

DOI: <http://dx.doi.org/10.18203/2320-1770.ijrcog20183771>

## Original Research Article

# Comparative study of oral iron (ferrous sulphate) versus intravenous (iron sucrose) therapy in treating iron deficiency anaemia in puerperium

Soniya Vishwakarma\*, Rajani Rawat, Pragati Dwivedi, Vaibhav Kanti

Department of Obstetrics and Gynecology, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, Uttar Pradesh, India

**Received:** 15 July 2018

**Accepted:** 06 August 2018

### \*Correspondence:

Dr. Soniya Vishwakarma,

E-mail: soniyaramesh17@gmail.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** Iron deficiency anaemia is one of the major morbidities during post-partum period. The aim of this study was to compare the efficacy, safety and compliance of intravenous iron sucrose complex with oral Iron therapy in treatment of postpartum anemia.

**Methods:** 100 postpartum anaemic patients randomized into two groups. In Group I oral iron ferrous sulphate tablets twice daily and in group II 200 mg of iron sucrose on every alternate day up to total calculated dose for 6 weeks. Hemoglobin and serum ferritin were measured on day 0, 2 week and 6 weeks. The side effects in both groups were noted.

**Results:** Majority of patients are multiparous, illiterate and belonged to low socioeconomic. Mean baseline hemoglobin in oral group (Group I) was  $7.90 \pm 0.905$  gm/dl and in i/v group (Group II) was  $7.81 \pm 0.849$  gm/dl. There was significant rise in hemoglobin and hematocrit in both groups after 2 weeks and 6 weeks. However, efficiency of iron sucrose was greater in between the groups (p value=0.0000). There was a rise in serum ferritin to  $58.35 \pm 14.537$  µg/L from  $8.30 \pm 1.461$  µg/L after 6 weeks in intravenous group with shorter duration of treatment indicating a high efficacy (p<0.001). Intravenous iron sucrose did not result in any serious adverse reactions.

**Conclusions:** This study illustrates clearly that intravenous iron sucrose complex is safe, convenient and effective in postpartum anemic women as compared with oral ferrous sulphate.

**Keywords:** Intravenous iron sucrose, Oral ferrous sulphate, Post-partum anemia

### INTRODUCTION

The postpartum period is a wonderful yet challenging time for mothers experiencing profound physical and mental challenges. Tiredness is expected during postpartum period; however, mother is concerned when their fatigue is disabling, stops them performing normal activity. Fatigue is usually attributed to anaemia. Iron deficiency anemia is the most common form of anaemia the world over and also the most common nutritional

disorder in the world. The overall mean global figure for the incidence of gestational anemia is 25%.<sup>1</sup> WHO (World Health Organization) has estimated that prevalence of anemia in developed and developing countries in pregnant women is 14% in developed and 51% in developing countries and 65 to 75% in India.<sup>2</sup>

As per WHO, anaemia during pregnancy is defined as hemoglobin concentration of less than 11 gm% (7.45 mmol/L) and hematocrit less than 33%.<sup>3</sup> Postpartum

anemia has been associated with postpartum depression, stress, anxiety, cognitive impairment.<sup>4</sup> Poor mother-infant interactions and delayed infant development.<sup>5</sup>

Management of postpartum iron deficiency anaemia (PPIDA) includes dietary modifications along with Pharmacotherapy (iron supplements). Dietary modification involves increasing total calorie intake along with increase in iron rich food stuffs such as spinach, green leafy vegetables, cereals, pulses (especially sprouts pulses), and jiggery.

The first choice in the treatment of iron deficiency anemia for almost all patients is oral iron replacement because of its effectiveness, safety, and lower cost. The major problem with oral iron therapy in its classic ferrous form is poor tolerability and up to 40% adverse reaction rate.<sup>6</sup> The most common complaints are nausea, abdominal pain, diarrhea and constipation. Parenteral iron administration by intramuscular injection is a painful alternative with a variable efficacy. Iron sucrose complex (ISC) is a relatively new drug, which is used intravenously for the correction of IDA.<sup>7</sup> Iron sucrose complex is a widely used in European countries and safe molecule, which has become major interest to prevent iron deficiency anemia. The objective of this study is to compare the efficacy, safety and tolerability of intravenous iron sucrose with that of oral ferrous sulphate in subjects who displays post-partum iron deficiency anaemia.

## METHODS

A prospective interventional study was carried out in Department of obstetrics and Gynaecology, Uttar Pradesh rural institute and medical sciences, Saifai, Etawah from May 2013 to August 2014. Study was conducted on 100 postpartum anaemic women.

### Inclusion criteria

- Post-partum patients age between 18-45 year.
- Hemoglobin level 6-9 gm/dl.
- No associated complicated factor.
- Demonstrate willingness to comply research protocol.

### Exclusion criteria

- Postpartum women with hemoglobin level < 6gm/dl and >10 gm/dl.
- Any medical disorder like tuberculosis, thyroid disease, diabetes, liver or kidney disease.
- Known hypersensitivity to oral or iv iron.
- Any obstetrical complicating factors like pre-eclampsia/ eclampsia.
- h/o of chronic severe bleeding.
- Hemochromatosis or iron storage metabolic disorder.

All patients were enrolled after a duly signed informed consent. 100 patients were recruited based on inclusion and exclusion criteria. A thorough history followed by clinical examination of all cases was carried out and antenatal investigations as per present institution protocol were undertaken. The cases were randomly divided into two groups of 50 each by randomly computers generated numbers.

Group I was given oral ferrous sulphate tablets containing 60mg of elemental iron twice daily for 6 weeks postpartum period

Group II In the intravenous group, the dose of total iron sucrose 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 8.

This dose of iron sucrose complex was administered as 200 mg (elemental iron) in 100 ml 0.9% sodium chloride intravenously over 20 to 30 min on alternate days 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.

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

The measurements recorded were: hemoglobin %, complete blood count, RBC indices (MCV, MCH, MCHC,) serum ferritin, reticulocyte count, peripheral smear for type of anemia. The results were recorded on day 1st day i.e. baseline, at 2 weeks and at 6 weeks after starting the treatment. The study results were expressed as mean±standard deviation. Further, to test the significance of difference between oral and I.V. mode of treatment in case of all parameters, student T test was used to verify the statistical significance. P-value <0.05 was taken as level of statistical significance.

## RESULTS

**Table 1: Distribution of patient according to age.**

Age in years	Oral iron group		i/v iron sucrose group	
	N=50	%	N=50	%
19-24	24	48	19	38
25-29	19	38	21	42
30 and above	7	14	10	20
Total	50	100	50	100

The mean age in oral group (Group I) was  $24.98 \pm 3.915$  years and in i/v group (Group II) was  $25.92 \pm 4.208$  years. No statistical significance between two group (p value=0.546) (Table 1).

**Table 2: Distribution of patients according to education and socioeconomic status.**

Education	Oral		Iron sucrose		P value=0.716
	N=50	%	N=50	%	
Illiterate	18	36	15	30	
Primary school	20	40	20	40	
Middle school	6	12	10	20	
High school	5	10	3	6	
Graduate	1	2	2	4	
Total	50	100	50	100	
Socioeconomic status	N=50	%	N=50	%	P value=0.288
Upper	nil	nil	nil	nil	
Upper-middle	2	4	3	6	
Lower-middle	10	20	11	22	
Upper-lower	23	46	14	28	
Lower	15	30	22	44	
Total	50	100	50	100	

In both the groups, the majority of patients were illiterate or educated up to primary school and also mostly were belongs to upper lower and lower class of socio economic status. There was no statistical significance between two

groups with respect to educational qualification (p value=0.716) and socioeconomic status (p value=0.288) (Table 2).

No statically significant difference was observed between the oral iron group and i/v iron sucrose group for any characteristic i.e. booking status (p value=0.405), parity of patients (p value=0.288), breast feeding status (p value=0.541) in either group (Table 3).

**Table 3: Distribution of patients according to booking status, parity and breast feeding.**

Booking status	Oral group		Iron sucrose		P value=0.405
	N=50	%	N=50	%	
Unbooked	34	68	30	60	
Booked	16	32	20	40	P value=0.288
Total	50	100	50	100	
Parity	N=50	%	N=50	%	
P 1	9	18	8	16	
P2	22	44	15	30	
P3	14	28	16	32	
P4 or >	5	10	11	22	
Total	50	100	50	100	P value=0.541
Breast feeding status	N=50	%	N=50	%	
Yes	45	90	46	92	
No	5	10	4	8	P value=0.541
Total	50	100	50	100	

**Table 4: Mean baseline hemoglobin and hematocrit in oral and IV group.**

	Oral iron	i/v iron sucrose	Minimum	Maximum
	Mean	Mean		
Hemoglobin mg/dl	$7.90 \pm 0.905$	$7.81 \pm 0.849$	6	9
Hematocrit	$23.47 \pm 3.446$	$22.88 \pm 3.016$	14.1	31.4

**Table 5: Mean hemoglobin and hematocrit in oral and IV group at 2 weeks and 6 weeks of treatment.**

		Oral iron	i/v iron sucrose	P value
Mean hemoglobin	At 2 weeks	$8.65 \pm 0.849$	$9.88 \pm 0.760$	0.00
	At 6 weeks	$10.16 \pm 0.877$	$10.91 \pm 0.770$	0.00
Mean hematocrit	At 2 weeks	$25.04 \pm 3.207$	$22.88 \pm 3.016$	0.00
	At 6 weeks	$29.25 \pm 2.891$	$31.34 \pm 2.474$	0.00

Mean baseline hemoglobin in oral group (Group I) was  $7.90 \pm 0.905$  gm /dl and in i/v group (Group II) was  $7.81 \pm 0.849$  gm /dl and mean hematocrit was  $23.47 \pm 3.446$  (Group I) and  $22.88 \pm 3.016$  (Group II). There was significant rise in hemoglobin and hematocrit in both groups after 2 weeks and 6 weeks. However, efficiency of iron sucrose was greater as highly significant difference was noted in mean Hb at 2 weeks and 6 weeks between the groups (p value=0.0000) (Table 4 and 5). Mean baseline serum ferritin of oral group was  $9.04 \pm 2.144$  and of i/v group was  $8.30 \pm 1.46$  µg/dL. A

high statistically significant difference was observed between oral and i/v group with respect to 6 weeks post-partum (Table 6 and 7).

On comparing the Adverse Drug Effect, oral iron had a little higher rate; 50% of overall side effects in comparison to Iron Sucrose group 10 %. Gastro-intestinal complaints topped the list of ADE in oral iron group. Irons sucrose was associated with injection site reactions like mild rashes, swelling or itching. 4%. Headache, muscle cramps and systemic reactions like fever,

dizziness were nil with oral irons but were noticed in parenteral groups i.e. 2% (Table 8).

**Table 6: Baseline serum ferritin of oral and IV group.**

Serum ferritin	Oral iron group		i/v iron sucrose group	
	n = 50	%	n = 50	%
5.6-8.7	25	50	34	68
8.8-11.9	20	40	16	32
12.0-15.0	5	10	nil	nil
Total	50	100	50	100
	Mean ferritin= 8.04±2.144		Mean ferritin= 8.30±1.461	

**Table 7: Comparison of mean serum ferritin between oral and IV group.**

	Baseline	At 6 weeks
Oral group	8.04±2.144	23.88±5.339
i/v group	8.30±1.461	58.35±14.537
P value	0.146	0.00

**Table 8: Adverse drug effects in Oral and IV group.**

	Oral iron group		i/v iron sucrose	
	N=50	%	N=50	%
Nausea, vomiting	3	6	nil	nil
Abdominal pain	1	2	nil	nil
Constipation	10	20	nil	nil
Diarrhea	1	2	nil	nil
Injection site reaction	nil	nil	2	4
hypotension	nil	nil	nil	nil
Dizziness	nil	nil	1	2
Metallic taste	6	12	1	2
Loss of appetite	5	10	1	2
No side effect	24	48	45	90
Total	50	100	50	100

## DISCUSSION

Iron deficiency anemia in pregnancy and postpartum period is a public health problem especially in developing countries. Anemia in pregnancy and in postpartum period is significantly associated with both fetal and maternal morbidity. 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.

Out of 100 patients 83 patients was in between 19-29 year of age. Mean age in oral group was 24.98±3.915 year and 25.92±4.208 in i/v iron group. The majority of patients were unbooked 64 % because of illiteracy and low socioeconomic status. In present study maximum

patients (72.5%) were illiterate or educated up to primary school. The majority of patients were multiparous 83%, mostly were para 2 and para 3. Study by Bodnar et al, 44.2 % multiparous patient have postpartum anemia. This signifies that multiparity as an important risk factor.<sup>9</sup>

The objective of this study was that in postpartum anemia which treatment results in higher Hemoglobin concentrations and improved iron stores i.e. giving iron by Intravenous route in form of ferrous sucrose to women with or using standard treatment with oral iron. In present study Group I received oral ferrous sulphate 200 mg twice daily for 6 weeks and in Group II, Iron sucrose injection were given up to calculated dose on alternate day. Hemoglobin, Serum Ferritin (measure of iron stores) and other parameter were measured on day 0, 2 weeks and 6 weeks. There was a rise in mean hemoglobin in the Intravenous iron group from 7.81±0.849 g/dl to 9.88±0.760g/dl (p value < 0.001) after 2 weeks and 10.91± 0.770 after 6 weeks. Whereas mean hemoglobin in oral group changed from 7.90±0.905 g/dl to 8.65± 0.849 at weeks and 10.16±0.877 at 6 weeks. So, it is evident that there is statistically significant (p value <0.001) rise of hemoglobin level in both Intravenous iron group and oral group but i/v iron group has shorter duration of treatment.

Westad et al reported a similar rise in hemoglobin level from baseline of 6.5gm/dl to 11.9±1 gm./dl after 4 weeks of treatment with Intravenous Iron sucrose 600 mg in 59 postpartum patients.<sup>10</sup> In a similar study by Dede et al on 50 postpartum women there was a rise in hemoglobin level from baseline of 8.2±0.6 gm./dl to 12.5±1.6 gm./dl after 4 weeks.<sup>11</sup> Bayoumeu et al also reported rise in hemoglobin from 9.6±79gm/dl to 11.11±1.3 in Intravenous group and from 9.7±.5 to 11.0±1.25 in oral group at day 30.<sup>12</sup> However Bhandal N and Russel R on day 40 after treatment found no difference in hemoglobin levels between the two groups.<sup>13</sup> Verma S et al compared efficacy of injection iron sucrose at 7, 15 and 30 days.<sup>14</sup> They found that mean rise of Hb was significantly higher in intravenous iron sucrose group in 7 days.

In present study rise in mean hematocrit was observed from 23.47±3.446 to 25.04±3.207 at 2 weeks to 29.25±2.891 at 6 weeks in oral iron group. In i/v group rise in hematocrit 22.88±3.016 to 22.88±3.016 at 2 weeks to 31.34±2.474 at 6 weeks. There was more significant improvement noted in i/v group.

The increasing iron stores of the body as depicted by rising serum ferritin levels were much more promising with the parenteral (i/v) preparations. There was a rise in Serum ferritin to 58.35±14.537µg/L from 8.30±1.461µg/L after 6 weeks in Intravenous group with shorter duration of treatment indicating a high efficacy (p<.001). Whereas in oral group there was a rise from baseline of 8.04±2.144µg/L to just 23.88±5.339 µg/l in 6 weeks. In a study by Dede et al in 2004, I was shown in his study that intravenous 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.<sup>11</sup> Bhandal and Russel also reported a statistical significant increase in Serum ferritin levels from the baseline values of 13microgm/dl to 42.2microgm/dl on day 40 in Intravenous iron group.<sup>13</sup> Similar significant rise was observed by Breyman et al, Momen et al, Bayoumeu et al, and Giannoulis C et al with the iron sucrose group.<sup>12,15-17</sup> Giannouslos et al also showed Hb rise from 8.1 to 10.3 g/dL and Verma et al from  $7.42 \pm 1.04$  to  $9.8 \pm 0.76$  g/dL after iron sucrose infusion.<sup>14,17</sup>

Adverse drug effect noted more commonly in oral iron group in present study, most frequent are constipation 20%, metallic taste 12%, loss of appetite 10 %, nausea and vomiting 6 %. Very few side effects with i/v iron sucrose group like injection site reaction 4%, dizziness 2%.

Seid et al reported lower incidence of adverse effects in parenteral group than oral group, no serious reactions in either group.<sup>18</sup> Most common adverse effect in parenteral group was urticarial and in oral group was constipation. Wyck V et al reported higher incidence of skin problems like purities and rashes with parenteral iron although very mild and transient in nature.<sup>19</sup> Momen et al and Bhandal and Russel described gastrointestinal adverse effects with a frequency of up to 30% and 33% in women treated with oral iron.<sup>13,16</sup>

## CONCLUSION

Present study illustrate clearly that intravenous iron sucrose complex is safe, convenient and effective in postpartum anaemic women as compared with oral ferrous sulphate.

Increase in values of hemoglobin, hematocrit, reticulocyte count, serum ferritin, RBC indices coupled with no serious side effect with Iron Sucrose as compared with Oral Iron over a shorter period of treatment duration, makes it as a safe and effective alternative in the management of postpartum anaemia.

## Recommendations

Authors recommend the use of IV Iron Sucrose in postpartum anaemia for safety, good compliance, for rapid correction of iron stores and shorter hospital stay in postpartum period.

## ACKNOWLEDGMENTS

Authors are extremely thankful to all the participants for their valuable contribution to carry out this study.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Breymann C. The use of iron sucrose complex for anemia in pregnancy and postpartum period. *Semin Hematol.* 2006;43 suppl 6:S28-31.
2. Kalaivani K. Prevalence and consequences of anemia in pregnancy. *Indian J Med Res.* 2009;130:627-33.
3. Indian Council of Medical Research. Evaluation of nutritional anaemia prophylaxis programme task force study New Delhi; 1989. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/2246014>.
4. Bodnar LM, Cogswell ME, Mc Donald. Have we forgotten the significance of postpartum iron deficiency? *Am J Obstet Gynecol.* 2005;193(1):36-44.
5. Perez EM, Hendricks MK, Beard JL, Murray KLE, Berg A, Tomlinson M, et al. Mother-infant interactions and infant development are altered by maternal iron deficiency anemia. *J Nutr.* 2005;135(4):850-5.
6. Sharma JB, Soni D. Oxidative stress in pregnancy - Role of iron therapy: oral iron therapy and risk of free radicals. *Obstet Gynecol.* 2001;6(12):705-6.
7. Perewusnyk KG, 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.
8. Kaur P, Kaur G, Bhatia R, Singh J, Aggarwal T, Kaur P. To study the comparison of oral iron versus parenteral iron sucrose in the treatment of postpartum anaemia. *J Evolution Med Dent Sci.* 2017;6(75):5337-9.
9. Bodnar LM, Cogswell ME, Scanlon KS. Low income postpartum women are at risk of iron deficiency. *J Nutr.* 2002;132:2298-302.
10. Westad S, Backe B, Salvesen KA, Nakling J, Okland I, Borthen I, et al. A 12- week randomized study comparing intravenous iron sucrose versus oral ferrous sulphate for treatment of postpartum anemia. *Acta Obstet Gynecol Scand.* 2008;87(9):916-23.
11. Dede A, Uygur D, Yilmaz B, Mungan T, Ugur M. Intravenous iron sucrose complex vs. Oral ferrous sulphate for postpartum iron deficiency anemia. *Int J Gynaecol Obstet.* 2005;90:238-9.
12. Bayoumeu F, Subiran-Buisset C, BakaNE, 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; 186:3: 518-522.
13. Bhandal N, Russell R. Intravenous versus oral iron therapy for postpartum anaemia. *BJOG.* 2006;113:1248-52.
14. Verma S, Inamdar SA, Malhotra N. Intravenous iron therapy versus oral iron in postpartum patients in rural area. *J SAFOG DVD.* 2011;3(2):67-70.
15. Breymann C. Treatment of iron deficiency anaemia in pregnancy and postpartum with special focus on

- intravenous iron sucrose complex. *J Med Assoc Thai.* 2005;88:108-9.
16. Al-Momen AK, Al-Meshari A, Al-Nuaim L, Saddique A, Abotalib Z, Khashoggi T, et al. Intravenous iron sucrose complex in the treatment of iron deficiency anemia during pregnancy. *Europ J Obstet Gynecol Reprod Biol.* 1996;69(2):121-4.
17. Giannoulis C, Daniilidis A, Tantanasis T, Dinas K, Tzafettas J. Intravenous administration of iron sucrose for treating anemia in postpartum women. *Hippokratia.* 2009;13(1):38-40.
18. Seid MH, Derman RJ, Baker JB, Banach W, Goldberg C, Rogers R. Ferric carboxy maltose injection in the treatment of postpartum iron deficiency anaemia: a randomized controlled clinical trial. *Am J Obstet Gynecol.* 2008;199(4):435:1-7.
19. Van Wyck DB, Martens MG, Seid MH, Baker JB, Mangione A. Intravenous ferric carboxymaltose compared with oral iron in the treatment of postpartum anemia: a randomized controlled trial. *Obstet Gynecol.* 2007;110:267-78.

**Cite this article as:** Vishwakarma S, Rawat R, Dwivedi P, Kanti V. Comparative study of oral iron (ferrous sulphate) versus intravenous (iron sucrose) therapy in treating iron deficiency anaemia in puerperium. *Int J Reprod Contracept Obstet Gynecol* 2018;7:3653-8.