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Original Research Article

Comparative study of efficacy and safety of intravenous ferric carboxymaltose versus iron sucrose in treatment of post-partum anemia

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ABSTRACT

Background: Ferric carboxymaltose has been recently introduced for the treatment of anaemia. The present study was planned to compare the efficacy, tolerability and safety of intravenous ferric carboxymaltose with intravenous iron sucrose in the treatment of iron deficiency anaemia among postpartum women.

Methods: A total of 60 postpartum women with haemoglobin levels between 7-10 g/dl were randomized into two groups: 30 in group A (received iron carboxymaltose) and 30 in group B (Received iron sucrose). Haemoglobin and serum ferritin levels were done on day 0 and after 6 weeks.

Results: The post treatment haemoglobin levels were found to be 10-10.9 g/dl in 66.7% of women in group A and 63.3% in group B. The mean post treatment haemoglobin levels in group A was 9.97 ± 0.3 g/dl and in group B was 10.9 g/dl ($p < 0.001$). The mean increase in haemoglobin levels post treatment were significantly high in group B (2.1 ± 0.5 gm%) compared to group A (1.3 ± 0.5 gm%). The mean post treatment S. Ferritin levels in group A was 91.2 ± 25.8 and in group B was 126.5 ± 23.2 gm%. The mean increase in S. Ferritin levels post treatment were significantly high in group B (96.9 ± 23.3) compared to group A (62.7 ± 22.6) ($p < 0.001$).

Conclusions: Intravenous iron carboxymaltose is more effective and better tolerated in the treatment of iron deficiency anaemia among postpartum women compared to intravenous iron sucrose.

Keywords: Intravenous iron sucrose, Iron carboxymaltose, Postpartum anaemia, Haemoglobin, Serum ferritin

INTRODUCTION

Anaemia is a condition in which the number of red blood cells or their oxygen carrying capacity is insufficient to meet physiologic needs.¹ It is defined by World Health Organization (WHO) as Haemoglobin levels less than 11 g/dL.² The functioning of the oxygen binding molecules such as haemoglobin depends largely on the availability of iron. Iron deficiency anaemia is accompanied by depleted iron stores and signs of a compromised supply of iron to the tissues. Iron deficiency anaemia is the most common cause of post-partum anaemia. The physiological effects

of pregnancy and blood loss at birth can exacerbate anaemia.³

In healthy women after normal delivery, the prevalence of anaemia 1 week postpartum is 14% in iron supplemented women and 24% in non-supplemented women.⁶

Treatment of anaemia is important because it is associated with reduced physical endurance, decreased work capacity and fatigue in child bearing women; and is associated with postpartum depression, stress, anxiety, reduced mother child interaction and cognitive impairment.^{4,7,8}

Although oral iron is easy and cost-effective method of iron replenishment, it has its limitations- gastrointestinal complaints, non-compliance (32% after 2 months of administration).⁵ Hence parenteral iron therapy is considered from 2nd trimester onwards and during postpartum period for women with confirmed iron deficiency according to the Obstetric Haematology group UK guidelines (2012) by British Society for Haematology.

Intravenous administration of iron sucrose has been available for several years, has excellent safety record and is administered in small doses of 200 mg over 30 minutes.⁹⁻¹¹

Intravenous ferric carboxymaltose is recently developed, gives rapid replacement of iron shortage and can be administered in a time of less than 15 minutes; though it is yet to find a place in India for routine use.¹¹⁻¹³ In this study, we compare and evaluate the safety and efficacy of intravenous ferric carboxymaltose and iron sucrose in the treatment of postpartum iron deficiency anaemia.

METHODS

The study design was comparative two group clinical study. The study period was from December 2015 to May 2017. The sample size was 60 (30 in each group).

All postpartum women admitted at Department of Obstetrics and Gynecology, KIMS Hospital, Bangalore, Karnataka, India.

Inclusion criteria

Postpartum women whose haemoglobin is in the range of 7-10g/dL.

Exclusion criteria

Women not willing to participate, medical disorders like hepatic or renal disorders, tuberculosis, diabetes, acute infections, known hypersensitivity to iron derivatives and parenteral iron treatment, haemolytic anaemia and thalassemia

Methodology

Demographic data was collected, along with detailed medical history and physical examination.

Haemoglobin, serum ferritin values were noted on day 0 and iron deficit was calculated according to the formula:

$$\text{Deficit} = (11 - \text{Hb of patient}) \times 2.4 \times \text{weight (kgs)} + 500$$

The women were divided into two groups of 30 each:

Group A (n=30) received iron sucrose in a dose of 200 mg intravenously in 200 ml normal saline over a period of

15-20 minutes on alternate days until a total dose was administered; not exceeding the maximum dose of 1000 mg/week.

Group B (30) received ferric carboxymaltose infusion as follows:

Dilute in 0.9% sodium chloride

500 mg: 100 ml NS – 6 minutes duration

1000 mg: 250 ml NS – 15 minutes duration

Not exceeding the maximum dose of 1000 mg/week.

All doses were given in the ward where equipment for cardiopulmonary resuscitation was available. Patients were observed for side effects or anaphylactic reactions. Any major side effects were documented.

Haemoglobin and serum ferritin estimation was repeated at the end of 6 weeks interval.

Statistical tool

The categorical data was expressed in terms of frequencies and percentages while continuous data was expressed as mean±standard deviation (SD). The two groups were compared using chi-square test for categorical data and independent sample 't' test was used to compare the means of different parameters. A 'p' value of less than or equal to 0.050 was considered as statistically significant.

Ethical approval

The study was approved by the Institutional Ethics Committee of Kempegowda Institute of Medical Sciences Hospital and Research Centre, Bangalore.

RESULTS

In this present study, most of the women (46.7%) were aged between 26 to 30 years in group A while in group B most of the women (40%) had also age between 26 to 30 years.

Most of the women in the study were booked outside in both group A (73.3%) and group B (63.3%).

In our study, most of the women had primi parity in group A (56.7%) and multi parity in group B (53.3%). However, the parity status of study population was comparable in both groups.

The present study had all women of group A (100%) and most of the women in group B (86.7%) had LSCS. In Group A, 15 patients needed 3 doses and 15 received 5 doses of iron sucrose; and in Group B, all received 1 dose of ferric carboxymaltose (Table 1).

Table 1: No. of doses given to study participants in Group A (Iron sucrose) and Group B (Ferric Carboxymaltose).

No. of doses given to study participants	Group A (Iron sucrose)		Group B (Ferric Carboxymaltose)		Total N (%)	P value
	N (%)	N (%)	N (%)	N (%)		
1	0 (0.0)	30 (100.0)	30 (50.0)			<0.001
3	15 (50.0)	0 (0.0)	15 (25.0)			
5	15 (50.0)	0 (0.0)	15 (25.0)			
Total	30 (100.0)	30 (100.0)	60 (100.0)			

*figures in parenthesis are percentages

Table 2: Pre and post treatment haemoglobin of study participants in Group A (Iron sucrose) and Group B (Ferric Carboxymaltose).

Haemoglobin in mg/dl	Group A (Iron sucrose)		Group B (Ferric Carboxymaltose)		Total N (%)		P value
	Pre treatment N (%)	Post treatment N (%)	Pre treatment N (%)	Post treatment N (%)	Pre treatment N (%)	Post treatment N (%)	
≤9.9	4 (13.3)	10 (33.3)	3 (10.0)	0 (0.0)	7 (13.3)	10 (16.7)	< 0.001
10.0-10.9	16 (53.3)	20 (66.7)	16 (53.3)	19 (63.3)	32 (53.3)	39 (65.0)	
≥11.0	10 (33.4)	0 (0.0)	11 (36.7)	11 (36.7)	21 (35.0)	11 (18.3)	
Total	30 (100.0)	30 (100.0)	30 (100.0)	30 (100.0)	60 (100.0)	60 (100.0)	

*figures in parenthesis are percentages

Table 3: Pre and post treatment serum ferritin levels of study participants in Group A (Iron sucrose) and Group B (Ferric Carboxymaltose).

Serum ferritin in mcg/ml	Group A (Iron sucrose)		Group B (Ferric Carboxymaltose)		Total N (%)		P value
	Pre treatment N (%)	Post treatment N (%)	Pre treatment N (%)	Post treatment N (%)	Pre treatment N (%)	Post treatment N (%)	
<75	12 (40.0)	10 (33.3)	11 (36.7)	0 (0.0)	23 (38.3)	10(16.7)	< 0.001
75-100	17 (56.7)	7(23.3)	18 (60.0)	3 (10.0)	35 (58.3)	10(16.7)	
>100	1 (3.3)	13(43.3)	1 (3.3)	27 (90.0)	2 (3.3)	40(66.7)	
Total	30 (100.0)	30 (100.0)	30 (100.0)	30 (100.0)	60 (100.0)	60 (100.0)	

*figures in parenthesis are percentages

Table 4: Reactions occurred among study participants in Group A (Iron sucrose) and Group B (Ferric Carboxymaltose).

Adverse reactions	Group A (Iron sucrose)		Group B (Ferric Carboxymaltose)		Total N (%)	P value
	N	%	N	%		
No reactions	29	96.7	30	100.0	59 (98.3)	0.313
Injection site reaction	1	3.3	0	0.0	1 (1.7)	
Total	30	100.0	30	100.0	60 (100.0)	

*figures in parenthesis are percentages

The mean pre-treatment haemoglobin levels were 8.8±0.6 gm% in Group A and 8.6±0.6 gm% in Group B (p=0.311). Post treatment Haemoglobin levels were found to be 10-10.9 in 66.7% women in Group A and 63.3% women in Group B (Table 2).

Majority of women in Group A (56.7%) and Group B (60.0%) had pre-treatment serum ferritin levels between 25-50 mcg/ml. Post treatment serum ferritin levels were found to be >100 mcg/ml in 43.3% women in Group A and 90% women in Group B (Table 3).

In this study, only 1 person in Group A (3.3%) had adverse reaction, which was injection site reaction. There was no adverse reaction seen in Group B (Table 4).

DISCUSSION

In this study majority of women in Group A (53.3%) and Group B (53.3%) had haemoglobin levels between 8.1-9.0 mg/dl ($p=0.909$). The mean pre-treatment haemoglobin levels were also comparable in Group A and B that is 8.8 ± 0.6 gm% in Group A and 8.6 ± 0.6 gm% in Group B ($p=0.311$). Majority of women in Group A (56.7%) and Group B (60%) had serum ferritin levels between 25-50 mcg/mL ($p=0.965$)

Post treatment Haemoglobin levels were found to be 10-10.9 in 66.7% women in Group A and 63.3% women in Group B. However, this difference was statistically significant.

In a similar study by Jose et al, mean rise in Haemoglobin at 12 weeks was significantly higher in ferric carboxymaltose group as compared with iron sucrose group (29 g/l versus 22 g/l; $p<0.01$).¹⁴ A similar study by Giannoulis et al in 52 postpartum women with anemia showed an increase in hemoglobin from <8 to 12.6 gm% post-treatment with iron sucrose.¹⁵ A study by Breymann et al in postpartum women with anemia showed an increase in hemoglobin from 9.67 to 15.2 post-treatment with ferric carboxymaltose.¹⁶

Post treatment serum ferritin levels were found to be >100 mcg/ml in 43.3% women in Group A and 90% women in Group B. However, this difference was statistically significant.

A similar study by Giannoulis et al in 52 postpartum women with anemia showed an increase in serum ferritin from <10 to 115 (ng/ml) post-treatment with iron sucrose.¹⁵ A study by Breymann et al in postpartum women with anemia showed an increase in serum ferritin from 39.9 mcg/l to 161.2 mcg/l post-treatment with ferric carboxymaltose.¹⁶

In this study, only 1 person in Group A (3.3%) had adverse reaction, which was injection site reaction. There was no adverse reaction seen in Group B.

In a similar study by Jose et al, no severe adverse effects were noted in either groups.¹⁴ In other similar studies, patients treated with ferric carboxymaltose had fewer side effects than those receiving iron sucrose, but the difference was not statistically significant.

The purpose of our study is to compare ferric carboxymaltose and iron sucrose in managing patients with postpartum anaemia and to avoid unnecessary blood transfusions. We found that both ferric carboxymaltose and iron sucrose regimens are effective and well tolerated when used in postpartum period but single dose and

efficacy of ferric carboxymaltose has better patient compliance.

Limitations

The sample size was small. Further, multi-centric study with more number subjects maybe justified.

CONCLUSION

In our comparative study among postpartum women within 6 weeks of delivery and Hb between 7.1 – 10.0 g/mL, Ferric carboxymaltose required was single dose compared to multiple doses of iron sucrose to achieve higher haemoglobin and serum ferritin values, lesser adverse effects, better patient compliance, and shorter treatment period, less hospital visits and did not require prolonged hospital stay. Though, ferric carboxymaltose is more expensive when compared to iron sucrose, when multiple doses of iron sucrose are required, the overall difference is not very significant. Hence, it was found that ferric carboxymaltose is a better drug when compared to iron sucrose.

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