International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2015): 6.391

Intravenous Iron Sucrose and Ferric Carboxymaltose (FCM) Versus Oral Iron in the Treatment of Postpartum Iron Deficiency Anaemia

Roy Bhramita[1], Sabzposh Noor Afshan[2], Akhtar Nishat[3]

[1]Junior resident, department of Obstetrics and Gynaecology, JNMC, AMU, Aligarh, UP, India

[2, 3]Professor Department of Obstetrics and Gynaecology, JNMC, AMU, Aligarh, UP, India

Abstract: ***Objectives: To evaluate the safety and efficacy of intravenous FCM & ferrous sucrose with oral iron in postpartum anaemic women. Study design: Random, prospective, interventional. Material and Methods: The study was conducted in the department of Obstetrics and Gynaecology, J.N.Medical College, AMU, Aligarh. A total of 90 postpartum anaemic women with haemoglobin < 10gm were assigned randomly to receive inj Ferric Carboxymaltose, oral iron or inj sucrose. Changes in haemoglobin and ferritin level were measured and analyzed among the groups using ANOVA and paired t –test. Results: A statistically significant increase in Haemoglobin and ferritin level was observed in all the three groups but maximum increase was observed in inj FCM group followed by inj Sucrose and Oral iron group .Mean increase in Haemoglobin in inj Ferric Carboxymaltose group was 2.157 ±.475 gm/dl followed by inj sucrose 1.221 ±.576 gm/dl and oral iron 0.609±.237 gm/dl at 2nd week. At 6th week increase in Haemoglobin were 4.737±.994gm/dl, 3.478 ±.799 gm/dl and 2.881±.752 gm/dl respectively in inj Ferric Carboxymaltose ,inj Sucrose, oral iron. Mean increase in serum ferritin were also significant in all the three groups both at 2nd and 6th weeks, but maximum increase was seen in inj FCM. Mean increase in serum ferritin level at 2nd weeks were 184.483±51.746 µ/l,93.275±26.972µ/l & 2.231±3.466µ/dl and at 6th week were 150.223±41.927µ/l, 75.489±25.586 µ/l and 31.940±7.177µ/dl respectively for inj Ferric Carboxymaltose, inj sucrose and oral iron. Conclusion: Haemoglobin and serum ferritin level increases fastest with Inj. Ferric Carboxymaltose followed by inj sucrose and oral iron.***

Keywords: Postpartum anaemia, Ferric Carboxymaltose, inj sucrose, oral iron

1. Introduction

Nutritional iron deficiency is the most common deficiency disorder in the world, affecting more than two billion people worldwide, with pregnant women particularly more at risk (Khalafallah & Dennis, 2012).. WHO has estimated that prevalence of anaemia in pregnant women is 14 percent in developed and 51 percent in developing countries, out of which 65-75 per cent in India. What is even more important is the fact that about half of the global maternal deaths due to anaemia occur in South Asian countries; India contributes to about 80 per cent of the maternal deaths due to anaemia in South Asia(Kalaivani, 2009) .The WHO (1972) defines anemia – regardless of its cause – as Haemoglobin(Hb) level of less than 11.0 g/dl during pregnancy and less than 10.0 g/dl during the postpartum period(Breymann, 2013). Postpartum anaemia is result of both, deficiency during pregnancy and haemorrhage during delivery. It has been associated with depression, stress, anxiety, cognitive impairment, decreased mother-infant attachment, and infant developmental retardation(Api et al 2015).

The routine management of iron deficiency anemia is oral supplementation. But even under the best of circumstances, oral iron is not well tolerated, and patients are often non-compliance for a variety of reasons, including intolerable side effects and the need for multiple daily doses(Koch et al 2015). The frequently poor absorption of oral iron, moreover, can contribute to suboptimal patient response. Blood transfusion is reserved for more severe or symptomatic cases and is associated with numerous risks which may be devastating for the young mother(Patel, 2015). Given the proven effectiveness as well as safety profile of IV iron, particularly of Iron Sucrose and FCM in a broad spectrum of diseases associated with IDA, the current paradigm of oral iron as first line therapy in moderate cases of postpartum anaemia should be reconsidered (Cançado & Muñoz, 2011).

2. Material & Methods

After approval from the ethical committee of the institution the study was conducted from December 2014 to November 2016 in the department of Obstetrics & Gynaecology on postpartum patients admitted in obstetrics wards.

Study design: It is a hospital based randomized prospective interventional open label single centre study.

Method

After informed consent hemodynamically stable postpartum women with IDA who delivered 24-48hrs before and fulfilled the inclusion criteria, i.e., Hb< 10gm, serum ferritin level <15µg/l were enrolled for the study. Women who were intolerant or hypersensitive to iron derivatives, or had history of anaemia due to other causes such as chronic blood loss, haemolytic anaemia, thalassaemia and sickle cell anaemia, preeclampsia, antepartum haemorrhage or parenteral therapy during current pregnancy, or peripartum blood transfusion, asthma, seizures, alcohol or drug abuse or had sign of infection or DVT, any evidence of hepatic, renal cardiovascular dysfunction were excluded. The enrolled women were divided into three groups: group I (30 women) received Injection FCM, group II (32 women) oral iron and group III (28 women) received injection sucrose.

Iron deficit was calculated by formula 2.4 × (target haemoglobin-Actual haemoglobin) ×weight+500mg for replenishment of stores. The calculated dose is to be rounded down to the nearest 100 mg and injections were given within 1 week of delivery. Group I received Inj. FCM by I.V route as single dose and maximum of 1000 mg (20ml) diluted in 250 ml sterile 0.9% sodium chloride solution over 15 minute not more than once a week and not exceeding 0.3ml of FCM injection(15mg of iron /kg body weight) or the calculated cumulative dose. Group II received intravenous Iron Sucrose (IS) on alternate day (500mg of elemental iron diluted in 500ml 0.9% normal saline). Patients were monitored for any hypersensitivity reaction. Injection FCM was given in single dose of 1000mg. Inj Iron Sucrose was given 500mg on two alternate days. Both were stopped after giving the calculated dose. Patients in groups I and III did not receive any additional oral iron. Group II received Oral iron (ferrous ascorbate) 100mg B.I.D was given for 6 wks.All patient were followed after 1-2 week and after 4-6 weeks. On each visit they were clinically evaluated and laboratory investigations were done to see the changes in haemoglobin level & serum ferritin. Patients and attendants were explained about the intervention properly in the local language and then informed consent was taken. The details of patient, her vitals and investigations were noted on a predesigned Proforma.

Statistical Analysis: The changes in Hb and serum ferritin levels at 2nd and 6th weeks after treatment were measured and analyzed (SPSS software) *IBM SPSS Statistics v23*

3. Result

Out of 150 cases initially enrolled in the study, only 90 cases could be followed up 2nd and 6th weeks post intervention, and analysis was done on 90 cases only. Patients of all three groups were comparable demographically as well as in baseline haemoglobin and serum ferritin (p value >.05) (Table-1.).Baseline Hb (gm/dl) for Inj. FCM (group I), Oral iron (group II) and inj. Iron Sucrose (group III) were 7.480 ±.702, 7.831±.631 & 7.911 ±.848 respectively, which post intervention increased to 9.637 ±.784, 8.441 ±.593 and 9.132 ±.667 at second week and 12.217 ± .725, 10.712 ± .803 and 11.389 ±.7355 gm at 6th week respectively (Table 2, Fig 1.). Mean rise in Hb (gm/dl) in group I, group II and group III, were 2.157 ±.475, .609 ±.237 and 1.221 ±.576. This rise was statistically significant (p value 0.000) and at 6th week the mean rise were 4.737±.994, 2.881±.752 and 3.478 ±.798 respectively which was also statistically significant (Fig. 3). Despite being the minimum Hb at recruitment the rise was maximum in FCM group both at 2nd & 6th week followed by injection iron sucrose and oral iron groups.

The other Haematological parameter for our study was serum ferritin level. The mean baseline values for group I, II, & III were 9.897,9.300 & 8.557 respectively, which were comparable (p value >0.05)(Table1). After intervention, at 2nd week the mean values for serum ferritin for all three groups I, II, and III increased to 194.380,11.531 & 101.832 respectively. This increase was statistically significant (p value <0.000) in all the groups. Sixth week post intervention also they remained significantly higher than initial values in all the groups. They were 160.120,41.241 & 84.046 for group I, II, III respectively (p value<0 .000) (Table 3, Fig 4). Although at 6th week, there was fall in serum ferritin level in injectable groups (FCM & Fe Sucrose) yet it was higher than baseline. In oral Fe group the level of serum ferritin consistently increased from enrolment and was found higher at 6th week than 2nd week but did not cross the level of 50µ/L. Within the group the rise in both Hb & serum ferritin was significant in all the three groups. Though the rise was slower in oral Fe group than the injectable groups. Both the injectable iron groups –group I & group III were able to replenish the iron store rapidly than oral iron. But injection FCM replenished the store better than injection sucrose both at 2nd and 6th week. A fall in serum ferritin level was noted in both the injectable groups at 6th week but the level of serum ferritin in FCM group was more than 150µ/l as compared to injection Fe sucrose which fell to 84.046µ/l.

By the end of 6th week 60% of the patients treated with injection FCM, 25% with injection sucrose and only 15.6% with oral iron were able to achieve Hb ≥12.There was no major side effects in all the three groups during the course of therapy and minor side effects were treated with medication. In injection FCM group only 6.7% cases complained of low grade fever, which responded to oral antipyretics. In oral iron group, most common complaint was constipation (25%), followed by nausea (18.75%) followed loose stools (6.25%). In injection Fe Sucrose group , incidence of fever, urticaria and discomfort were equal (10.71% each) , in addition to thrombophlebitis in 7.14% cases (Table 4, fig 5).

4. Discussion

Iron deficiency anaemia is the most common cause of postpartum anaemia in India. It is due to preexisting iron deficiency, repeated pregnancy at short intervals, poor dietary intake, malaria and worm infestations. The aim for the treatment of anaemia is to improve the Hb level as well as to replenish the iron store. There are various modalities for the treatment like oral formulations and injectable iron preparations. Oral iron is preferred due to ease of administration, but the non-compliance and side effects make them unpopular. Parenteral iron therapy is expensive and invasive but helps to restore Hb and iron stores rapidly and efficiently. For moderate grade parenteral iron like Dextran used in past were associated with adverse reactions making them unsafe(Cançado & Muñoz, 2011).Blood transfusion is the choice for severe anaemia but is associated with hazards, so the search for alternative is always welcomed. Inj FCM & inj. Fe Sucrose are better than IM preparation with less side effects.

There are many studies which has been conducted to compare the efficacy and safety of oral iron(sulphate) with inj. Fe sucrose and Inj. FCM, but there are only few studies which has compared oral iron(ascorbate)with both inj FCM and inj Sucrose viz., Rathod et al (2015)& Singh et al(2016).In both the studies the age group of the cases are comparable to our studies.

Haemoglobin

In our study the rise in Hb at 2nd week was comparable to the two studies (Rathod et al 2015 & Singh et al, 2016) .Rise in

Hb at 2nd week was 2.156gm/dl,0.609gm/dl and 1.22gm/dl for inj FCM, oral iron and inj Sucrose respectively in our study ,which is quite similar to Rathod et al and Singh et al which were 3.2gm/dl,.8gm/dl & 2.4gm and 1.56gm/dl,0.64gm/dl and 1.31gm/dl respectively. Hb at 6th week for study was 4.73gm/dl,2.88gm/dl and 3.47gm/dl and for Rathod et al and Singh et al were 4.4gm/dl,2.1gm/dl and 3.4gm/dl and 2.95gm/dl,2.64gm/dl and 1.30 gm/dl respectively

Serum Ferritin

Other parameter for our study was rise in serum ferritin at 2nd and 6th week. Mean Serum ferritin at 2nd week for our study was 184.483, 2.231 & 93.275 for inj FCM , oral iron & inj Sucrose. The serum ferritin for Rathod et al & Singh et al were 307.1, 2.5 & 193.1 and 263.35,18.5 &109.9 respectively for inj FCM, oral iron & inj Sucrose. At 6th week value of ferritin for our study was 150.22,41.24 & 84.04 and for Rathod et al and Singh et al were 106.7,14.2 & 64 and 218.99 ,11.9 & 81.6 respectively. There is fall in the serum ferritin level in injectable group in our study group as well as Rathod et al(2015) and Singh et al (2016).But in Rathod et al & our study there is rise in serum ferritin level in oral iron group which in contrast has fall in Singh et al.

Adverse reactions

There was no serious side effects during the course of treatment. Minor side effects were seen in all the three groups. In oral iron group 50% cases reported adverse effects which included constipation (25%), nausea (18.7%) and loose stools (6%). In inj Sucrose group 39% cases reported fever (11%), utricaria(11%), uneasiness(11%) and thrombophlebitis(7%) which were treated and no further complication was seen.In inj FCM group 6% complaint of fever after infusion. Similar side effects have been reported from various studies((Damineni & Thunga, 2016). but fever in Inj FCM group was reported from our study only.

5. Conclusion

Anaemia is a public health problem in India like other developing countries but it is significantly high among the pregnant women due to lack of proper diet, increase body demand ,& underlying causes. Several programmes are being run by government and non-government organizations to correct it during pregnancy, but have proved futile, because of illiteracy poverty and practices delay in seeking health services. In puerperium it further deteriorates and with subsequent pregnancies it is at its worst due to depleted iron stores.In our study we found both inj. Iron SUCROSE and inj. FCM efficient and safe in treatment of postpartum anaemia. They not only improved Hb level but also replenished the body stores. Although oral Iron Group achieved 9gm/dl or more in the 6th week but it failed to replenish the stores**.** Whereas 100% cases enrolled in the FCM group achieved ≥10 gm/dl and replenished the stores. Inj. FCM was found safe even in severe anaemia (refusal for transfusion by patient) and blood transfusion was prevented. In future FCM should be tried in stable severe anaemic patients.

Table 1: Baseline characteristics at the time of recruitment

	Inj.Fcm group (n=30)	Oral group (n=32)	Inj. Fe.Sucrose group(n=28)	P value
Age	25.00 ±4.1287	25.06±3.975	24.84±4.00	>.05
Baseline Hb	7.4807±.7024	7.831±.6311	7.911±.8478	>.05
Baseline ferritin	9.897±3.0627	9.300±2.5278	8.557±1.7124	>.05

Table 2: Showing Hb levels at enrollment, and 2 and 6 weeks after intervention

At enrollment	Study groups	Hb (µ/gm) ±SD	Minimum Hb	Max, Hb
	Inj. FCM (GpI)	7.480± .702	6.3	8.5
	Oral Fe (Gp II)	7.831 ±.631	6.0	8.6
	Inj. Fe. Sucrose (GpII)	7.911±.848	6.5	9.4
After 2 week	Inj. FCM (Gp I)	9.637±.784	8.0	10.9
	Oral Fe (GpII)	8.441±.593	7.0	9.3
	Inj. Fe. Sucrose	9.132±.667	7.9	10.7
After 6 weeks	Inj.FCM (GpI)	12.217±.725	11.0	14.4
	Oral Fe	10.712±.803	9.00	12.2
	Inj. Fe. Sucrose	11.389±.736	10.00	12.7

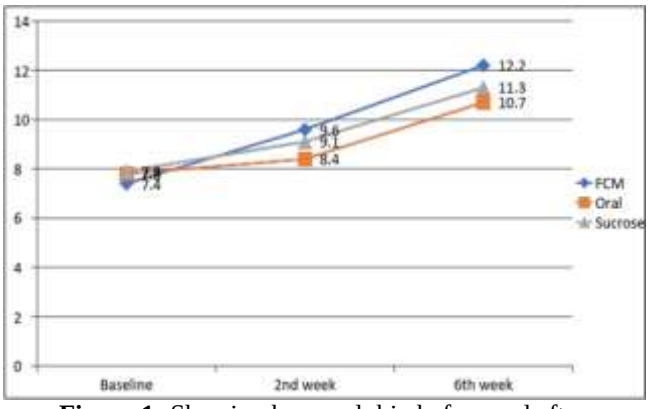

Figure 1: Showing haemoglobin before and after intervention

Table 3: Comparison of serum ferritin before intervention and 2nd & 6 weeks after intervention

		Mean ±Std. Deviation	95% C.I		Mini ferritin	Maxi ferritin
			Lower Bound	Upper Bound		
ferritin Baseline	Inj. FCM	9.897±3.063	8.753	11.040	5.0	15.0
	oral	9.300±2.528	8.389	10.211	6.0	15.0
	Sucrose	8.557±1.712	7.893	9.221	6.0	12.3
ferritin 2nd week	FCM	194.380±51.348	175.206	213.554	90.0	297.0
	oral	11.531±4.581	9.880	13.183	7.2	28.0
	Sucrose	101.832±26.840	91.425	112.240	8.4	149.0
ferritin 6th week	FCM	160.120±40.695	144.924	175.316	93.3	227.0
	oral	41.241±6.302	38.968	43.513	29.0	52.1
	Sucrose	84.046±25.639	74.105	93.988	10.1	135.0

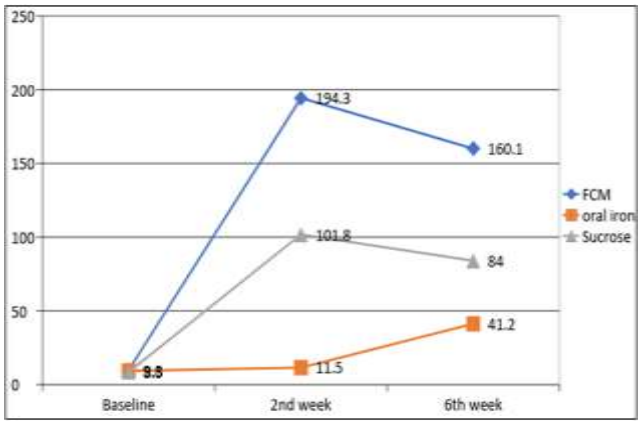

Figure 2: Showing serum ferritin before and after intervention

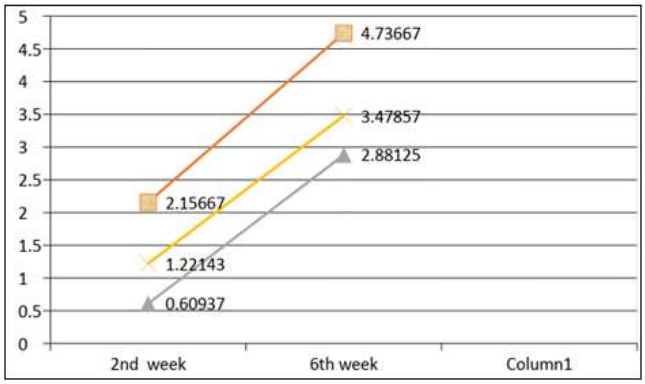

Figure 3: Rise in Hb over 2nd and 6th week

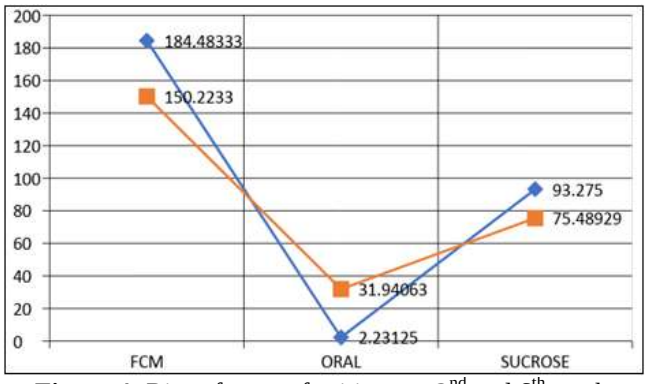

Figure 4: Rise of serum ferritin over 2nd and 6th week

Table 4: Side Effects during Therapy

Side Effects	Inj. FCM % (n)	ORAL % (n)	Inj.Fe Sucrose %(n)
Nausea	0	18.75 (6)	0
Vomiting	0	0	0
Constipation	0	25 (8)	0
Loose Motion	0	6.25 (2)	0
Urticaria	0	0	10.71(3)
Fever	6.7 (2)	0	10.71(3)
Thrombophlebitis	0	0	7.14(2)
Discomfort	0	0	10.71(3)
Total	30	32	28

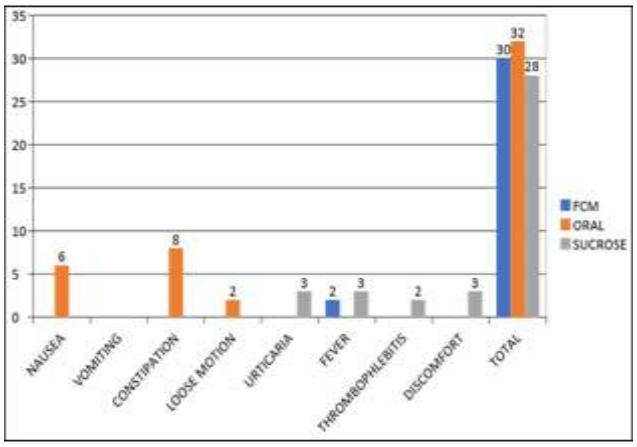

Figure 5: Adverse effects

6. Source of support

NIL

7. Conflict of Interest

None

References

[1] Api, O., Breyman, C., Çetiner, M., Demir, C., & Ecder, T. (2015). Diagnosis and treatment of iron deficiency anemia during pregnancy and the postpartum period: Iron deficiency anemia working group consensus report. *Journal of Turkish Society of Obstetric and Gynecology*, *12*(3), 173–181. https://doi.org/10.4274/tjod.01700

[2] Bhandal, N., & Russell, R. (2006). Intravenous versus oral iron therapy for postpartum anaemia. *BJOG: An International Journal of Obstetrics and Gynaecology*, *113*(11), 1248–1252. https://doi.org/10.1111/j.1471-0528.2006.01062.x

[3] Breymann, C. (2013). Iron deficiency anemia in pregnancy. *Expert Review of Obstetrics and Gynecology*, *8*(6), 587–596. https://doi.org/http://dx.doi.org/10.1586/17474108.2013.842683

[4] Cançado, R. D., & Muñoz, M. (2011). Intravenous iron therapy: how far have we come? *Revista Brasileira de Hematologia E Hemoterapia*, *33*(6), 461–9. https://doi.org/10.5581/1516-8484.20110123

[5] Damineni, S. C., & Thunga, S. (2016). IV ferric carboxymaltose vs oral iron in the treatment of post-partum iron deficiency anaemia. *Journal of Clinical and Diagnostic Research*, *10*(11), QC8-QC10. https://doi.org/10.7860/JCDR/2016/19375.8937

[6] Kalaivani, K. (2009). Prevalence & consequences of anaemia in pregnancy. *Indian Journal of Medical Research*, *130*(5), 627–633. https://doi.org/10.1542/peds.2005-1156

[7] Khalafallah, A. A., & Dennis, A. E. (2012). Iron deficiency anaemia in pregnancy and postpartum: Pathophysiology and effect of oral versus intravenous iron therapy. *Journal of Pregnancy*, *2012*, 1–12. https://doi.org/10.1155/2012/630519

[8] Koch, T. A., Myers, J., & Goodnough, L. T. (2015). 763576, *2015*.

[9] National, T., Health, F., & Iron, U. N. (n.d.). National Iron Plus Initiative for Anaemia Control Among 6 Months Onwards Population.
[10] Patel, J. (2015). Comparison of Intravenous Iron Sucrose and Ferric Carboxymaltose Therapy in Iron Deficiency Anemia during Pregnancy and Postpartum Period. *J Pharm Sci Bioscientific Res*, *5*(53), 239–243.
[11] Singh, S., Singh, R. K., & Singh, S. (2016). Comparison of Oral Iron, Iron Sucrose and Ferric Carboxymaltose (Fcm) To Treat Post Partum Anaemia. *Journal of Evidence Based Medicine and Healthcare*, *3*(20), 832–835. https://doi.org/10.18410/jebmh/2016/190
[12] Rathod, S., Samal, S. K., Mahapatra, P. C., & Samal, S. (2015). Ferric carboxymaltose: A revolution in the treatment of postpartum anemia in Indian women. *International Journal of Applied and Basic Medical Research*, *5*(1), 25–30. http://doi.org/10.4103/2229-516X.149230