

Study on Effect of Oral vs Injectable Iron Treatment in Anemic Pregnant Women on Hematological Parameters

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ABSTRACT

Objective- To compare the effect of intravenous iron.(Iron sucrose) to oral iron (Ferrous sulphate) in improving the haematological parameters in anemic pregnant women and to assess the safety and compliance of the two treatments. **Methods-** The present study is prospective, comparative, interventional randomized OPD based study done at Gauhati Medical College, Guwahati, from June 2011 to May 2012. Sample size was 100 women in each group. Data was analyzed using SPSS version 11. **Results-** The study shows that there is significant difference in rise in Hb (haemoglobin), serum iron and serum ferritin between injection iron and oral iron group. Also the side effects are lesser in injection iron group. **Conclusion-** The study proved that both oral iron and injectable iron are effective way of treating the iron deficiency anemia, but injectable iron associated with faster improvement of hematological parameters with better replenishment of iron stores & lesser side effects.

KEYWORDS: Anemia, Injection Iron Sucrose, Oral Iron

INTRODUCTION

Anemia is major public health problem throughout the world. WHO defines anemia in pregnancy as Hb less than 11 g/dl.¹ The Centre for Disease Control and Prevention defines anemia in pregnant women as Hb less than 11 gm/dl in first and third trimester and less than 10.5 gm/dl in second trimester.² Iron deficiency is thought to be the most common cause of anemia in world, although other conditions such as folate or vitamin B12 deficiency, chronic inflammation, parasitic infections and inherited disorders can all cause anemia. In its severe form, it is associated with fatigue, weakness, dizziness etc. In India >90% of anemia cases are estimated to be due to iron deficiency¹, because high iron requirements during pregnancy are not easily fulfilled by food, especially when iron bioavailability is poor. Most of the Indian women are already deficient in iron stores before pregnancy. Diet alone cannot supply the 30–40 mg iron that is required for absorption of the 4–6 mg iron/day needed during the later stages of pregnancy and postpartum. Oral iron intake is the treatment of choice and almost all women can be treated effectively with oral preparations. However, parenteral administration of iron is necessary under certain circumstances and may be suitable under the following situations like inability to tolerate the side effects of orally administered iron,

inflammatory bowel disease, peptic ulcer, noncompliance with oral regimens, iron malabsorption and pregnancies near term. Also iron treatment is safer and cost effective than blood transfusion for treatment of anemia. In developing countries the prevalence of anemia in pregnant women varies anywhere between 50 to 90% among different population. In India 16% of maternal deaths are due to anemia.³

Iron folic acid supplementation is recommended for all pregnant women in area with high prevalence of anemia (>40%). Fortification of food is successful in many developed & developing countries but is experimental and required multisectoral involvement. Currently, the standard treatment for anemia is oral iron supplementation. However, this is limited by patient noncompliance and gastrointestinal symptoms such as nausea, vomiting and diarrhea.⁴ Absorption of oral iron is influenced by the dosage, the patient's iron storage and the proximity of taking the medication relative to mealtime.⁵ This method of treatment is slow to take effect, often requiring several weeks for results to transpire. Alternative treatment methods for anemia include intravenous (IV) iron therapy or blood transfusion.

Hematologic changes, like Hb and ferritin are rapid with IV iron therapy have a positive effect on the body's

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iron storage which is measured by the ferritin level. Intravenous iron administration with iron sucrose has been available for several years and is routinely used in a number of European countries to treat severe anemia.⁶ Iron sucrose has an excellent safety profile, unlike older IV formulations like ferrous dextran, which has been associated with a significant risk of anaphylactic reactions.⁷ Intravenous iron sucrose can be administered as an infusion in small doses (about 200mg) over a 30-minute time period.⁸ A new IV iron preparation, ferric carboxymaltose, has been recently developed. It provides rapid replacement of iron storage and can be administered in higher single doses of up to 1000mg during a minimum administration time of less than 15 minutes.^{5,7,8} In present study we have used iron sucrose for parenteral iron therapy.

MATERIALS & METHODOLOGY

The present study was approved by ethical committee. Period of study- The study was conducted from June 2011 to May 2012.

Study Design: Short term, comparative, interventional, randomized, prospective study.

Patient's Selection: Pregnant women with anemia were randomly selected from antenatal clinic and assigned either to intravenous or to oral iron group. Sample size was decided to be 100 anemic women in each group. More women were enrolled in both groups as in the course of study there was high chance of loss of follow up of patients. The cases were included in the study after fulfilling the given criteria.

INCLUSION CRITERIAS:

- Age group 18 to 34 years.
- Hemoglobin concentration 7 to 10 g/dl
- Gestational age between 12 to 32 weeks
- No other systemic illness

EXCLUSION CRITERIAS:

- Hemoglobin concentration <7 or >10 g/dl
- Multifetal pregnancy.
- Pre-existing illness of mother,
- History of late miscarriage or stillbirth,
- Unwilling subjects
- Anemia not caused by iron deficiency (e.g. aplastic, megaloblastic or hemolytic anemia) or related to hemoglobinopathies, chronic diseases and autoimmune diseases.
- Previous iron therapy or blood transfusion

Consent: An informed and written consent was taken from each patient

Methodology: Detailed history was taken. Complete systemic and obstetric examination was carried out. Period of gestation was calculated from last menstrual period (LMP) or first trimester obstetric scan, if patient not sure of her dates.

Investigations: Following investigations are done in all cases before trial

- Blood- Blood group & Rh typing
- Hemoglobin
- Reticulocyte count
- Peripheral blood smear
- Hematocrit
- PCV, MCV, MCHC, MCH, TIBC
- S. Iron, S. Ferritin
- RBS
- S. Creatinine
- HIV
- Urine RE-albumen, pus cell, sugar etc.
- Stool RE- Ova for hook worm/ round worm, occult blood
- Other investigation- USG, Hemoglobin typing

Investigations were done in central laboratory of Gauhati Medical College & Hospital, with the help of automated analyzer (VITROS 5600 integrated system) and automated cell counter (SYSMEX xs800).

Procedure-We had enrolled 150 women in each group. Each patient of the oral iron group was given iron tablets (Iron sulphate) in adequate doses. Each study patient in intravenous therapy group was given calculated amount of intravenous iron (Iron sucrose). All patients were monitored for adverse effects, clinical and laboratory responses. Deworming done in the patients with investigation reports positive for ova. Deworming done with Mebendazole 100mg twice daily for three days.

Study Group: Oral iron (Ferrous sulphate) - The participants of oral iron group were given oral tablets of 100 mg elemental Iron (Ferrous Sulphate) & 500 mg of Folic acid (FOLIFER-Ministry of health) thrice daily after food. During next visit they were asked about intake of tablet and color of stool to ensure the intake of iron tablets.

Study group: I.V. Iron Group

Total dosage of Injection Iron sucrose is calculated by the following formula:

Total Iron deficit (mg) = amount of Iron deficit+ amount of Iron to replenish stores

Total Iron deficit (mg) = W X 0.24 X (desired Hb% - Patient's Hb %) + 500

(rounded up to the nearest multiple of 100 mg).

Method of administration: Iron dosage calculated and administered direct intravenously slowly, without dilution in not less than 5 minutes, on alternate day as 100-200 mg injection, not exceeding 600 mg/week. Adrenaline, Hydrocortisone, Pheneramine maleate and Oxygen kept ready to combat any serious allergic reaction.

Assessment of the results: Patients of both groups were asked to attend antenatal clinic after 3 weeks and 6 weeks interval from the date of starting the treatment. At each visit improvement of general conditions and disappearance of the symptoms and sign of anemia were looked for. Before initiation of the treatment, Hb, Hematocrit, Reticulocyte count, S, Iron, S. Ferritin, TIBC, MCV, PCV, MCH, MCHC and peripheral blood

smear done. To assess the result, changes in different hematological parameters noted after 3 weeks and 6 weeks. Data was analyzed using SPSS version 11 (Statistical Package for Social Sciences). The mean changes in hematological parameters between the groups receiving oral iron versus I.V. iron sucrose were compared using the paired t-test, while the chi-square test was used to compare the quantitative data.

RESULTS

Total 150 antenatal women were registered in each oral and intravenous group. Sample size was decided to be 100 anemic women in each group. More women were enrolled in both groups, as in the course of study, the loss of follow up was high. In oral group (Ferrous sulphate), 32 women did not come for follow up, 9 women had not taken iron tablets regularly because of side effects, 3 women were diagnosed with megaloblastic anemia and 3 women were found to be having haemoglobin E disease. So in oral group only 103 women completed the study. In I.V. iron (Iron sucrose) group- 30 women did not come for follow up, 2 women were found to be having megaloblastic anemia, 2 women were found to be having hemoglobin E disease, 1 woman had preterm labour and 1 woman was found to be having pulmonary tuberculosis, so 114 women had completed the study in IV group. First 100 women in each group had compared, among the total 217 women, who had completed the study.

It is observed that no significant difference existed between the two groups in age, literacy, parity, weight, socioeconomic status and gestational age at the start of the study ($P > 0.05$). It is observed that no significant difference existed between the two groups in Hb, S.Iron, S. Ferritin and other Red Blood Cell indices; MCV, MCH, MCHC, PCV and Reticulocyte count at the start of the study and both groups were comparable ($P > 0.05$). It is seen from data that Hb increment (Table no. 1) in both groups were significant at 3 weeks and 6 weeks interval (P value < 0.0001). Increment in Hb in oral group was 1.63 g/dl and in I. V. iron group was 2.52 g/dl in 6 weeks duration ($P < 0.0001$). So increment in Hb in I.V. iron group was significantly higher than oral group. It is observed from the data that there was significant rise in serum iron (Table no. 2) level in I.V. iron group than oral iron group ($P < 0.0001$). It is observed that rise in S. ferritin (Table no. 3) in I.V. iron group is statistically significant than oral iron group. It is seen that there is no significant difference in rise of other haematological indices (Table no. 4). It is seen that side effects (Table no. 5) were more common in oral iron group in comparison to I.V. iron group.

	Before TX	After 3 wks	After 6 wks	Rise in 6 wk	P value
Oral iron group	8.492	9.38	10.162	1.630±0.47	P<0.00001
Inj. Iron group	8.332	9.396	10.794	2.528±0.79	

Table -1 Rise in Haemoglobin (mean value)

Side effects including gastrointestinal upset, constipation, nausea and noncompliance etc. more common in oral iron group, while I.V. iron group have few side effects which includes pain at the site of injection and metallic taste.

	Before TX	After 3 wks	After 6 wks	Rise in 6 weeks	P value
Oral iron group	46.608	72	89.752	43.144	P<0.00001
Inj. Iron group	49.72	82.28	104.16	54.44	

Table-2 Rise in serum Iron (μ g/dl)

S. Ferritin (μ g/L)	Oral iron group	I.V. iron group
Before treatment	8.73	8.99
After 3 wks	11.83	12.01
After 6 wks	14.93	16.10
P value	<0.0001	

Table-3 Rise in S. Ferritin

	N=50	Before TX	After 3 wks	After 6 wks	P value
PCV%	Oral iron	27.074	29.552	31.672	0.12 = NS
	Inj iron	27.514	30.032	32.254	
MCV(fl)	Oral iron	78.286	81.532	84.618	0.95 =NS
	Inj iron	77.318	81.45	84.658	
MCH (pgm)	Oral iron	24.908	28.268	30.356	0.96 =NS
	Inj iron	24.88	27.8872	30.342	
MCHC (g/dl)	Oral iron	29.128	30.91837	32.412	0.68 =NS
	Inj iron	28.808	30.8	32.538	
RC(%)	Oral iron	1.478	1.78	1.962	0.092
	Inj iron	1.37	1.726	2.304	

Table-4 Rise in other haematological indices

	Oral iron group	I.V. iron group
Constipation	26	3
Nausea	4	2
Dark stool	10	0
Metallic taste	6	8
Local pain	0	7
Thrombophlebitis of vein	0	0
Anaphylactic reaction	0	0
Others	0	0

Table-5 Side effects

DISCUSSION

The two groups matched in all respect including age, literacy, parity, weight, socioeconomic status, gestational age, Hb, S.Iron, S. Ferritin and other Red Blood Cell indices; MCV, MCH, MCHC, PCV and Reticulocyte count at start of the study and both groups were comparable ($P > 0.05$). It is observed from our study that the mean hemoglobin in oral iron group was 8.49+0.53g/dl and in I.V. group was 8.332+ 0.68 g/dl and Hb increment in oral group was 1.630+0.47 g/dl and in I.V. Iron group was 2.528+ 0.7 g/dl in 6 week duration. P value is < 0.0001 and highly significant. So rise in Hb in I.V. iron group was significantly higher than oral iron group. Similar result found by study of Kumar et al and study of Diwakar et al, Al Momen et al, Al Ra et al. In study conducted by Diwakar et al, 30.7% of the women

receiving oral iron showed an increase in Hb while 92.8% women receiving iron-sucrose showed a significant increase in Hb level.⁹ They found that mean rise in Oral iron group was 0.5g/dl and in I.V. group mean rise in Hb was 1.3 g/dl.⁹ Al Momen et al found that the intravenous iron therapy resulted in higher levels of Hb, with the time to achieve maximal Hb concentration also significantly shorter in this group compared with controls (mean 6.9 vs. 14.9 weeks).¹⁰ Al Ra et al found that the change in Hb from baseline was significantly higher in the intravenous group than the oral group at each measurement; the changes with respect to subsequent Hb were significantly higher on the 14th (P = .004) and 28th (P = .031) days.¹⁰

It is observed from present study that S. ferritin level at the end of 6 weeks was 14.91 µg/L in oral group and 16.1 µg/L in I.V. iron group and the rise in S. ferritin was significantly higher after 6 weeks in I.V. group than oral iron group (P<0.0001). The result is comparable to the study conducted by Bayoumeu et al they found that on day 30, there was a highly significant difference in ferritin levels between the 2 groups with iron reserves restored only in the IV group (P < .0001).¹¹ Al Momen et al found that the intravenous iron therapy resulted in higher levels of S. Ferritin (P<0.05).¹⁰ Al Ra et al, found that S. Ferritin values were higher in patients receiving intravenous iron throughout pregnancy (P<0.001).¹⁰ Exceptionally high level of Serum ferritin seen in the study of Breyman et al, after 4 weeks of I.V. iron therapy.¹² The cause might be that they had given injection iron sucrose at 200 mg/ week and the S. Ferritin level tested on 28th day, might be in close proximity to the day of intravenous iron injection. So present study is comparable to all other studies and shows iron sucrose not only increases the Hb level, but also leads to restitution of iron stores.

Rise in other red cell indices- It is observed from our study that there was significant improvement in all red blood cell indices PCV, MCV, MCH and MCHC in both oral and I.V. iron groups after 6 weeks of treatment. But there was no significant difference between both groups and both oral and I.V iron had similar effect (P>0.05) on haematological parameter.

Side effects: In the present study it is seen that side effects were more common in oral iron group in comparison to I.V. iron group. 46% patients in oral iron group had some side effect among that 26% women complained constipation, but only 20% patients in I.V iron group had mild side effects among that 8% complained pain at site of injection, 7% complained metallic taste, 2% complained nausea and 3% women complained constipation. No patient had suffered from any severe reaction. Diwakar et al showed that in I.V. iron group minor adverse reactions, which included burning at the infusion site, itching, giddiness and GI symptoms occurred in 18.89% of the women, but there were no major adverse reactions, while in oral iron group 5 patients has discontinued the oral tablets due to constipation and 4 patients stopped due to gastric

irritation and 39% patient had other minor complaints like nausea, constipation and metallic taste.

CONCLUSION

The study proved that both oral iron tablet and I.V. iron sucrose are effective in treating the iron deficiency anaemia, but injection iron sucrose is more effective in replenishing the iron stores with more speedy increase in haemoglobin and Serum ferritin level than oral iron treatment. Also I.V. iron sucrose therapy is a safe, efficient and quick method to treat iron deficiency anaemia with lesser side effects and good compliance. Intravenous Iron therapy has a role in developing countries like India, where poor compliance to oral therapy is a great hindrance to effective eradication of anaemia in pregnant women. With regard to cost, definitive cost effective studies need to be done. But use of injection iron sucrose is very much cost effective when considered number of maternal mortality by virtue of iron deficiency anaemia.

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