, and economic in comparison to the repeated and painful intramuscular iron injections. Although the incidence of anaphylaxis and other adverse reactions with IV iron sucrose is markedly lower, multiple doses and prolonged infusion times are typically required.[8] IV ferric carboxymaltose (FCM) has a neutral pH (5.0-7.0) and physiological osmolarity, which makes it possible to

administer its higher single doses over shorter time periods (single dose up to 1000 mg over 15 min) than other parenteral preparations.[9] It does not contain dextran; therefore, the risk of anaphylaxis or serious hypersensitivity reactions is very low, and a test dose is also not required. In this study, we compare and evaluate the safety and efficacy of IV FCM and iron sucrose in treatment of postpartum iron deficiency anemia.

METHODS

This comparative study was conducted in VIMS from October 2013 to June 2015. Research and academic committee approved the study protocol prior to initiation. All subjects gave written informed consent before enrollment. 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.

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 22. 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, 83 from iron sucrose group and 90 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
	Frequency	Percent	Frequency	Percent	
18-25	62	74.7	64	71.1	0.642
26-30	14	16.9	20	22.2	
> 30	7	8.4	6	6.7	
Total	83	100.0	90	100.0	
Mean±SD	23.66 ± 4.12		24.02 ± 3.64		0.543

Table 2: SES wise distribution of the study subjects among the two groups.

SES	Iron sucrose group		Ferric carboxy maltose group		P-value
	Frequency	Percent	Frequency	Percent	
BPL	57	68.7	61	67.8	0.899
APL	26	31.3	29	32.2	
Total	83	100.0	90	100.0	

SES: Socio economic status

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, 2, 3). 75 to 80 % of women in either group had some visits to the healthcare provider and were advised regarding anemia correction during antenatal period, 20 to 25 percentage were unbooked in both the group. Postpartum anemia was more common in multiparous women in this study, 70 to 75% in both the

groups (Table 3).Hb levels increased from base line in both the treatment group at 30 days (Table 4). Mean pre-treatment Hb was 7.9±0.6 and 8.01±0.5 in iron sucrose and ferric carboxy maltose group respectively. There was statistically significant rise (P <0.001) of Hb in FCM group 4.68 g/dl compare to iron sucrose group 3.92 g/dl (Table 4).

Table 3: Distribution of the study subjects based on obstetric profile among the two groups.

	Iron sucrose group		Ferric carboxy maltose group		P-value
	Frequency	Percent	Frequency	Percent	
Parity					
Multi gravida	62	74.7	64	71.1	0.596
Primi gravida	21	25.3	26	28.9	
Total	83	100.0	90	100.0	
Mode of delivery					
Vaginal	54	65.1	57	63.3	0.812
LSCS	29	34.9	33	36.7	
Total	83	100.0	90	100.0	

Table 4: Descriptive statistics of hemoglobin at different stages of treatment.

Hemoglobin parameter	Iron sucrose group	Ferric carboxy maltose group
Hb pre treatment		
N	83	90
Mean	7.93	8.01
Std. Deviation	0.695	0.551
Minimum	6	7
Maximum	9	9
Hb post treatment		
N	83	90
Mean	12.083	12.701
Std. Deviation	1.1692	1.0427
Minimum	10	10
Maximum	15	14
Hb difference		
N	83	90
Mean	3.92	4.68
Std. Deviation	1.118	0.958
Minimum	2	3
Maximum	6	6

Mean rise of serum ferritin was 71.07±27.23 and 95.39±45.84 in iron sucrose and ferric carboxy maltose group (Table 5, 6, 7).

Table 5: Descriptive statistics of serum ferritin at different stages of treatment.

Serum ferritin	Iron sucrose group	Ferric carboxy maltose group
S.Ferritin pre treatment		
N	83	90
Mean	15.23	14.82
Std. Deviation	8.366	7.039
Minimum	3	4
Maximum	30	29
S.Ferritin post treatment		
N	83	90
Mean	86.37	110.22
Std. Deviation	28.658	45.293
Minimum	46	45
Maximum	194	205
S Ferritin difference		
N	83	90
Mean	71.07	95.39
Std. Deviation	27.233	45.844
Minimum	23	19
Maximum	165	186

Table 6: Comparison of hemoglobin levels among the two groups.

Hb levels	Iron sucrose group	Ferrics carboxy maltose group	T statistic	P-value
	Mean±SD	Mean±SD		
Pre treatment	7.93±0.69	8.01±0.55	-0.878	0.381
Post treatment	12.08±1.17	12.70±1.04	-3.674	<0.001
Hb difference	3.92 ± 1.12	4.68 ± 0.96	-4.827	<0.001

Table 7: Comparison of serum ferritin levels among the two groups.

Serum ferritin levels	Iron sucrose group	Ferric carboxy maltose group	T-statistic	P-value
	Mean±SD	Mean±SD		
Pre-treatment	15.23±8.37	14.82±7.04	0.347	0.729
Post-treatment	86.37±28.66	110.22±45.29	-4.099	0
S. Ferritin difference	71.07±27.23	95.39±45.84	-4.197	0

Table 8: Distribution of the study subjects based on adverse effects among the two groups.

Adverse effects	Iron sucrose group		Ferric carboxy maltose group		P-value
	Frequency	Percent	Frequency	Percent	
Yes	6	7.2	3	3.3	0.249
No	77	92.8	87	96.7	
Total	83	100.0	90	100.0	

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 6 (7.2%) iron sucrose group and chest discomfort was noted in 2, nausea in 1, (3.3%) of FCM group (Table 8).

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.[10]

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.[11] To overcome this problem I.V. iron preparations were used.[12] 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. 4.68 g/dl and 3.92 g/dl respectively 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.[9] 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.[9]

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).[8]

Retrospective study was conducted to assess the efficacy and safety of FCM and found effective.[13] In a prospective trial FCM was better tolerated than iron sucrose in postpartum anemia with superior efficiency.[14] 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.[10]

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. Unlike other studies Hb rise was more than 3.5 in both the groups, this may be because of our total dose used in both the groups. In this study adverse effects occurred in 7% of women in iron sucrose group but were not severe enough to affect compliance. It has to be noted that this group of women were highly motivated and therefore may have completed the multiple dose of the drug. Women who received FCM also expressed better-overall satisfaction to administration of treatment.

CONCLUSION

Due to properties like ultra-short duration of treatment i.e. ability to administer 1000 mg doses in a single sitting, fewer adverse reactions and better compliance makes FCM the first-line drug in the management of postpartum iron deficiency anemia causing a faster and higher replenishment of iron stores and correction of Hb levels. Also use of high doses reduces the number of infusions, enabling the possibility of cost reductions compared to multiple administrations.[15-18]

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