International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Assessment of Efficacy and Safety of Intravenous Iron Sucrose Compared to Oral Iron Sulphate Therapy in Anemia among Antenatal Women Visiting Primary Health Centres, District Ambala, Haryana

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Received: 29/08/2016 *Revised: 21/09/2016* *Accepted: 26/09/2016*

ABSTRACT

Background: Anemia is the most common disorder of the blood, affecting a quarter of the world's population globally. WHO defines anemia as hemoglobin level (HB) <11g/dl in pregnancy. In India, prevalence of anemia ranges between 33%-89%. [1] About half of the global maternal deaths due to anemia occur in south Asian countries; India contributes to about 80% of this mortality ratio. [2]
Objectives: 1) To compare the efficacy of intravenous iron sucrose with oral iron sulphate therapy to treat anemia in pregnant women visiting the Primary Health Centers of Ambala District, Haryana.
2) To evaluate the side effects and complications of Intravenous Iron Sucrose and Oral Iron Sulphate therapies in these patients.
Sample size: A total of 400 (rounded) 200 antenatal cases for intravenous therapy and 200 for oral sulphate therapy.
Materials and Methods: A community based prospective study was conducted and all eligible Antenatal females (20-24 weeks of gestation) visiting Primary Health Centers and with hemoglobin level 7.1-8.9 g/dl, having received IV Iron sucrose or Oral Iron sulphate therapy were evaluated.
Results: The target haemoglobin was achieved in 37.0% antenatal women in Group A whereas only 12% achieved the target haemoglobin in Group B. 14.5% of the Intravenous group A had side effects as compared to 25.4% of Oral group B (p=0.009).
Conclusion: This study concluded that intravenous iron sucrose is safe and highly efficacious for the treatment of iron deficiency anemia in pregnancy as compared to oral iron sulphate therapy.

Keywords: Intravenous iron sucrose, iron deficiency anemia, oral iron sulphate, antenatal.

INTRODUCTION

Anemia is the most common disorder of the blood, affecting a quarter of the world's population globally. WHO defines anemia as hemoglobin level (HB) <11g/dl in pregnancy. The ICMR-1989 classification of anemia is: 10-10.9 g/dl mild, 7.0-9.9 g/dl moderate, 4.0-6.9 g/dl severe anemia. In India, prevalence of anemia ranges between 33%-89%. [1] About half of the global maternal deaths due to anemia occur in south Asian countries; India contributes to about 80% of this mortality ratio. [2] The National Family Heath Survey (NFHS-3) conducted in 2005-06 shows a disturbing presence of anemia in pregnant women; the disease troubles 59% cases of pregnancy while 63% of lactating women are anemic. [3]

Anemia during pregnancy has been shown to be associated with a high risk of preterm delivery [4] and three-fold risk for

low birth weight and stillbirth as well as maternal mortality. [5] According to recent studies, the prevalence of iron deficiency anemia in the first trimester ranges from 3.5%-7.4% and this rate increases to 15.6%-55% in the third trimester.

With adequate iron stores, the daily iron requirement in pregnancy increases from an average of 2mg-3mg/day in early trimester to 6mg-8mg/day in the last trimester. Approximately 900 mg of iron is needed during a singleton pregnancy. [6] 300 mg for development of placenta and fetus and 500 mg is required to support maternal hemoglobin mass. Approximately 200 mg is shed through the gut, urine and skin. The total amount thus is 1000 mg, which considerably exceeds the iron stores of most women, despite a 20% increase in absorption of iron during pregnancy. [7]

There are multiple causes of anemia during pregnancy including inadequate nutrition, dysfunctional uterine bleeding, gastrointestinal bleeding, chronic kidney disease, frequent pregnancies, multiple gestations, hookworm infestations, malaria, TB etc. However, it is generally estimated that half of anemia cases in pregnancy are related to iron deficiency. [8] Vegetarians are more likely to develop iron deficiency as the vegetarian food contains phytates, phosphates, tannates, oxalates and carbonates which make non-heme iron nonabsorbable.

Iron deficiency anemia (IDA) is the most common nutritional disorder in the world, affecting approximately 25% of the world's population. [9] The prevalence of iron deficiency anemia in pregnant women is estimated to be 35%-75% (average 56%) in the developing countries, whereas in industrialized countries the average prevalence is 18%. [10,11]

The first choice in treatment of iron deficiency anemia is oral iron sulphate therapy because of its effectiveness, safety and low cost. However there are dose related side effects, noncompliance or iron intolerance, decreased absorption as in ulcerative colitis, delay in replenishment of iron stores of the body as once the anemia is corrected with oral iron, absorption slows down and thus the iron stores are not replenished. This is significant in our country where women may become anemic again during lactation, especially when their iron stores have not been corrected.

Contrary to the above Intravenous Iron Sucrose releases iron rapidly to the endogenous iron binding proteins, resulting in a significant raise of ferritin and regulation of marrow proliferation. [12] It has a half-life of 6 h, so it produces a more rapid increase in hemoglobin concentration than oral iron and even iron dextran. [13] It can be administered without a test dose [14] and has a lower incidence of allergic reactions.

As per guidelines and directions for the prevention of Maternal Anemia issued by (NRHM) [15] Government of India, Intravenous Iron Sucrose therapy has been included in the treatment of Anemia in antenatal women at all levels of Government Health Institutions. The initial estimation of hemoglobin level is to be recorded at the gestation age of 14-16 weeks, thereafter at 20-24 weeks of gestation period a mandatory second estimation of hemoglobin has to be done and if the hemoglobin level is between 7.1 to 8.9 g/dl, IV Iron Sucrose Infusion is initiated once a day x 4days over a period of 2 weeks (with 2-4 days of interval between each infusion). Oral iron therapy is withheld while receiving iron sucrose infusion. The third and fourth hemoglobin estimation will be done at gestation period of 26-30 weeks and 30-34 weeks respectively with an interval of minimum four weeks. Additional hemoglobin estimation will be done at the time of delivery.

The literature regarding efficacy and safety of intravenous iron sucrose in treatment of anemia in pregnant women is limited and few studies have been done on this subject especially in this part of our country. Therefore this study was planned to compare the efficacy and safety of iron sucrose with oral iron, which may prove to be a good alternative to oral iron therapy in

patients who are either intolerant to oral iron or are noncompliant and may also reduce the incidence of blood transfusion and its associated risks.

MATERIALS AND METHODS

This prospective study was carried out in district Ambala of Haryana from 1st Nov 2014 to 31st Oct 2015 among all eligible antenatal women who were screened for anemia between 20-34 weeks of gestation period. Using the formula n = 16 s^2 /d^2 (where's' is standard deviation of outcome variable and'd' is difference to be detected in the outcome variable of the two groups) and assuming the standard deviation to be 0.83 (average of 0.94 [16] to 0.73 [17]) sample size of 176 antenatal women (in each group) was required to detect a hemoglobin difference of 0.25g/dl (d) with a power of 80%. On the assumption of an overall loss rate of 10% a total of 400 eligible women (200 in group A i.e. Intravenous Iron Sucrose and 200 in group B i.e. Oral Iron Sulphate) were included in this study.

The study was conducted in four Primary Health Centres, selected by simple random sampling technique, out of the total 18 Primary Health Centres in district Ambala. From each of the 4 PHC's a total of 100 eligible antenatal women were selected (50 on treatment with IV Iron Sucrose and the other 50 on oral Iron sulphate therapy). Screening was done in the laboratory attached to the facility. Antenatal women with hemoglobin level between 7.1-8.9 g/dl, singleton live pregnancy and gestation age between 20-34 weeks were included in this study while women with history of hematological disease, blood transfusion during current pregnancy, chronic blood loss and placenta previa were excluded.

Pretested and semi-structured proformas was used to obtain the required information. Socio-economic status was determined by updated BG Prasad Socio-economic Classification for the year 2014. [18] Gestation period was assessed by the last menstrual period and by ultrasonography and hemoglobin estimation was done by Sahli Hemoglobin meter (available at Primary Health Centres).

Group A subjects received intravenous iron sucrose (Infusion of Normal Saline 100ml including the part dose of Iron Sucrose completed within 30 minutes; during the first 5 minutes rate of infusion was set at 20-30 drops/minute, then the rate was increased to 80-90 drops/minute), Group B subjects received100 mg iron sulphate orally twice daily for 90 days. All Group B patients were advised to take tablets on empty stomach, 2 hours prior or after meals, preferably with lemon juice but not with milk. Both groups were supplemented with 0.5 mg folic acid and vitamin B12 (15 mcg) + vitamin C 100mg per day.

Table 1: Distribution of antenatal cases in both groups A and B as per target (Hb 11gm/dl) achieved.

Target Hb Achieved	GROUP A		GROUP B			
	No	%	No	%	Total	%
YES	74	37.0%	24	12.0%	98	24.5%
NO	126	63.0%	176	88.0%	302	75.5%

P value 0.001

Table 1 shows distribution of antenatal case in both the Groups as per target haemoglobin achieved (11gm/dl) at the time of delivery. It was observed that desired level of Haemoglobin was achieved by more number of antenatal cases (37.0%) in group A i.e. who received Intravenous Iron Sucrose than antenatal cases in Group B (12%) i.e. who received Oral Iron Sulphate. The difference in proportion of antenatal women achieving the target is statistically significant. (P=0.001)

Table 2: Side effects of Intravenous and Oral iron therapy.

Side Effects	Group A		Group B	
	No	%	No	%
Absent	171	85.5%	149	74.6%
Present	29	14.5%	51	25.4%

p value 0.009

Table 2 shows the side effects after intravenous and oral iron therapy in both the groups. In Group B (oral iron) 51 antenatal cases (25.4%) reported side effects whereas only 29 cases (14.5%) had the side effects as a result of the intravenous iron therapy

Group A. This difference was found to be statistically significant. (p=0.009)

Table 3: Distribution of side effects in Group A and Group B

Side Effects	Group A		Group B	
	No	%	No	%
Constipation	0	0.0%	9	4.5%
Diarrhoea	0	0.0%	3	1.5%
Epigastric Pain	0	0.0%	10	5.0%
Gest. Hypertension	2	1.0%	2	1.0%
Giddiness	3	1.5%	0	0.0%
Black Stools	0	0.0%	6	3.0%
Nausea	12	6.0%	4	2.0%
Pain Site	2	1.0%	0	0.0%
tachycardia	2	1.0%	0	0.0%
Taste change	1	0.5%	0	0.0%
Vomiting	7	3.5%	16	8.5%

Table 3 shows the various types of side effects after intravenous and oral iron therapy in both groups. In Group A (intravenous iron) 12 case (6.0%) reported nausea, 7 cases (3.5%) reported vomiting, 3 cases (1.5%) reported giddiness, 2 cases each (1.0%) reported pain at site, tachycardia and 2 cases had gestational hypertension respectively.

In Group B (oral iron), majority had Gastro-intestinal side effects and more comparatively to the Group A. 17 case (8.5%) reported vomiting, 10 cases (5.0%) reported epigastric pain, 9 cases (4.5%) reported constipation, 6 cases (3.0%) reported black-stools, 4 cases (2.0%) cases reported nausea and 3 cases (1.5%) cases reported diarrhoea, 2 cases (1.0%) had gestational hypertension.

RESULTS

The target haemoglobin was achieved in 37.0% patients in group A whereas only 12.0% achieved target haemoglobin in group B. The gastrointestinal related side effects were nil in groups A as compared to group B. None of the patients from either group had any blood transfusion. Higher number of antenatal women reported side effects in Group B (25.4% in group B and 14.5% in group A) Fear of prick was the most common reason given for refusal of Intravenous Iron therapy in Group A at 38%.

DISCUSSION

In the study it was observed that desired level of Haemoglobin (11.0gm/dl) was achieved by more number of antennal cases (37.0%) in group A i.e. who received Intravenous Iron Sucrose than antenatal cases in Group B (12%) i.e. who received Oral Iron Sulphate. The difference in proportion of antenatal women achieving the target is statistically significant. (P=0.001) In another prospective randomized clinical trial registered under the Clinical Trial Registry, India, in the year 2008 to September 2010 by Neeru et al [19] target hemoglobin of 11 g/dL was attained by 66% of the patients in the IVIS group after 1 month of treatment as compared with 61% of patients in the OI group, which was not statistically significant.

In the present study some side effects after intravenous and oral iron therapy were reported in both groups. In Group A (intravenous iron) 12 case (6.0%) reported nausea, 7 cases (3.5%) reported vomiting, 3 cases (1.5%) reported giddiness, 2 cases each (1.0%) reported pain at site, tachycardia and 2 cases had gestational hypertension respectively, whereas in Group B (oral iron), majority had Gastro-intestinal side effects and more comparatively to the Group A. 17 cases (8.5%) reported vomiting, 10 cases (5.0%) reported epigastric pain, 9 cases (4.5%) reported constipation, 6 cases (3.0%) reported black-stools, 4 cases (2.0%) reported nausea and 3 cases (1.5%) cases reported diarrhoea, 2 cases (1.0%) had gestational hypertension. In another study by Kochar et al [20] it was concluded that the adverse effects from iron treatment were mild but more prominent in Oral Iron therapy group B. In another similar study by Kriplani A et al [21] it was concluded that intravenous iron sucrose was associated with fewer adverse events and was more effective than regular oral iron therapy.

CONCLUSIONS

This study concluded that intravenous iron sucrose is safe and highly

efficacious for the treatment of iron deficiency anaemia in pregnancy. It restores iron stores more rapidly and promptly. Therefore it is an effective alternative to oral iron therapy without side effects, especially when patients are non-tolerant to oral iron therapy or when oral iron preparations are ineffective because of poor absorption. Further it may reduce the requirement of blood transfusion in pregnant women with severe anaemia at term.

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How to cite this article: Singh AJ, Goel RKD, Bhardwaj A et al. Assessment of efficacy and safety of intravenous iron sucrose compared to oral iron sulphate therapy in anemia among antenatal women visiting primary health centres, district Ambala, Haryana. Int J Health Sci Res. 2016; 6(10):10-15.

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