e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(8); 1277-1282

Original Research Article

A Comparative Study between Standard Oral Iron Tablets Versus Single Dose Intravenous Iron Sucrose in Post-Partum Anaemic Women Attending A Tertiary Care Hospital in Tripura

Debbarma B[1], Chakrabarti SB[2], Rakshit AK[3], Saha(Ray) M[4], Shil A[5]

[1]Post graduate student, Department of Obstetrics & Gynaecology, AGMC & GBP Hospital
[2,3]Associate Professor, Department of Obstetrics & Gynaecology, AGMC & GBP Hospital
[4]Professor, Department of Pathology, AGMC & GBP Hospital
[5]Assistant Professor, Department of Obstetrics & Gynaecology, AGMC & GBP Hospital

Received: 30-5-2023 / Revised: 30-06-2023 / Accepted: 30-07-2023
Corresponding author: Shil A
Conflict of interest: Nil

Abstract:

Background: Postpartum anaemia is one of the under-appreciated global maternal health burden. There are various comorbidities found relating to postpartum anaemia such as fatigue, depression, impaired cognition. Postpartum anaemia can impact on both maternal-child bonding & neonatal care. Most women with postpartum anaemia have antepartum iron deficiency. Oral or intravenous iron is choice of correcting anaemia with various side effects. The current study had been taken to compare the effectiveness of oral iron tablet & intravenous iron sucrose.

Result: Mean haemoglobin level was found to be increased more significantly from baseline to post 6 weeks therapy in both the groups: 1. Group A from 9% (baseline) to 10.58% (after 6 weeks) and 2. Group B from 8.5% (baseline) to 10.50% (after 6 weeks). The mean changes both in between the group and within the group were also found to be significant. However, it was observed that the mean changes were more in group A (2.091 ± 0.8121) who were treated with IV iron sucrose than group B (1.442 ± 0.7354) who were treated with oral iron folic acid tablets.

Conclusion: The haemoglobin concentration at 6 weeks postpartum was higher in women who received intravenous iron compared to oral iron therapy. The current findings suggest that intravenous iron can be considered as a viable option for postpartum anaemia over oral iron concerning rise in hemoglobin level & risk of side effects.

Keywords: Postpartum Period, Anaemia, Iron, Nausea, Anaphylaxis.

Introduction

Anemia is a condition in which the number of red blood cells or their oxygen carrying capacity is insufficient to meet the body's physiological requirements, and is conventionally taken as hemoglobin (Hb) value that is less than the lower limit of the normal, which vary by age, sex, and during pregnancy. According to World Health Organization (WHO), anemia affects more than 1.5 billion people worldwide. WHO defines anemia in pregnancy as Hb value less than 11g/dl and value less than 10g/dl as post-partum anemia. Iron deficit being the most common cause [1]. Even though iron supplementation reduces anemia and is standard prenatal care in most countries, anemia continues to persist at relatively high rates among postpartum women. Globally, iron deficiency anemia (IDA) is considered directly (20%) and indirectly (50%) responsible for maternal death and feto-maternal morbidity [2,3]. According to National Family Health Survey-4 (NFHS-4), 45.7% (urban) and 52.1% (rural) antenatal women in India are anemic [4]. Women in the reproductive age frequently have anemia and iron deficiency due to menstrual loss. Frequently these women are already anemic by the time they get pregnant especially in under privileged population. Iron requirement during pregnancy is about 40–60mg/day. At least 40–60 mg of dietary iron is required to meet this demand since iron absorption is about 10%. Government of India recommends universal oral iron–folic acid supplementation for antenatal and post-partum women [5]. Studies on postnatal anemia are limited in India and the Government of India has been addressing the problem of anemia, through National Nutritional Anemia Control Programmed and adopting the National Iron Plus Initiative (NIPI), Ministry of Health and Family Welfare (MoHFW), Government of India [6]. Post-

partum anemia imposes a negative influence on the well-being of not only to the mother, but also on the interactive mother-baby relationship as it can lead to hemorrhage, puerperal sepsis, fatigue, lactation failure, varied maternal psychological and cognitive variations [7]. If iron stores are not restored soon after childbirth, the negative consequences may continue through other stages of the reproductive cycle, particularly among women consuming diets that are low in iron and who have short inter-pregnancy intervals (less than 18 months); leading to continued adverse maternal and infant outcomes [8].

Poor iron intake during pregnancy and blood loss at the time of delivery are the major causes of post-partum anemia. Iron can be administered either by oral or parenteral route. Although the best method of treating post-partum anemia has not been clarified, the current treatment guideline is oral iron supplementation and parenteral iron is to be considered only after a failed trial of oral iron [9]. Oral iron results in hemoglobin rise of 0.3–1.0gm/week [10]. However, the efficacy of oral irons may be questioned due to its faulty intake, faulty absorption, and adverse gastrointestinal side effects such as nausea, vomiting and constipation resulting in reduced treatment adherence and persistent anemia [11,12].

Parenteral iron may be preferred because the gastrointestinal side effects and absorption challenges of oral iron are mitigated. Moreover, in some non-obstetric literature, there is increasing interest in the use of intravenous (IV) iron for the primary treatment of iron deficiency anemia [13]. Some obstetricians in middle-eastern countries started using IV iron sucrose for treatment of anemic pregnant women. However, iron infusion can sometimes cause adverse or anaphylaxis reactions (especially high molecular weight iron dextran) which may be due to oversaturation of transferrin releasing free iron [14]. IV iron sucrose is a complex of polynuclear iron (III) hydroxide in sucrose. Following intravenous administration, it is dissociated by reticulo-endothelial system into iron and sucrose. It is quickly cleared from serum with terminal half-life of approximately 5–6 hours and, hence, is more rapidly available for erythropoiesis [15,16].

Aim: To compare the efficacy of single dose (500mg) intravenous (IV) iron sucrose and standard oral iron folic acid tablet (IFA) in post-partum anemic women.

Objective:

1. To estimate the rise in hemoglobin level after a single dose of IV iron sucrose (500mg) at six weeks among women with post-partum anemia attending at AGMC and GBP hospital.
2. To estimate the rise in hemoglobin level after standard oral IFA tablet at six weeks among women with post-partum anemia attending at AGMC and GBP hospital
3. To find out any significant difference at the rise in haemoglobin level between the IV iron sucrose (500mg) and standard oral IFA tablet groups

Materials & Methods:

Study type: Observational study

Study Design: Cross-sectional study

Study Setting: Department of Obstetrics and Gynecology, Agartala Government Medical College (AGMC) & Govind Ballabh Pant (GBP) Hospital

Study Period: 18 months

Study Population: Post-partum anemic women attending at AGMC and GBP hospital

Inclusion criteria: Booked post-partum women with moderate anemia

Exclusion criteria:

1. Any bleeding disorders
2. Hemoglobinopathies like thalassemia
3. Co-morbidities like, hypertension, diabetes, liver or kidney disease, thyroid disorder etc.
4. Known sensitivity to oral or injection form of iron
5. Indication of blood transfusion.

Sample size: Sample size calculated using the formula (N) = Here, P = Prevalence Q= 100-P L = 8 (Absolute allowable error at 95% confidence interval) 18 According to study by Selvaraj R et al35 prevalence of postpartum anemia is 76.2%. So, sample size (N) = =113 Adding 10% non-response rate, sample size = 113+11.3=124.3=125 So, final sample size was 125 in each group. Total sample size calculated was 250 in this study.

Study variables: 1. Independent: Age in years, parity, dietary pattern, gestational age, mode of delivery, baseline Hb and iron therapy (IV and Oral). 2. Outcome measures: Comparison of Hb% between IV iron sucrose and oral IFA tablet therapy after 6 weeks.

Study Tools: A predesigned proforma was used to collect data, it consists of: 1. Baseline characteristics of the participants 2. Outcome details

Recruitment and Study Procedure: Mothers who had delivered at AGMC and GBP hospital fulfilling the inclusion criteria was conveniently selected for participation in the study and a written informed consent was then obtained in either English or Bengali or Kokborok depending on the patient's

preference. Baseline information including hemoglobin level was collected from all participants in predesigned proforma. At the end of the interview, participants were given either 500mg elemental iron in the form of iron sucrose in 200 ml of 0.9% sodium chloride intravenously over 3 hours or were advised to take oral IFA tablet containing 19 100mg elemental iron twice daily as per the protocol. After discharge, follow-up was done after 6 weeks for blood hemoglobin level estimation.

Data analysis:

Data was checked for completeness and consistency. Collected data was analysed using SPSS version 21.0 software for windows. Descriptive statistics like mean, standard deviation, frequency, percentage were used to summarize the findings. To see the changes of Hb level in different time and comparing between the groups, Student's T test was applied.

Ethical issues: The protocol of the thesis was submitted to the Institutional Ethics Committee, Agartala Government Medical College & GBP Hospital, for processing and approval. The study was conducted after due approval from the committee

Result

Total 250 postpartum anemic women had participated in the study. Group A (N=125) were given injection iron sucrose and Group B (N=125) were given oral iron tablet.

The mean age of the participant was (24-34) years ± 4.09 ranging from (16 – 46) years.

Table 1: Age Comparison (N=250)

Variable	Groups of study	N	Mean	SD	P value
Age	Group A	125	24.58	5.238	0.43
	Group B	125	24.10	4.562	

Above mentioned table 1 shows the mean age in between the study groups is comparable as p value is 0.43 (not significant). The mean age is almost similar in both the groups (24.58 years and 24.10 years respectively).

Table 2: Age group distribution in the study group (N=250)

Study group	Age group (years) N (%)			P value
	Teenage pregnant	20-29 years	Above 29 years	
Group A	26 (20.8)	74 (59.2)	25 (20.0)	0.607
Group B	28 (22.4)	78 (62.4)	19 (15.2)	

Table 2 depicts teenage pregnancy more in group B (22.4%), and pregnancy among 29 years or above was more in group A (20%). However, the distribution of age group in the two study group is comparable with p value of 0.607 (insignificant).

Table 3: Diet pattern distribution among the study group (N=250)

Diet pattern	Study group		P value
	Group A (IV iron)	Group B (Oral iron)	
Mixed diet	122 (49.6%)	124 (50.4%)	0.622
Vegetarian	3 (75%)	1 (25%)	

Majority of the participants followed mixed diet pattern (246 out of 250). The distribution among the study group is comparable (p value 0.622).

Table 4: Distribution of parity status among study group (N=250)

Parity type	Study group		P value
	Group A (IV iron)	Group B (Oral iron)	
Single parity	72 (47.7%)	79 (52.3%)	0.365
Multi-parity	53 (53.5%)	46 (46.5%)	

Parity distribution among the group is comparable (p value 0.365), almost equally distributed.

Table 5: Mean comparison of period of gestation (POG), (N=250)

Group study	N	Mean POG at delivery	Std. Deviation	P value
Group A	125	38.54	1.84	0.803
Group B	125	38.61	2.18	

Table 5 shows that the mean gestational age of the participants was 38.54 ± 1.84 weeks and 38.61 ± 2.18 weeks respectively which is statistically not significant i.e. comparable with a p value of 0.803.

Table 6: Distribution of gestational age among the study group (N=250)

Gestational age (POG)	Study group		P value
	Group A	Group B	
Preterm delivery	25 (50%)	25 (50%)	
Term delivery	99(50.3%)	98 (49.7%)	
Postdated delivery	1(33.3%)	2 (66.7%)	0.844

Table 6 depicted that the distribution of the gestational status at delivery among the study groups was almost equally comparable but post-dated delivery was more among the group B participants (66.7% vs 33.3%). However, it is still comparable (p value 0.844).

Table 7: Comparison of mode of delivery (N=250)

Mode of delivery	Study group		P value
	Group A (IV iron)	Group B (Oral iron)	
Vaginal delivery	61 (50.4%)	60 (49.6%)	
Cesarean delivery	64 (49.6%)	65 (50.4%)	0.899

Both vaginal and cesarean delivery was comparable, almost equally distributed among the study group (p value 0.899).

Table 8: Mean Hb% among the group (N=250)

Hb%	Group study	N	Mean	Std. Deviation	P value
Baseline	Group A	125	8.557	1.0070	0.310
	Group B	125	9.040	0.6222	
After 6 weeks	Group A	125	10.583	0.8220	0.410
	Group B	125	10.500	0.8044	

Table 8 shows Hb% at baseline (8.5% and 9.0%) and after 6 weeks of therapy (10.58% and 10.50%) in the two groups. The Hb% was comparable between the groups (p value 0.310 and 0.410 at baseline and 6 weeks later).

Table 9: Mean changes Hb% (Hb% at 6 weeks – baseline Hb%)

Group study	Mean change	Mean changes/differences	P value
Group A	Hb% at 6 weeks – Hb% at baseline (within the group)	2.091 ± 0.8121	0.000
Group B	Hb% at 6 weeks – Hb% at baseline (within the group)	1.442 ± 0.7354	0.000
Mean changes of Hb% Between the group		P value – 0.000	

The mean changes of Hb% after the therapy, where it shows that the mean changes were more (2.091 ± 0.8121) in group A than group B (1.442 ± 0.7354). The changes from baseline to 6 weeks in group A was found to be statistically significant (p value 0.000) and the changes from baseline to 6 weeks in group B was also found to be statistically significant (p value 0.000).

Discussion

Treatment of post-partum anemia is very important to build up iron reserves in the puerperal, to have a better quality of life and to minimize incidence of anemia in next pregnancy. Although oral irons are the most convenient and affordable form of iron supplementation, parenteral irons are better tolerated than oral iron due to adverse gastrointestinal effects [17]. Irrespective of mode of delivery, blood loss is a contributing factor, with 5% of deliveries involving loss of more than 1 liter [18]. In healthy women after normal delivery, the prevalence of anemia is 14% in iron-supplemented women and 24% in non-supplemented women. In current study both vaginal delivery and caesarean delivery was comparable i.e almost equally distributed among the study group (p value 0.899) Table 7. The baseline mean Hb level in the oral iron therapy group was 9.04 ± 0.62 g/dl and in the injectable iron therapy group it was 8.55 ± 1.00 g/dl which are comparable i.e. not much differences (p value 0.310) Table 8. Almost two-third women belongs to 20-29 years of age pointing that most of them are entering their reproductive age with insufficient iron stores who is likely to succumb to increasing iron demands of pregnancy and with peripartum blood loss further depleting maternal iron reserves. Major causes of higher prevalence of anemia in India, is malnutrition, low dietary intake of iron and high prevalence of infections like malaria and hookworm infestations [19].

After 6 weeks of iron therapy, it was observed that the rise in Hb levels in the injectable iron group was from 8.55 ± 1.00 g/dl to 10.58 ± 0.82 g/dl, which was found to be statistically significant (p value 0.000). In oral group also there was a significant (p value 0.000) increase in Hb levels (from 9.04 ± 0.62 g/dl to 10.50± 0.80 g/dl) Table 8. Chaurasia Amrita et al [17] in their study had similar results after 6 weeks of iron therapy, achieving almost similar increase in Hb level (2.6 gm% and 2.8 gm% respectively, p>0.05) in both the modalities. Westad et al [20] while studying

128 postpartum anemic women also reported oral iron and intravenous iron to be equieffective treatments for correcting postpartum anaemia as there was no significant differences in the mean hemoglobin values in both the groups after 4 weeks (11.9g/100ml vs. 12.3g/100ml, p value 0.89). Becuzzi N et al [21] also support our results as they showed similar rise in mean Hb levels in both the groups (from 10.1 g/dl to 13.3 ± 0.83 g/dl in oral versus from 9.1 g/dl to 13.3 ± 0.84 g/dl in IV group, p value 0.68). Owing to intolerance to oral iron therapy, one should consider the use of iron infusion therapy. One disadvantage with IV iron sucrose regimen is the need of multiple infusions to deliver the required iron dose due to limited maximum permissible dose per week that required prolonged hospital stay. Administering higher single doses of iron sucrose makes it possible to overcome these challenges. On comparing the response to the two modalities of iron therapy we found that the mean changes of Hb after the therapy were more (2.091 ± 0.8121) in group A than group B (1.442 ± 0.7354), thus proving that IV iron was more effective than oral iron (p value 0.000) in correcting anemia. Similar to our study, Giannoulis et al [22] while comparing the efficacy of oral and intravenous administration of iron supplements for treating postpartum anemia found a significant difference in the increase of hemoglobin level (p value 0.0001) in between the two groups (increase of mean Hb level in IV group was 4.6 g/dl and in oral group it was 2.3 g/dl). Dede et al [23] also reported similar trend of responses in haemoglobin level both in intravenous iron sucrose and oral iron route (P<0.001). Similarly, Halimi S et al [24] in their study also concluded parenteral iron therapy in the form of iron sucrose to be a better choice to correct iron deficiency anaemia related to pregnancy as they observed rise in haemoglobin concentration from 9.20±1.69 to 12.65±1.06 g/dl in intravenous group as compare to 9.35±1.62 to 11.20±0.28 g/dl in oral group on day 30 after therapy.

However, in contrast to our study, Bhandal N et al [25] in their prospective randomised controlled trial reported that there was no significant difference in mean increase of Hb level at day 40 between the oral and IV iron therapy groups (Hb level increased from 7.3g/dl to 11.5g/dl with intravenous iron and from 7.5g/dl to 11.2g/dl with oral iron). Breymann C et al [26] also reported insignificant difference of efficacy between oral iron group and IV iron group after 6 weeks of iron therapy.

IV iron therapy also has a role in patients with refractory anaemia not responding to oral iron e.g. chronic infections, chronic kidney disease, and inflammatory bowel disease. This is especially important in low- resource countries with high prevalence of chronic diseases like TB and endemic malaria5. Intravenous iron–sucrose also undoubtedly allows some blood transfusion to be avoided in postpartum women, even though the need for blood transfusion is unquestionable in life threatening situations [19].

Limitations

1. As this is a hospital-based study, therefore may not represent the actual incidence of post- partum anemia in the general population.
2. Though the sample size was calculated statistically, it was a small sample size.
3. Due to unavailability of thalassemia screening tests in the institute, exclusion of thalassemia was based on patient's history.

Conclusion

There is a significant increase of mean hemoglobin level from baseline to post 6 weeks therapy in both the groups (in group A from baseline 9% to 10.58% and in group B from 8.5% to 10.50%). The mean changes both in between the group and within the group were also found to be significant. However, it was observed that the mean changes were more in the women treated with IV iron sucrose than the women treated with oral iron folic acid tablet. Given that postpartum injection of intravenous single high dose of iron sucrose is more effective than oral alternatives in raising hemoglobin level, we would advocate its use as the treatment of choice in moderate post-partum anemia. However, further studies are needed to determine its precise impact.

References

1. World Health Organization. Reduction of maternal mortality: a joint WHO/UNFPA/UNICEF/World Bank statement. World Health Organization 1999. https://apps.who.int/iris/handle/10665/42191. Accessed October 15, 2020.
2. Galloway R, Dusch E, Elder L, et al. Women's perceptions of Iron deficiency and anaemia prevention and control in eight developing countries. Soc Sci Med. 1982; 55(4):529–544.
3. Drukker L, Hants Y, Farkash R, et al. Iron deficiency anemia at admission for labor and delivery is associated with an increased risk for Cesarean section and adverse maternal and neonatal outcomes. Transfusion. 2015; 55(12):2799.
4. International Institute for Population Sciences (IIPS) and ICF. National Family Health Survey (NFHS-4), 2015-16: India. Mumbai: IIPS 2017.
5. Radhika AG, Sharma AK, Perumal V, Sinha A, Sriganesh V, Kulshreshtha V, Kriplani A. Parenteral Versus Oral Iron for Treatment of Iron Deficiency Anaemia During Pregnancy

and post-partum: A Systematic Review. J Obstet Gynaecol India. 2019; 69(1):13-24.
6. WHO. Guideline: Daily iron supplementation in postpartum women. Geneva, World Health Organization 2016. (http://www.who.int/nutition/publications/micronutrients/guidelines/daily iron_supp_postpartum_women/en). Accessed on December 12, 2020.
7. Milman N. Post-partum anaemia I: definition, prevalence, causes and consequences. Ann Hematol. 2011; 90(11):1247–53.
8. King JC. The risk of maternal nutritional depletion and poor outcomes increases in early or closely spaced pregnancies. J Nutr. 2003; 133(5):1732–6.
9. Munoz M, Pena-Rosas JP, Robinson S, et al. Patient blood management in obstetrics: management of anaemia and haematinic deficiencies in pregnancy and in the post-partum period: NATA consensus statement. Transfus Med 2018; 28:22–39.
10. Cook JD. Iron-deficiency anemia. Baillieres Clin Haematol. 1994; 7(4):787–804.
11. Goodnough LT, Nemeth E, Ganz T. Detection, evaluation, and management of iron restricted erythropoiesis. Blood 2010; 116:4754–61.
12. Peyrin-Biroulet L, Williet N, Cacoub P. Guidelines on the diagnosis and treatment of iron deficiency across indications: a systematic review. Am J Clin Nutr 2015; 102:1585–94.
13. Petewusnyk G, Huch R, Huch A, Breymann C. Parenteral iron therapy in obstetrics: 8 years' experience with iron-sucrose complex. Br J Nutr. 2002; 88:3–10.
14. Camaschella C. New insights into iron deficiency and iron deficiency anemia. Blood Rev 2017; 31:225–33.
15. Silverstein SB, Rodgers GM. Parenteral iron therapy options. Am J Hematol. 2004; 76:74–8.
16. Khalafallah AA, Dennis AE. Iron deficiency anaemia in pregnancy and postpartum: pathophysiology and effect of oral versus intravenous iron therapy. J Pregnancy. 2012; 2012:630519.
17. Chaurasia A, Singh N, Gupta V, Gupta B. A prospective study comparing the efficacy of oral iron, intra-venous Iron sucrose and Ferric-carboxy-maltose in postpartum anemia. Int J Med Res Health Sci. 2016;5:107-11
18. Kotto-Kome AC, Calhoun DA, Montenegro R, Sosa R, Maldonado L, Christensen MD. Effect of administering recombinant erythropoietin to women with postpartum anemia: a meta-analysis. J Perinatol 2004;24:11–5
19. Vijayalakshmi S, Mahendra G, Ravindra S. Pukale, Rajkumari Linthoingambi. "Intravenous Iron versus oral Iron Therapy in Postpartum Anaemia in Rural India". Journal of Evolution of Medical and Dental Sciences 2015;4:1666-71
20. Westad S, Baker B, Salvensen KA. A 12 week randomized study compared intravenous ferrous sucrose versus oral ferrous sulfate for treatment of postpartum anemia. Acta Obstet Gynecol Scand 2008;87:916–17
21. Becuzzi N, Zimmermann R, Krafft A. Long-term efficacy of postpartum intravenous iron therapy. Biomed Res Int. 2014;2014:815437
22. Giannoulis C, Daniilidis A, Tantanasis T, Dinas K, Tzafettas J. Intravenous administration of iron sucrose for treating anemia in postpartum women. Hippokratia. 2009;13:38-40
23. Dede A, Uygur D, Yilmaz B, Mungan T, Ugur M. Intravenous iron sucrose complex vs. oral ferrous sulfate for postpartum iron deficiency anemia. Intl J Gynecol Obstet. 2005; 90:238-39.
24. Halimi S, Halimi SMA, Shoaib M. Oral versus parenteral iron therapy for correction of iron deficiency anaemia in pregnancy. Gomal J Med Sci. 2011;9(1):3-5
25. Bhandal N, Russell R. Intravenous versus oral iron therapy for postpartum anemia. BJOG 2006; 113:1248–52.
26. Breymann C, Gliga F, Bejenariu C, Strizhova N. Comparative efficacy and safety of intravenous ferric carboxymaltose in the treatment of postpartum iron deficiency anemia. Int J Gynaecol Obstet. 2008;101(1):67-73.