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A prospective study comparing the efficacy of oral iron, intra-venous Iron-sucrose and Ferric-carboxy-maltose in postpartum anemia

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ABSTRACT

Post partum anemia needs a major concern not only to ensure healthy puerperum, better mother baby bonding, build up iron reserves in the puerpurae to have a better quality of life but also to ensure minimised incidence of anemia in next pregnancy. The current treatment for postpartum anemia is oral iron supplementation but this has been associated with several gastrointestinal side effects, So Intravenous iron treatments have become more popular. To evaluate the efficacy of oral iron, intravenous Iron sucrose and ferric carboxymaltose for treatment of postpartum anemia. Prospective study conducted at MLN Medical College from 2014 to 2015 in 350 postpartum anemic women given different iron preparation and changes in various haematological parameters compared. Although both forms of iron achieved almost similar increase in Hb level, parenteral Iron preparations had a quicker response with better restoration of iron stores. The rise in all the red cell indices were significantly more in the intravenous group then in oral iron group with no difference between ISR&FCM. The restoration of iron stores were maximum in FCM group. Parenteral iron therapy replenishes iron stores more rapidly and ensures iron therapy in population with poor compliance. Compared to ISR, FCM had advantage of lesser dose requirement and lesser side effects.

Keywords: Post partum anemia, oral iron, intra-venous Iron-sucrose(ISR) and Ferric-carboxy-maltose(FCM).

INTRODUCTION

The problem of anemia both antepartum and postpartum is far more prevalent in developing countries than in western societies[1].According to the WHO, anemia affects up to one-quarter of the global population, approximately 62 billion people[2,3] and prevalence of postpartum anemia in an ICMR study covering 11 states in 2009 was 87.65%[4].

Postpartum anemia needs a major concern as about 20% of maternal deaths worldwide and 36% maternal deaths in India had been attributed to it[5,6]. It is mostly continuum of antepartum anemia or may be sometimes precipitated by postpartum hemorrhage as a Nutrition Surveillance System estimated 29.8% of non anemicantepartum women became anemic after delivery[7].

Postpartum anemia imposes a disproportionately substantial disease burden during a critical period of maternal–infant interaction causing lactation failure, sepsis, prolonged hospitalization, secondary hemorrhage, heart failure, varied maternal psychological and cognitive variations, postpartum depression[8].

Postpartum anemia requires prevention and treatment not only for that particular period but also to ensure good health with enough iron stores atthe start of next pregnancy. Currently, the Center for Disease Control and Prevention recommends selective anemia screening at 4–6 weeks postpartum in woman having anemia continued through the third trimester, postpartum hemorrhage and multiple births [1].

Oral iron preparations are being used since centuries as an easy, cost-effective and preferred method to treat anemia, but in certain circumstances the efficacy of oral irons may be questioned due to it's faulty intake, faulty absorption, related side effects, different bioavailability of different iron preparations and unpredictable attitude of the patient. Parentral iron preparation offers a benefit over the oral iron in being more reliable, better bioavailable, no gastrointestinal side effects and thus better response, though, sometimes they may cause allergic and anaphylaxis reactions.

MATERIAL AND METHODS

The present study was conducted in the Department of Obstetrics and Gynecology at Swaroop Rani Nehru Hospital, MLN Medical College, Allahabad over a period of one year(2014-15).Approximately 500 postpartum women (post delivery and post caesarean) who had no pregnancy related complications except antepartum or postpartum hemorrhage if any, no medical and endocrine disorders were enrolled in the study after taking valid informed consent. A detail history, thorough general and systemic examination were carried out. All 500 patients were subjected to complete blood count, out of these 362 patients were found to be anemic as per the criteria's laid down by Center for Disease Control and prevention for iron deficiency anemia: Hb<10g/dl, MCV<80fl, MCH<27pg, MCHC<34g/dl, hematocrit<40%S.Ferritin<15µg/ml. Out of these 362 patients,12 patients withdrew from study before completion due to some or the other reason. Patients were properly counseled regarding various treatment modalities and were freely allowed to choose between oral iron, intravenous Iron sucrose or intravenous FCM. Out of 350 anemic patients, 200 women received oral iron containing 200mg of elemental iron in divided doses for 4 weeks (as recommended by CDC for the treatment of anemia) (Group I) ,100 patients received intravenous Iron sucrose(ISR) as multiple shots of 200mg each, diluted in 200ml normal saline infused over 15-20 minutes on alternate days (Group II) and 50 patients received intravenous Ferric carboxymaltose (FCM) as single shot of 1000mg in 250 ml normal saline over 15 minutes (Group III). Total iron to be infused in a particular patient was calculated using Ganzoni formula [Weight (kgs)×(Target Hb – Patient's baseline Hb)×2.4+500.Target Hb was 11 g/dl, 2.4 is unitless conversion constant and 500 is the target iron stores in mg. The response to the therapy was assessed by estimating FSS(Fatigue Severity score) score, Haemoglobin(g/dl), Haematocrit (%), Serum ferritin (µg/ml) , MCV(fl),MCH(pg),MCHC (g/dl), Reticulocytes count (%) initially before starting treatment and on day 7 and day 28 of the treatment. Statistical analysis was done by applying ANOVA and t-Test to test each pair of means. For all statistical purposes, p value < 0.05 was considered significant.

RESULTS

Out of 500 postpartum women, 362 (72%) had Hb<10 gm/dl with other features of iron deficiency in Complete blood count [Table-1]. More than half of the patients,222 (63%) were illiterate and in age group 20-25years (P<0.05), almost two third, 235 (67%) were from rural background(p<0.05) and up to three forth 271(77%) belonged to middle socioeconomic status(p<0.05).The demographic variables and baseline haematological parameters; Haemoglobin(g/dl), Haematocrit (%), Serum ferritin (µg/ml) , MCV(fl),MCH(pg),MCHC (g/dl) in oral iron group-I, ISR-II and FCM group- III were statistically comparable(p>0.05) to avoid result bias . At day 7 the mean rise in Hb in groupI, II and III was 0.7,1.6 and 2.3 gm% respectively that was significantly higher in parenteral group (p<0.05) with even better response with FCM. But at day 28, the mean rise of haemoglobin in all the groups was comparable; 2.6,2.8 and 2.85 gm% respectively (p>0.05).The iron stores as reflected by serum ferritin increased significantly (p<0.05) with the parenteral irons both at day 7 and day 28, with the difference of rise being 19.5 and 43.4 µg/dlat 7^{th} day and 10.5 and 24µg/dlat 28^{th} day with ISR and FCM respectively. The response to FCM was prompt and better than ISR. Whereas, the response to oral iron in improving the stores were only minimal (p>0.05) with marginal increase in serum ferritin, 1.3 and 4.3µg/dl at day 7 and 28 respectively [Table-7].Other hematological parameters like PCV, MCV, MCH and MCHC showed improvements on day 7 but better results were obtained on day 28. The mean increase in these parameters except PCV were statistically nonsignificant (p>0.05) with oral iron, whereas both the parenteral groups showed a significant improvements (p<0.05) in all these parameters with the most significant response in rise in PCV by 9.5% and 10% on day 28 with ISR and FCM. The fall in the mean FSS scores were significant (p<0.05) in all the groups both at day 7 and 28 but with no statistical difference between the 3 groups. On comparing the ADE, oral iron had a little higher rates;

32.5% of overall side effects in comparison to ISR; 30%. Whereas FCM had relatively better tolerance with the rates of overall side effects of 24% only. Gastro-intestinal complaints topped the list of ADE in oral iron group; 21% as compared to 2 % in ISR and nil in FCM group .Parenteral irons were more commonly associated with injection site reactions like mild rashes, urticaria, swelling or itching, that were higher in ISR than in FCM (12% vs 4%).Headache, muscle cramps and systemic reactions like fever, dizziness were either nil or minimal; 0-1.5% with oral irons but were noticed in parenteral groups ranging between 2-8% [Table-6].

DISCUSSION

The prevalence of postpartum iron deficiency anemia was as high as 72% similar to various other studies like Somdatta et al in 2009 and Kriti Ayer et al in 2012[9,10]. Almost two-third (63%) were belonging to 20-25 years of age pointing that most women are entering their reproductive age with insufficient iron stores who is likely to succumb to increasing iron demands of pregnancy and postpartum period thus develop anaemia. Most of these patients were illiterate and belonged to rural areas and of lower middle class. On comparing the response to the various modalities of iron therapy we found that parenteral iron preparations caused relatively rapid rise in Hb at day 7, but at 28th day both the modalities oral and parentral, achieved almost similar increase in Hb level ($p>0.05$). All the red cell indices (MCV,MCH,MCHC, Haematocrit) showed statistically significant difference in improvement with the intravenous group than in oral iron group($p<0.05$). The increasing iron stores of the body as depicted by rising serum ferritin levels were much more promising with the parenteral preparations, FCM showing a relatively much rapid and higher restoration of the iron stores (<0.05). Breyman et al in 2008 [11] followed their patients for 12 weeks and found that oral iron caused only a marginal increase in ferritin levels even by the end of 12 weeks while response to FCM was significantly appreciable at 1 week of treatment only. Similar trend of responses to the oral and parenteral irons had been shown by previous studies [12,13,14,15,16] who compared oral iron with ISR and or FCM. Whereas, a little variation had been observed by the authors like Quinibi et al and Giammoulis et al in 2008 [17,18] who showed that parentral iron preparations both ISR and FCM caused a significantly higher rise in Hb than oral iron at all points of time in their study. Iron deficiency in postpartum period is associated with decrease physical endurance and impairs mother's ability to engage in child care, household and social activities. Apart from the biochemical response to the therapy, we also assessed the general well being of the patient by observing fatigue severity score (FSS) that showed comparable improvements in all the three groups. Except for few injection site reaction, FCM and ISR were better tolerated than oral iron. No anaphylactic reactions were noticed with these preparations. Whereas oral irons were associated with frequent gastrointestinal complaints adding to the problems of her day to day routine is definitely a cause for poor adherence to the therapy. The upper handedness of parenteral irons in relation to the side effects and compliance had been proved by the other studies also like Brymann et al(3.5%in FCM vs 24%in oral), van Wyck et al(24.5%vs2.4%) Morre et al(13% vs32%) [11,14,19].

Table 1:The prevalence of post-partum anemia in total study population

Total no. of patients	Patients without Postpartum anemia (Hb≥10gm%)		Patients with Postpartum Anemia (Hb<10gm%)	
	No.	%	No	%
500	138	28	362	72

Table 2-Demographic factors in postpartum anemia (N=350)

	Habitat		Education		Age groups(years)				SE-Status		
	R	U	IL	L	15-20	20-25	25-30	30-35	High	Middle	lower
No.	235	115	220	130	41	222	54	33	9	271	70
%	67	33	63	37	12	63	14	11	3	77	20
P	<0.05		<0.05			<0.05				<0.05	

(R=rural,U=urban,IL=illiterate,L=literate)

TABLE 3-Mean Haematological parameters before& after Oral Iron Thearpy

	Hb (gm/dl)	S. Ferritin (µ/dl)	PCV (%)	MCV (fl)	MCH (pg)	MCHC (g/l)	FSS Score
Baseline	8.2	12.9	25.6	74.5	25.1	32.4	49
Day 7	8.9	14.2	27.8	75.1	25.2	32.7	42
Day 28	10.9	17.2	32.2	76.2	26	33	26
Difference	2.6	4.3	6.5	1.7	0.9	0.6	23
P Value	0.0267	0.0143	0.0120	0.0734	0.1843	0.1956	0.0063

TABLE 4- Mean Haematological parameters before& after IV. Iron Sucrose

	Hb (gm/dl)	S. Ferritin (µ/dl)	PCV (%)	MCV (fl)	MCH (pg)	MCHC (g/l)	FSS Score
Baseline	8.1	12.6	25.3	74.6	25	31.5	50
Day 7	8.9	32.1	30.9	76.6	26.3	32.8	40
Day 28	10.9	23.1	34.8	79.6	27.1	33.1	28
Difference	2.8	10.5	9.5	5	2.1	1.6	22
P Value	0.0129	0.0056	0.0052	0.0264	0.0245	0.0388	0.0093

TABLE- 5 Mean Haematological parameters before& after IV.FCM

	FERRIC CARBOXYMALTOSE						
	Hb (gm/dl)	S. Ferritin (µ/dl)	PCV (%)	MCV (fl)	MCH (pg)	MCHC (g/l)	FSS Score
Baseline	7.9	12.7	25.7	74.1	24.8	30.8	47
Day 7	10.2	56.1	31.7	76.4	26.2	32.4	39
Day 28	10.8	36.7	35.7	79.7	27.2	32.7	25
Difference	2.9	24	10	5.6	2.4	1.9	22
P Value	0.0113	0.0019	0.0049	0.0249	0.0201	0.0257	0.0078

Table 6: Drug related adverse reactions in each group

	Oral(N=200)		ISR(N=100)		FCM(N=50)		
Adverse reactions	NO.	%	NO.	%	NO.	%	P Value
Nausea & Vomiting	18	9	3	3	1	3	<0.05
G.I. Complaints	42	21	2	2	0	0	<0.05
Muscle Cramps	0	0	1	1	2	4	<0.05
Headache	2	1	6	6	4	8	<0.05
Injection site reactions	0	0	12	12	2	4	<0.05
Systemic reactions	3	1.5	6	6	2	4	<0.05
Overall side effect	65	33	30	30	12	24	<0.05

Table 7: differences of variables on day 28 from baseline in all the three groups

	Hb (gm/dl)	S. Ferritin (µ/dl)	PCV (%)	MCV (fl)	MCH (pg)	MCHC (g/l)	FSS Score
Oral iron	2.6	4.3	6.5	1.7	0.9	0.6	23
IV iron sucrose	2.8	10.5	9.5	5	2.1	1.6	22
IV FCM	2.9	24	10	5.6	2.4	1.9	22
P Value	>0.05	<0.05	<0.05	<0.05	<0.05	<0.05	>0.05

CONCLUSION

Although oral irons are the most convenient and affordable form of iron supplementation, in cases of any doubt, parenteral irons are definitely better chosen with preferences for FCM if the cost is not the limiting factor as it require fewer episodes of administration and are associated with lesser side effects and have the best response amongst all the available iron preparations.

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