International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Thobbi VA et al. Int J Reprod Contracept Obstet Gynecol. 2020 Sep;9(9):3852-3857
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20203495

Original Research Article

A comparative study of efficacy, safety and compliance of oral iron versus intravenous iron sucrose in treatment of iron deficiency anaemia of pregnancy

Vidya A. Thobbi, Zeba Naz M. Bijapur*

Department of Obstetrics and Gynecology, Al-Ameen Medical College, Vijayapur, Karnataka, India

Received: 23 July 2020
Accepted: 29 July 2020

***Correspondence:**
Dr. Zeba Naz M. Bijapur,
E-mail: zebabijapur99@gmail.com

ABSTRACT

Background: Iron deficiency anemia is the most common form of anemia and nutritional disorder worldwide. Oral iron therapy and blood transfusion has many drawbacks like noncompliance and risk of transmittable infections and transfusion reaction. The modern alternative therapy is treatment with intravenous iron. Present study compares the efficacy, safety and tolerability between intravenous iron sucrose and oral iron in iron deficiency anemia during 20-36 weeks of pregnancy.
Methods: It was a randomized controlled study between December 2017 to September 2019. 200 patients attending antenatal OPD in Al Ameen Medical College, with haemoglobin levels between 7-9.9 gm/dl and serum ferritin of <15 ng/ml were enrolled. In intravenous group, 200 mg iron sucrose in 100ml normal saline was infused alternate day till the required dose was met. The oral group received 200 mg of oral iron ascorbate along with folic acid 1.5 mg per day for 6 weeks. Treatment efficacy was assessed by Hb and serum ferritin after 3 and 6 weeks.
Results: Out of 200 patients, an increase in Hb was observed in both groups, rising from 9.7 g/dl to 10.3 g/dl and 10.9 g/dl after 3 weeks and 6 weeks respectively in oral group and from 8.6 g/dl to 9.8 g/dl and 10.8 g/dl after 3 weeks and 6 weeks respectively in intravenous group. Similar results were seen in ferritin levels. Rise in Hb and ferritin levels were greater in intravenous group than in oral group.
Conclusions: Intravenous iron sucrose appears to be a better treatment option in comparison with oral iron, without serious side effects, better compliance and improved efficacy in correction of anaemia of pregnancy.

Keywords: Ferrous ascorbate, Haemoglobin, Intravenous iron sucrose, Iron deficiency anaemia, Micronutrients deficiency

INTRODUCTION

The importance of anaemia as a major public health problem is widely recognised throughout the world. In pregnancy it is associated with a number of maternal and foetal complications. The women's reserve to tolerate bleeding either during or after pregnancy is decreased and makes prone to infections.[1]

According to World health organisation statistics, anaemia is seen in 41.8% of pregnant women worldwide.[1] The condition is prominent in Southeast Asian countries where about half of all global deaths are due to anaemia in South Asia. WHO has estimated that prevalence of anaemia in developed and developing countries in pregnant women is 14% and 51% respectively and 65 to 75% in India.[2,3] India contributes to about 20% of maternal deaths directly due to anaemia.[4] In India, there is a marginally decrease in prevalence of anaemia in pregnant women from 58% in NFHS-3 (National Family Health Survey-2005-06) to 50% in NFHS-4 survey (2015-16).[5]

Among the various causes of anaemia in women like poor nutrition, malaria, infections and chronic infections, iron deficiency anaemia is the most common type of anaemia, primarily due to their recurrent menstrual loss and secondarily due to poor supply of iron in the diet.[6] During pregnancy anaemia is common due to increase in demand of iron for growing foetus and placenta; increase in red cell mass, which is further aggravated with other factors like early age of childbearing, repeated pregnancies, short inter delivery intervals and poor access to antenatal care and supplementation.[7] It impairs the oxygen delivery through the placenta to the foetus and interferes with the normal intrauterine growth leading to foetal loss and perinatal deaths. It causes increased preterm labour (28.2%) and low birth weight, possibly placental abruption, preeclampsia (31.2%), maternal sepsis and increased peripartum blood loss.[8,9]

Hence anaemia continues to take a heavy toll of maternal lives in India either directly or indirectly as a consequence like cardiac failure, haemorrhage, infections, preeclampsia, and puerperal sepsis.

Over the past years, various oral, intramuscular and intravenous preparations of iron have been used for the correction of IDA in pregnant patients. The mainstay treatment of iron deficiency anaemia is oral iron replacement because of its safety, and cheap cost.[10]

The Indian market is abundant in a variety of oral iron preparations like ferrous sulphate, ferrous fumarate, ferrous succinate, ferrous gluconate, ferrous poly maltose, carbonyl iron and parenteral preparations like iron dextran, iron gluconate, iron sorbitol citric acid and iron hydroxide-sucrose.[11]

The major problem with oral iron therapy in its classic ferrous form is the poor tolerability. The most common complaints are nausea, abdominal pain, diarrhoea and constipation. Ferrous iron is best absorbed on an empty stomach, but this also increases the complications due to increased amounts of free iron in the GIT.

Further, food decreases the bioavailability of ferrous salts, leading to poor efficacy.[12] Conventional ferrous salts increase the susceptibility of the atherogenic lipoproteins to oxidation. This increase in the free radicals could lead to pre-eclampsia and pregnancy induced hypertension.

Intravenous iron has reduced usage as it can lead to severe consequences. Iron sucrose complex (ISC) is a relatively new drug, used intravenously for the correction of IDA. Iron sucrose complex is a widely used and safe molecule, which has become major interest to prevent iron deficiency anaemia.[13]

Furthermore, research was needed more insight on this topic, in this context, an attempt has been made in this study to compare the efficacy, safety and patient acceptability of oral iron formulation and intravenous iron sucrose during 20 to 36 weeks of pregnancy.

METHODS

Patients between 20 to 36 weeks of pregnancy with haemoglobin level between 7 to 9.9gm/dL who attended obstetrics and gynecology department of Al-Ameen Medical College hospital, Vijyapur were taken for consideration for the study between December 2017 and September 2019. A total of 200 (100 per arm) cases were considered for the present study. Among patients enrolled for study, 198 patients completed the study, 1 patient had an IUD in the intravenous group and 1 patient delivered pre term in oral group.

Inclusion criteria

Inclusion criteria of this study were pregnant women of 20-36 weeks of gestational age between haemoglobin level 7 to 9.9 gm/dL and serum ferritin level <15 ng/ml were enrolled in the study.

Exclusion criteria

Exclusion criteria of this study were patients with severe or very severe anaemia (Hb <7 gm/dL) were excluded due to possible history of bleeding tendency, blood transfusion within the prior 120 days, allergic conditions or asthma and acute inflammatory state.

In the oral group (Group A): The patients received two tablets of oral iron (ferrous ascorbate containing 100 mg of elemental iron per day with 1.15 mg of folic acid with zinc 22.5 mg) for 3 weeks on an empty stomach either 2h before or after their meals. Patients were told to carefully note treatment compliances on a calendar provided for that purpose. Women were asked to bring back empty packs and were asked about intake of tablets and the colour of the stools to ensure that they consumed the tablets and to continue for another 3 weeks.

In the intravenous group (Group B): The total iron sucrose dose to be administered was calculated from the following formula;

Total dose required = weight in kg × (target Hb in g/L - actual Hb in g/L) × 0.24 + 500 mg. rounded up to the nearest multiple of 100 mg.[14]

Target haemoglobin in g/L set at 110 g/L because of physiologic haemodilution during pregnancy. Actual haemoglobin in g/L: patient's haemoglobin level on inclusion.

This dose of iron sucrose complex was administered as 200 mg (elemental iron) in 100 ml normal saline intravenously over 20 to 30 minutes daily up to the total dose. No test dose was given. This treatment was supplemented with 5 mg of oral folic acid daily for 4

weeks to prevent an eventual folic acid deficiency and to eliminate the influence of such a deficiency on the results. Additional oral administration of iron was excluded during the 6 weeks of study.

The two groups were monitored both clinically, biologically and adverse reaction linked with it. Biologic monitoring was carried out on inclusion (day 0) in addition to the data required at the start of the study.

After 3 weeks, haemoglobin and serum ferritin levels were repeated in both groups. And again, after 6 weeks from the start of study, haemoglobin and serum ferritin were repeated.

Statistical analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi square test for association, Unpaired t-test, ANOVA test were used to compare the means. Data were analyzed using SPSS software v.23.0 and Microsoft office 2007.

RESULTS

Majority of patients 106 (53.5%) were between 21 to 25 years of age. 73% were multigravidas and 26.8% were primigravida. Non vegetarians consist of 68.7% of cases. The mean gestational age at which patients were found to be anaemic and included in this study was 30 weeks in the IV group which was significantly higher than 25 weeks in the oral group. Out of 99 patients, 52 (52.5%) patients belonged to 31-34 weeks of gestational age in the IV group, whereas only one third 16 (16.2%) comprised the oral group. In the oral group 43 (43.4%) patients were of 21-25 weeks of gestational age, on the other hand only 10 (10.1%) patients belonged to 21-25 weeks of gestation.

Among the intravenous group 43 patients (21.7%) needed 4 doses of 200 mg iron sucrose in 100 ml normal saline, 36 patients (18.2%) and 20 patients needed 3 doses according to their individual requirement.

Table 1: Change in mean parameters between study groups.

Treatment	Parameter	Pre treatment		Post treatment (3 weeks)		Post treatment (6 weeks)		p value
		Mean	SD	Mean	SD	Mean	SD	
I.V.	Hb	8.6	0.9	9.8	1.0	10.8	1.3	<0.001*
	Sr Ferritin	15.1	22.2	65.0	41.3	108.2	74.1	<0.001*
Oral	Hb	9.7	1.0	10.3	1.0	10.9	1.1	<0.001*
	Sr Ferritin	9.9	5.9	27.5	17.9	43.7	25.5	<0.001*

Note: * significant at 5% level of significance (p<0.05).

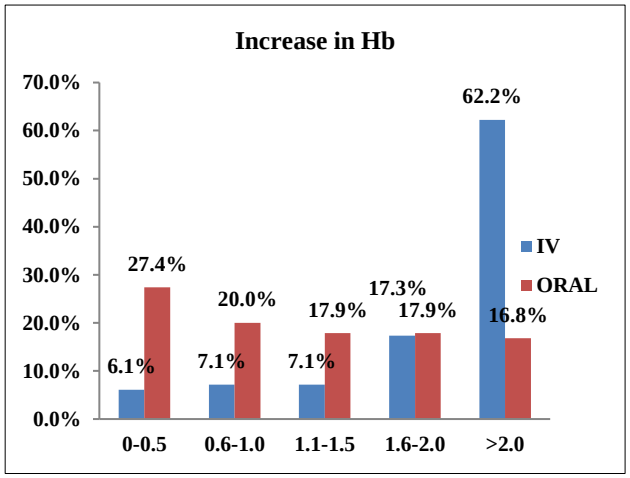

Figure 1: Increase in Hb between study groups.

Table 1 show that the there is significant post treatment increase in mean haemoglobin and serum ferritin from pre-treatment. The mean change in the Hb 6 weeks post treatment was 2.2 and 1.2 in IV and oral groups respectively. While that was 93.0 and 35.3 in serum ferritin 6 weeks post treatment in IV and oral groups respectively.

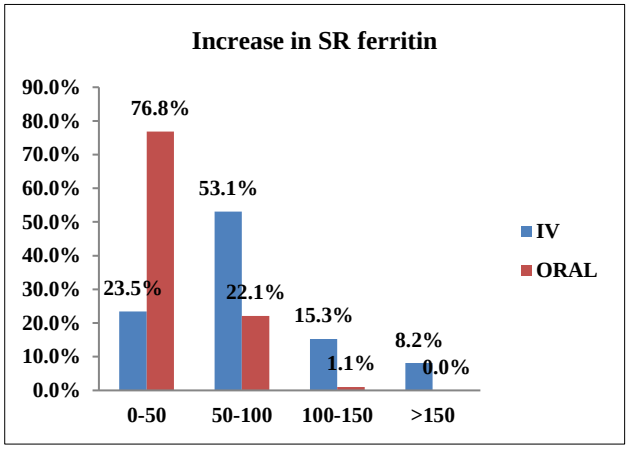

Figure 2: Increase in Sr Ferritin between study groups.

The rise of Hb being approximately being 1 gram every 3 weeks in IV group, while in the oral group, the rise was 0.6 grams every 3rd week. This shows that although both the groups had a significant rise, but the rise in IV group was significantly higher compared to the oral group.

According to Figure 1, it was evident that 35.8% of women who took oral iron showed an increase in Hb of 1.1 to 2 gm %, where as 62.2% women in the IV group showed a greater improvement of > than 2 gm % Hb and such a rise was seen in only 16.8 % of the oral iron group. The differences in the responses were highly significant (p< 0.001).

In the Figure 2, it was found that, out of 99 patients treated with oral iron, 76 patients (76.8%) showed an increase in serum ferritin levels up to 50 ng/ml and only 1 patients (1.1%) had increase in serum ferritin between 100 to 150 ng/ml whereas in the I.V. group 53 patients (53.1%) showed increase in serum ferritin levels between 51 to 100 ng/ml. 15 patients treated with I.V. iron (15.3%) had increase in serum ferritin by 101 to 150 ng/ml and 8 patients (8.2%) had increase in serum ferritin by more than 150 ng/ml and none of the patients in orally treated group had any rise in serum ferritin levels >150 ng/ml. The differences in the responses were significant (p< 0.001).

Table 2: Side effects between study groups.

Side effects	I.V.	Oral
Diarrhoea	0	2
Gastritis	0	2
Nausea	0	6
Vomiting	0	3
Pain	3	0
Burning	2	0
Swelling	1	0

Table 2 represent the side effects between study groups. The oral group reported more side effects as compared to the IV group. Maximum number of patients 6% complained of nausea in the oral group. 3% complained of vomiting and 2 % each complained of diarrhoea and gastritis. 3% in the IV group complained of pain and only 2% and 1% each of the same group complained of burning and swelling respectively.

DISCUSSION

Present study observed that parentally administered iron-sucrose elevates haemoglobin and restores iron stores better than oral iron during the treatment of iron deficiency anaemia in pregnancy. The mean changes in haemoglobin and ferritin levels throughout the treatment were significantly higher in the intravenously administered iron group than in the orally administered iron group. In clinical experience, iron sucrose has been approved for use in 54 countries as hematinic therapy for variety of disorders associated with pregnancy and during the post-surgical period.[14]

In a study 500 patients received 200 mg ferrous sucrose twice per week to a target of Hb of 11 g/dl or for a maximum of 4 weeks.[13] Anaemia was corrected in all patients, with a mean increase in Hb of 1.9 g/dl and significant increases in mean corpuscular volume and mean corpuscular Hb. In this study Mean increase in Hb of 1.1 to 2 gm % in oral group, whereas the I.V iron sucrose group showed a greater improvement of > than 2 gm %.

All Momen et al reported intravenous treatment resulted in higher haemoglobin levels in shorter periods compared with the oral treatment group (mean 6.9 versus 14.9 weeks). In their study, however, 30% of the patients had poor compliance with oral treatment whereas only 14% in the oral group in this study took tablets irregularly; otherwise the compliance was excellent with ferrous fumarate.

Ferrous sucrose appears to be effective because it is rapidly removed from the plasma and used for erythropoiesis.[16] After a bolus of saccharated iron, plasma levels peak at 10 minutes. 24 hours after administration, the plasma level is negligible, indicating rapid incorporation. This has been shown by positron emission tomography studies, which show immediate incorporation into the bone marrow while the plasma levels fall.[17] These studies, mostly investigating renal patients with severe IDA, have shown that 70-97% of the iron is used for erythropoiesis with only 4-6% elimination.

In present study, I.V. ferrous sucrose was well tolerated and not associated with any serious adverse effects and was only associated with burning, pain and swelling at the injection site in 6 patients. It was reduced by elevation of the limb, thrombophobe ointment, ice pack and by injecting 5 cc of normal saline or distilled water at the end of I.V. sucrose infusion. This finding is supported by previous larger studies that have investigated the safety profile of intravenous ferrous sucrose both during pregnancy and in the postpartum period.[18]

In this study, compliance with oral treatment was good. This contrasts with compliance findings described in other studies.[19] Singh et al, compared 50 women treated with I.V. iron polymatose complex to 50 women treated with oral iron fumarate, and found that I.V. treatment resulted in significantly higher rates of increased hemoglobin, as well as higher levels of hemoglobin.[20] Whereas in this study the increase in levels of Hemoglobin after 4 weeks of treatment was same in both IV and oral group. Singh et al also reported significantly higher levels of serum ferritin (p<0.001) with no reports of any adverse reactions in the IV group, compared to the oral group which was similar to this study.

Dede et al showed that I.V. iron therapy with an iron sucrose complex significantly increased serum ferritin levels within a short time with fewer adverse effects than oral iron therapy in women with post-partum iron deficiency anemia.[21] The results of this study were similar to this study.

The USA, Food and Drug Administration (FDA) approved the use of iron sucrose for the treatment of iron deficiency anaemia in chronic hemodialysis patients since November 2000. The Indian FDA gave their approval for the use of iron sucrose in pregnancy and the postpartum period in 2005.[14] Many studies of the use of iron sucrose during pregnancy and the puerperium, have demonstrated a high level of efficacy and safety.

CONCLUSION

Iron deficiency anaemia is the most common form of anaemia and the most common nutritional disorder in the world. The consequences of IDA include increased maternal and perinatal morbidity and mortality including intrauterine growth restriction, preterm birth and postpartum haemorrhage and their attended sequel. Traditional iron therapy which is based on either oral administration of iron or blood transfusion has many drawbacks like non-compliance and risk of infection, immunologic impact and transfusion reaction. Intravenous iron sucrose tolerance seems to be excellent in this study without serious adverse effects and associated with only minor side effects like pain, burning and swelling at the injection site. I.V. iron sucrose complex (ISC) may be safe and effective in the treatment of iron deficiency anaemia during pregnancy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Anemia during pregnancy. Available at: https://www.nhp.gov.in/disease/gynaecology-and-obstetrics/anaemia-during- pregnancy-maternal-anemia. Accessed on 27th July 2020.
2. Iron deficiency anaemia: assessment, prevention and control. A guide for programme managers. 2001. Available at: https://www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/WHO_NHD_01.3/en. Accessed on 27th July 2020.
3. Kalaivani K. Prevalence and consequences of anemia in pregnancy. Indian J Med Res. 2009;130:627-33.
4. Low MS, Grigoriadis G. Iron deficiency and new insights into therapy. Med J Aust. 2017;207(2):81-7.
5. International Institute for Population Sciences-IIPS/India and ICF. National Family Health Survey NFHS-4, 2015-2016. Mumbai, India: India; IIPS; 2017.
6. Malagi U, Reddy M, Naik R. Evaluation of national nutritional control programme in Dharward (Karnataka). J Hum Ecol. 2006;20(4):279-81.
7. Helping hematologists conquer blood diseases worldwide. Available at: https://www.hematology.org/education/patients/anemia. Accessed on 27th July 2020.
8. Yip R. Prevention and control of iron deficiency: policy and strategy issues. The J Nutrit. 2002;132(4):802S-5S.
9. Kotecha PV. Micronutrient Malnutrition in India: Let Us Say "No" to it Now. Indian J Community Med. 2008;33(1):9-10.
10. Bayoumeu F, Subiran-Buisset C, Baka NE, Legagneur H, Monnier-Barbarino P, Laxenaire MC. Iron therapy in iron deficiency anemia in pregnancy: intravenous route versus oral route. Am J Obstet Gynecol. 2002;186:518-22.
11. Sharma JB, Soni D. Oxidative stress in pregnancy - Role of iron therapy: oral iron therapy and risk of free radicals. Obs Gynac. 2001:6(12):705-6.
12. De Gruchy's. Clinical hematology in medical practice. Chapter 3 hypochromic anaemia: iron deficiency and sideroblastic anaemia. 5th edition; 1989:54.
13. Perewusnyk KG, Huch R, Huch A, Breymann C. Parenteral iron therapy in odstretics: 8 years experience with iron-sucrose complex. Br J Nutr. 2002;88:3-10.
14. Divakar H, Manyonda I. Battling with rising prevalence of gestational diabetes mellitus: screening and diagnosis. Int J Infertil Fetal Med. 2011;2:96-100.
15. Al-Momen AK, al-Meshari A, al-Nuaim L, Saddique A, Abutalib Z, Khashogi T, et al. Intravenous iron sucrose complex in the treatment of iron deficiency anemia during pregnancy. Eur J Obstet Gynecol Reprod Biol. 1996;69:121-4.
16. Bhandal N, Russell R. Intravenous versus oral iron therapy for postpartum anemia. An Int J Obstet Gynecol. 2006;113:1248-52.
17. Beshar S Lundqvist H, Sundin J, Lubberink M, Tolmachev V, Valind S, Antoni G, et al. Pharmacokinetics and red cell utilization of iron (III) hydroxide-sucrose complex in anemic patients: a study using positron emission tomography. Br J Haematol. 1999;104:296-302.
18. Breymann C. Modern therapy concepts for severe anaemia in pregnancy and postpartum. Prevention and management of anemia in pregnancy and postpartum hemorrhage. Schellenberg Druck AC, Zurich, Switzerland. 1998:107-122.
19. Hallberg L, Ryttinger L, Solvell. Side effects of oral iron therapy. A double-blind study of different iron compounds in tablet form. Acta Mdd Scand Suppl. 1996;459:3-10.
20. Singh K, Fong YF, Kuperan P. A comparison between intravenous iron polymaltose complex (Ferrum Haussmann) and oral ferrous fumarate in the

treatment of iron deficiency anemia in pregnancy. Eur J Hematol. 1998;60:119-24.
21. Dede A, Uygur D, Yilmaz B, Mungan T, Ugur Zekai M. Intravenous iron sucrose complex vs. oral ferrous sulfate for postpartum iron deficiency anemia. Int J Gynecol Obstet. 2005;90:238-9.

Cite this article as: Thobbi VA, Bijapur ZNM. A comparative study of efficacy, safety and compliance of oral iron versus intravenous iron sucrose in treatment of iron deficiency anaemia of pregnancy. Int J Reprod Contracept Obstet Gynecol 2020;9:3852-7.