

A Comparative Randomised Research to Assess the Efficacy of Parenteral Iron Sucrose and Oral Iron in the Treatment of Iron Deficient Anaemia in Pregnancy.

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Received: 07-02-2021 / Revised: 20-03-2021 / Accepted: 14-04-2021

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Conflict of interest: Nil

Abstract

Aim: To compare and observe the effect of parenteral iron sucrose and oral iron in the treatment of iron deficiency anaemia in pregnancy.

Methods: Total 120 Pregnant women with gestational age between 26 to 34 weeks with mild to moderate iron deficiency anemia (Hb 7-10 g/dl) who gave informed consent were selected from ANC clinic were included in this study. Two groups were made and in each group 60 patients were included. The women in group A received IV iron sucrose. The women in the group B received ferrous sulphate as oral iron BD for 6 weeks. Women were instructed to take the tablets on an empty stomach either two hour before or after meal. Each tablet contained 200 mg as salt (60 mg elemental iron). The each and every patient of these two groups was followed up every week for six weeks. At the end of six weeks all the initial investigation viz: haemoglobin, red blood cell count, reticulocyte count, PCV, MCHC, serum iron, serum ferritin and total iron binding capacity of serum were estimated. All the haematological parameters were repeated at the time of delivery and one week after delivery.

Results: Mean age of the patients in oral group was 28.69±1.77 and in the intravenous group it was 26.98±0.79 years. The baseline mean Hb level in the oral iron therapy group was 8.81±0.17g/dl and parental iron therapy it was 8.77±0.11g/dl, which was found to be statistically insignificant between the groups. 6 weeks after starting the therapy, there was a high significant change ($p<0.05$) in the Hb level in both oral and injectable iron group. The mean Hb rise in the injectable iron group was 3.26 g/dl ($p<0.05$) and in the oral iron group was 1.52 g/dl ($p<0.05$). The significant difference ($p<0.05$) in increase in serum iron, serum ferritin and TIBC was also observed in two group A and B in our study, whereas the rise of other haematological parameters i.e. red cell count, packed cell volume, mean corpuscular haemoglobin concentration and reticulocyte counts were non-significant. Indicate that IV group respond better than the oral group ($p<0.05$). To compare the weekly change in haemoglobin level in two

groups, independent sample t-test was performed. Two group differ significantly ($p < 0.05$) change in haemoglobin per cent in all the weeks.

Conclusion: The intravenous iron sucrose appeared to be more efficacious in increasing hemoglobin level more rapidly than prolonged course of oral iron therapy.

Keywords: Hb, Pregnancy, Iron therapy

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Introduction

Iron is a critical element in function of all cells of human body and takes major role in oxygen transport as a part of hemoglobin (Hb). Iron deficiency anemia is worldwide health problem and also is the commonest form of nutritional deficiency[1]. It occurs as a late manifestation of prolonged negative iron balance, which can be due to nutritional deficiency, chronic blood loss, impaired iron absorption from gastrointestinal tract, multiple pregnancy, or worm infestations[2]. Historically the oral route of administration of iron was given much attention but the effectiveness of oral formulations are compromised by poor absorption, poor compliance and side effects. Blood transfusions for iron deficiency anemia depend upon severity of anemia. The hemoglobin level at which blood transfusion to be given varies from clinicians to clinicians with a possibility of unnecessary transfusions[3]. There are also chances of mismatched transfusions, infections particularly HIV and hepatitis, and transfusion related acute lung injury which are difficult to handle. Therefore searching an alternative to raise hemoglobin in iron deficiency anemia, we can think of parenteral iron formulations. Early parenteral formulations are associated with much adverse reactions and are withdrawn from many countries. They were surpassed with introduction of iron sucrose, modified formulations of iron dextran and ferric

gluconate. These formulations have much improved safety profiles, lower rates of adverse events[4,5] and also reduce the frequency of hospital or clinic visits by the patients[6]. Compared with blood transfusions, intravenous (IV) iron therapy is safe and cost effective for restoration of hemoglobin and body iron stores[7]. IV iron sucrose formulations are being used in many countries for the said purpose. Although another IV iron preparation, that is, ferric carboxymaltose is now available and claims to be safe but it is very costly and not affordable by everyone. Our study will help primary physicians to prioritize IV iron sucrose which is safe and easily affordable to treat iron deficiency anemia. Hence the aim of our study to observe the effect of parenteral iron sucrose and oral iron in the treatment of iron deficiency anaemia in pregnancy.

Material and methods

This prospective, randomized, comparative study was done in the Department of Obstetrics and Gynecology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India., from September 2019 to September 2020, after taking the approval of the protocol review committee and institutional ethics committee. After taking informed consent detailed history was taken from the patient or relatives. total 120 Pregnant women with gestational age between 26 to 34 weeks with mild to moderate iron deficiency anemia (Hb 7-10 g/dl) who gave

informed consent were selected from ANC clinic were included in this study. We set the target Hb level of 11 g/dl. The initial iron status of the woman was assessed by the clinical and laboratory examinations. Features of iron deficiency were evidenced by: low red cell count, MCHC, reticulocyte count, serum ferritin and serum iron and increased TIBC. The Pregnant women with gestational age less than 26 weeks and more than 34 weeks, anemia due to causes other than iron deficiency, any other medical or obstetric complicating factors like hypertension, diabetes, reaction to IV iron sucrose are excluded from the study.

Methodology

After careful history analysis, clinical examination and minimal investigations, other cause of anaemia was ruled out. Two groups were made and in each group 60 patients were included. The women in group A received IV iron sucrose. The dose of iron sucrose was calculated as follows: $2.4 \times \text{Body weight (in kg)} \times (\text{target Hb} - \text{actual Hb})$. To replenish iron stores 10 mg/kg of iron sucrose was added. Total calculated dose was given in divided doses either on alternate day or twice weekly. Maximum dose is 200 mg per dose infused IV over 1 h. The stability of iron sucrose in normal saline has been shown in studies at concentration of 0.5 to 2 mg/ml for a period of 24 h. So 100 mg iron sucrose diluted in 100 ml saline (1 mg/ml) is stable and should be given in 15-20 min. So the dilutions and administration were: 5 ml iron sucrose (100 mg iron) in 100 ml of 0.9% NaCl infused over at least 15 min. No test dose was given.

The women in the group B received ferrous sulphate as oral iron BD for 6 weeks. Women were instructed to take the tablets on an empty stomach either two hour before or after meal. Each tablet contained 200 mg as salt (60 mg elemental iron). The each and every patient of these two groups was

followed up every week for six weeks. At the end of six weeks all the initial investigation viz: haemoglobin, red blood cell count, reticulocyte count, PCV, MCHC, serum iron, serum ferritin and total iron binding capacity of serum were estimated. All the haematological parameters were repeated at the time of delivery and one week after delivery.

Statistical Analysis

Data were analyzed using SYSTAT 7.0 (SPSS Inc. USA). Differences between mean percentages were analyzed by independent -'t' test. A value of $P < 0.05$ was considered to be statistically significant. All means have been expressed as mean \pm standard error.

Results

In this prospective study, 120 pregnant women were included according to selection criteria and randomly assigned in the one of the two groups, i.e. iron sucrose (group A, n = 60) or ferrous sulphate (group B, n = 60). At 6 weeks, 54 pregnant women from the iron sucrose group (two develops hypersensitivity reaction) and 42 pregnant women from the ferrous sulphate group (19 patients did not take tablet regularly) could be included for the analysis. Majority of the patients were in the age group of 20 to 30 years in both oral and intravenous group. Mean age of the patients in oral group was 28.69 ± 1.77 and in the intravenous group it was 26.98 ± 0.79 years.

In the present study the baseline mean Hb level in the oral iron therapy group was 8.81 ± 0.17 g/dl and parental iron therapy it was 8.77 ± 0.11 g/dl, which was found to be statistically insignificant between the groups. 6 weeks after starting the therapy, there was a high significant change ($p < 0.05$) in the Hb level in both oral and injectable iron group. The mean Hb rise in the injectable iron group was 3.26 g/dl ($p < 0.05$) and in the oral iron group was 1.52 g/dl ($p < 0.05$).

The significant difference ($p < 0.05$) in increase in serum iron, serum ferritin and TIBC was also observed in two group A and B in our study, whereas the rise of other haematological parameters i.e. red cell count, packed cell volume, mean corpuscular haemoglobin concentration and reticulocyte counts were non-significant. Indicate that IV group respond better than the oral group ($p < 0.05$).

To compare the haematological parameters of two groups (Group- A and Group- B), independent sample t-test was performed. There was significant differences ($p < 0.05$) was observed in Hb, serum iron level and

total iron binding capacity, whereas other parameters were found to be non-significant ($p < 0.05$) (Table 1 and Table 2).

To compare the weekly change in haemoglobin level in two groups, independent sample t-test was performed. Two group differ significantly ($p < 0.05$) change in haemoglobin per cent in all the weeks (Table 3).

No significant differences between the two groups in pregnancy outcomes were observed. Systemic side effects were more common in the parenteral iron group, whereas gastrointestinal side effects were more common in the oral iron group.

Table 1: Haemoglobin level before and after treatment

Group	Hb level (g/dl)		Differences
	Before treatment	After treatment	
Group A	8.77±0.11	12.03±0.17	3.26
Group B	8.81±0.17	10.33±0.19	1.52

Table 2: Change in various Haematological parameters

Haematological parameters	Change in haematological parameters after treatment		P value
	Group- A	Group- B	
Haemoglobin level (g/dl)	3.26	1.52	0.0015
Red cell count (million/ mm ³)	0.95	1.06	4.33
Packed cell volume (%)	10.03	11.87	4.88
Mean corpuscular haemoglobin concentration (%)	5.03	4.47	3.63
Reticulocyte counts (%)	0.81	0.63	2.21
Serum iron level (µg %)	70.03	42.36	0.048
Serum ferritin (µg/l)	65.03	15.23	0.0015
Total iron binding capacity (µg %)	-326.74	-152.36	0.0015

Table 3: Weekly change in level of haemoglobin

Weeks	Group - A average %	Group - B average %	P - Value
First	14.03 ± 0.69	10.68 ± 0.74	0.0001
Second	19.01 ± 0.93	6.07 ± 0.56	0.0001
Third	5.36 ± 0.47	1.78 ± 0.16	0.008
Fourth	2.88 ± 0.36	1.36 ± 0.11	0.0041
Fifth	1.25 ± 0.07	0.68 ± 0.06	0.0005
Sixth	0	0.41 ± 0.03	0.0000
At time of delivery	44.98 ± 3.01	28.11 ± 1.63	0.0012
One week after delivery	32.99 ± 2.42	17.02 ± 1.42	0.0133

Discussion

The safety and effectiveness of iron sucrose has been demonstrated in several clinical trials of patients with chronic kidney disease with refractory anemia[8]. In anaemic pregnant women, Govan and Scott reported a case series as early as in 1949 demonstrating the benefits of intravenous iron[9]. Subsequently, small observational studies, quasi-experimental studies, and small randomized clinical trials have shown improvement in haematological indices with intravenous iron sucrose in pregnant women.

Iron deficiency anemia during pregnancy is the commonest medical disorder in pregnancy in developing world and deserves special attention because of its potential consequences[10]. Although oral iron supplementation is widely used for the treatment of IDA, not all patients respond adequately to oral iron therapy[11]. Previously, the use of intravenous iron had been associated with undesirable and sometimes serious side effects and therefore is under utilized[12]. However, in recent years, new type II and III iron complexes have been developed, which offer better compliance and toleration as well as high efficacy with a good safety profile[13]. There are few studies comparing intravenous iron sucrose versus oral iron for the treatment of iron deficiency anaemia in pregnancy[14].

In the present study the baseline mean Hb level in the oral iron therapy group was 8.81 ± 0.17 g/dl and parental iron therapy it was 8.77 ± 0.11 g/dl, which was found to be statistically insignificant between the groups. 6 weeks after starting the therapy, there was a high significant change ($p < 0.05$) in the Hb level in both oral and injectable iron group[15]. The mean Hb rise in the injectable iron group was 3.26 g/dl ($p < 0.05$) and in the oral iron group was 1.52 g/dl ($p < 0.05$). The similar findings of increased Hb% in oral and

IV group were also reported by earlier workers[16]. The significant difference ($p < 0.05$) in increase in serum iron, serum ferritin and TIBC was also observed in two group A and B in our study, whereas the rise of other haematological parameters i.e. red cell count, packed cell volume, mean corpuscular haemoglobin concentration and reticulocyte counts were non-significant. Indicate that IV group respond better than the oral group ($p < 0.05$). The other workers also reported increase in serum iron in both the groups, but there was no significant difference between oral and IV groups[17]. When analyzed across time it was found that two group differ significantly ($p < 0.05$) change in haemoglobin per cent in all the weeks[18]. Intravenously administered iron sucrose (Group A) was significantly more likely to have higher haemoglobin from baseline than those patients with orally administered iron at every point at measurement (at 1st week, 2nd week and at term) during the course of the study similar to other studies[19,20].

Conclusion

In our study, intravenous iron sucrose appeared to be more efficacious in increasing hemoglobin level more rapidly than prolonged course of oral iron therapy. It also replenishes iron stores more rapidly than oral iron. The high dose regimen saves time for both patient and health professionals. Intravenous iron therapy in form of iron sucrose provides complete treatment in most of cases within a short period of time and overcomes the issue of noncompliance. We also recommend further studies with newer IV iron formulations to overcome the issue of affordability and the risks of infusion related complications

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