



Comparative Study of Oral versus Parenteral iron therapy in Anemia complicating Pregnancy

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Abstract

Background and Objective: Iron deficiency anemia is the most common form of anemia in pregnancy and also the most common nutritional disorder. Anemia during pregnancy is a significant concern because of its association with adverse pregnancy outcomes. According to WHO, the prevalence of iron deficiency anemia in pregnancy is 40.1%. The objective of this study is to compare the efficacy of oral versus parenteral iron therapy in the treatment of anemic pregnant women.

Materials and Methods: It was a randomized controlled clinical trial conducted in Regional Institute of Medical Sciences. A total of 50 anemic pregnant women meeting the inclusion criteria and giving the informed consent were taken into the study. Those are in the oral group(25), taken two 100 mg ferrous ascorbate and in parenteral (iron sucrose) group(25), was administered 200mg elemental iron in 200ml of normal saline. Results were interpreted after taking Hb % and Serum ferritin levels after 14 and 28 days of administration.

Results: The haemoglobin in oral group after 14 and 28 days of treatment were (9.19±0.49) and (10.76±0.49) and for intravenous group (9.64± 0.45) and (11.41± 0.51) respectively. Serum ferritin values after 28 days of oral and intravenous treatment are (50.68± 2.64) and (60.92± 6.90) respectively. So the p value < 0.001, which was significant.

Conclusion: Intravenous iron sucrose was well tolerated and good patient complaint with comparable efficacy than oral ferrous ascorbate in treating anemic pregnant women.

Keywords: Iron deficiency anemia in pregnant women, iron sucrose, ferrous ascorbate,

Introduction

Iron deficiency anemia is the most common form of anemia in the pregnancy and also the most common nutritional disorder. According to the World Health Organization (WHO), anemia is defined as hemoglobin concentration of less than 11gm/dl (7.45mmol/L) and a hematocrit of less than 33%.

World Health Organisation (WHO) has estimated that prevalence of anemia in developed and developing countries in pregnant women is 18% in developed and 35-75% in developing countries.^(1,2) About 16-40% maternal deaths occur due to anemia. Anemia interferes with normal intrauterine growth leading to fetal loss and perinatal deaths. It is associated with

increased preterm labour(28%), pre eclampsia (51%) and maternal sepsis.^(3,4)

The standard treatment in majority of the institutions is oral iron (OI), with blood transfusion reserved for severe or emergency cases. However, it is unreliable in the treatment of severe anemia. Blood transfusion has its own hazards, including transfusion of wrong blood and deadly infections like HIV, CMV, hepatitis and anaphylaxis.⁽⁵⁾ Thus, there is a need for a safe and effective alternative to OI or blood transfusion in the treatment of anemia. Iron dextran, the first parenteral iron used, lost its popularity due to anaphylaxis. Iron sucrose was then discovered as a parenteral iron that could be safe and effective.

Over the past years, various oral, intravenous and intramuscular preparations of iron have been used for correction of Iron deficiency anemia in pregnant patients. 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.⁽⁶⁾ Parenteral iron is a useful treatment, although iron dextran use decreased due to anaphylaxis. Iron sucrose is a newer agent that has overcome the shortcomings of iron dextran.

The major problem with oral iron therapy in its classic ferrous form is poor tolerability and upto 40% adverse reaction rate.⁽⁷⁾ The most common complaints are nausea, abdominal pain, diarrhoea and constipation. Severe systemic adverse effects associated with iron dextran and iron gluconate limited the use of intravenous iron. Iron sucrose complex (ISC) is a relatively new drug which is used intravenously for the correction of iron deficiency anemia. Iron sucrose complex is a widely used and safe molecule, which has become major interest to prevent iron deficiency anemia.

Iron sucrose is complex of polynuclear iron (III) hydroxide in sucrose for intravenous use. The polynucleariron (III) hydroxide cores are superficially surrounded by large number of non-covalently bound sucrose molecules resulting in a

complex a molecular weight of approximately 60,000 DA, prohibiting renal elimination. The iron in the polynuclear cores is bound in a similar structure to that of physiologically occurring ferritin. The complex is stable and does not release ionic iron under physiologic conditions. Following intravenous administration, iron sucrose is dissociated by the reticulo-endothelial system into iron and sucrose. Common side effects are headache, dizziness, pruritis, rashes etc.

Materials and Methods

The study was conducted at Regional Institute of Medical Sciences, Imphal, Manipur. This was a randomized clinical trial conducted between September 2017 and March 2019. The study protocol was ethically permitted from Institutional Review Committee, Imphal, Manipur.

Inclusion Criteria

- Singleton pregnancy
- Gestational age between 14-34 weeks
- Hemoglobin concentration between 7 gm% to 9 gm%
- Who gave informed consent

Exclusion Criteria

- Medical disorders like tuberculosis, diabetes mellitus, renal and hepatic disorders
- Obstetrics complications like pregnancy induced hypertension, antepartum haemorrhage
- Women with multiple pregnancy
- Intolerance to iron derivatives
- Having history of asthma, eczema or other atopic disease
- Patients with risk of preterm labour
- Recent blood transfusion
- Women who diagnosed with other causes of anemia (sickle cell anemia, haemochromatosis, hemosiderosis, thalassemia)
- Who are not willing to participate in the study

In the group, whom iron was administered intravenously, hospital admission was required for

few patients and the dose for total iron-sucrose was calculated from the following formula: $\text{Weight} \times (\text{target haemoglobin} - \text{actual haemoglobin}) \text{ g/dl} \times 2.4 + 500\text{mg}$, rounded upto the nearest multiple of 100 mg, described by Naz F, Iqbal K et al.⁽⁸⁾

Iron sucrose (inj. Venofer containing ferric hydroxide complex with sucrose equivalent to elemental iron 50 mg in 2.5ml, Wanburry Pvt. Ltd.) was given by intravenous injection on alternate day according to iron deficit calculated for each individual. In each infusion, the maximum total dose administered was 200mg elemental iron in 200 ml of 0.9% NaCl (1:1) initially given at 100ml/hr for few minutes and patient was monitored for any sign of allergic reaction. Later, rest of the infusion was given at 400ml/hr over 30 minutes. The remaining doses were given on alternate days. Infusions were given as outpatient basis in labour room with facilities for acute emergency care.

In the group whom iron was administered orally, two 100mg iron tablets per day (cap. Autrin containing ferrous ascorbate equivalent to elemental iron 100mg, Acme Foundation Pvt. Ltd.) were given for 28 days. No admission into the hospital was needed. Patients were instructed to take the tablets in an .stomach, 2 hours before or after their meals.

Laboratory evaluation was performed at the time of inclusion in the study, on the 14th and 28th days. Initial evaluation included complete blood count and serum ferritin level. On 14th day, haemoglobin concentration was estimated. Finally, haemoglobin concentration and serum ferritin were determined on the 28th day of initiation of therapy. All patients were seen every 2 weeks. During each visit, all adverse events related to the drugs were recorded after physical examinations and direct enquiries of the patients. Adherence to oral treatment was assessed by the number of returned tablets and asking the colour of the stool.

Results

A total of 50 women after fulfilment of inclusion criteria were included in the study. Written informed consent were collected prior to randomization.

Table 1 Hemoglobin level after 14 and 28 days of intravenous iron sucrose and oral iron treatment

Parameter	Treatment with iron		Total	P value
	Intravenous	Oral		
Hb% after 14 days of treatment (gm/dl)	9.64±0.45	9.19±0.49	9.42±0.52	0.002
Hb% after 28 days of treatment (gm/dl)	11.41±0.51	10.76±0.49	11.09±0.59	<0.001

Table – 1 shows that on 14th day, intravenous group had mean ±SD haemoglobin level of 9.64 ± 0.45 gm/dl while in oral group it was 9.19 ± 0.49 gm/dl. This was found to be statistically significant with p-value of 0.002. On 28th day, intravenous group had mean ± SD haemoglobin level of 11.41 ± 0.51gm/dl while in oral group had 10.76 ± 0.49 gm/dl. This was also found to be statistically significant with p-value of <0.001.

Table 2 Comparison of serum ferritin levels after 28 days of treatment

Parameter	Treatment with iron		Total	P value
	Intravenous	Oral		
Serum ferritin after 28 days of treatment (ng/ml)	60.92±6.90	50.68±2.64	55.80±7.31	<0.001

Table- 2 shows that serum ferritin level in both the intravenous and oral group was higher than the baseline level but it was more in intravenous iron- sucrose. Intravenous group had mean ± SD serum ferritin level of 60.92 ± 6.90 ng/ml while in oral group had 50.68 ± 2.64 ng/ml and this was found to be statistically highly significant with p-value of <0.001.

Table 3 Comparison of Side effects/ Reactions between intravenous iron sucrose and oral iron therapy

Side effects/ Reactions	Treatment with iron		Total (n=50)
	Intravenous (n=25)	Oral (n=25)	
Nil	20(80%)	17(68%)	37(74%)
Epigastric discomfort	1(4%)	2(8%)	3(6%)
Nausea	2(8%)	1(4%)	3(6%)
Constipation	0(0%)	2(8%)	2(4%)
Hotflush	2(8%)	0(0%)	2(4%)
Metallic taste	0(0%)	2(8%)	2(4%)
Vomiting	0(0%)	1(4%)	1(2%)

P=0.333, Not Significant

Table -3 shows that only 20% of intravenous group (5 patients) had side effects/ reactions while 80% (20 patients) did not have any side effects. In oral group, 32% (8 patients) experienced side effects while 68% (17 patients) did not have any side effects. Out of the reactions in intravenous group, 1 patient (4%) had epigastric discomfort, 2 patients (8%) experienced nausea, 2 patients (8%) had hot flush, none of the patients had vomiting, metallic taste, constipation. In oral group, 2 patients (8%) had nausea, 1 patient (4%) had nausea, 2 patients (8%) experienced constipation. 2 patients (8%) had epigastric discomfort, 2 patients (8%) had metallic taste, 1 patient (4%) had vomiting, none of the patients had hot flush. This was statistically not significant with p-value of 0.333.

Discussion

Anaemia in pregnancy continues to be a major public health problem affecting 54.96% of the pregnant population. Despite launching the National Anaemia Prophylaxis Programme in 1972, anaemia complicating pregnancy continues to be a major problem with adverse maternal and foetal outcome. Inadequate intake of iron-rich foods, poor environmental sanitation, unsafe drinking water, iron loss due to parasite infestation, adolescent anaemia, along with teenage pregnancies and repeated pregnancies in low resource countries, are the predominant causes for the

disproportionately increased prevalence of iron deficiency anaemia in pregnancy.

The present study was conducted to find out an alternative iron therapy in the form of intravenous iron-sucrose and to determine its therapeutic effectiveness, safety and compliance in the management of anaemic expectant mothers and to compare it with that of oral iron therapy. For this purpose, 50 pregnant anaemic women with gestational age of 14-34 weeks with haemoglobin between 7 – 9 gm/dl were selected, 25 patients were administered intravenous iron sucrose and 25 patients received oral iron.

In this study, haemoglobin level after 14 days of treatment was 9.64 ± 0.45 gm/dl in intravenous group, while in oral group it was 9.19 ± 0.49 gm/dl. Increase in haemoglobin level after 14 days of treatment showed significantly higher level in intravenous group than oral group (p-value = 0.002). This findings are similar to the findings reported by Al Ragip A, Eylem U, et al⁽⁹⁾ where the rise in haemoglobin was significantly higher in intravenous group than oral group after 14 days of treatment with p-value of 0.004.

In this study, haemoglobin level after 28 days of treatment in intravenous group was 11.41 ± 0.51 gm/dl, while in oral group it was 10.76 ± 0.49 gm/dl. The findings of this study are similar to the findings reported by many studies. Naj F, Iqbal K et al⁽⁸⁾ reported an increase in haemoglobin level from 8.7 ± 1.2 gm/dl to 11.1 ± 1.97 gm/dl. Raja KS, Janjua NB et al⁽¹¹⁾ observed that haemoglobin level increased from 7.5 gm/dl to 11.0 gm/dl in 4 weeks. Breyman C⁽¹⁰⁾ in his study found the haemoglobin to be raised from 9.1 gm/dl to 11.0 gm/dl in 4 weeks.

In this study, there was remarkable rise in the haemoglobin level after 28 days of treatment in both oral iron and intravenous iron-sucrose group but more with intravenous iron-sucrose which was statistically significant.

In this study, serum ferritin level in intravenous group was 60.92 ± 6.90 ng/ml with increase from 19.24 ± 3.76 ng/ml after 28 days of treatment. The findings are similar to the findings reported by many studies. Al Ragip A, Eylem U et al⁽⁹⁾ reported increase in serum ferritin from 4.1 ± 2.5 ng/ml to 28 ± 2.6 ng/ml. Sharma JB, Jain S et al⁽¹²⁾ reported increase in serum ferritin level from 7.0 ± 1.67 ng/ml to 23.1 ± 2.27 ng/ml. A slightly higher increase in serum ferritin from 13 to 42 ng/ml was reported by Bhandal N, Russell R.⁽¹³⁾

In the oral group, serum ferritin level after 28 days of treatment was 50.80 ± 2.64 ng/ml from 19.26 ± 3.49 ng/ml. Al Ragip A, Eylem U et al⁽⁸⁾ reported an increase from 5 ± 2.2 ng/ml to 11 ± 1.1 ng/ml. Sharma JB, Jain S et al⁽¹²⁾ in their study found that the increase in serum ferritin after 28 days of oral iron therapy was 7.5 ± 1.84 ng/ml. Kumar A, Jain S et al⁽¹⁴⁾ reported increase in serum ferritin level from 10.93 ± 3.05 ng/ml to 16.68 ± 6.49 ng/ml. Asma S, Boga C et al⁽¹⁵⁾ found the treatment with iron-sucrose to be more expensive than the oral iron.

Thus, this study found that after 28 days of treatment, the difference in serum ferritin levels between the two groups were highly significant with much higher increase in intravenous iron-sucrose group.

Conclusion

It was clearly evident from the present study that parenterally administered iron-sucrose molecule increases the haemoglobin level and restores iron reserve better and earlier than oral iron, which is of paramount importance especially if the patient is in late stage of pregnancy. The mean haemoglobin and serum ferritin levels throughout the treatment were significantly higher in the intravenous iron-sucrose group than in the oral iron group and a significantly higher number of patients achieved the target haemoglobin of 11.0 gm/dl after 28 days of treatment.

Funding: No funding source

Conflict of interest: None declared

Ethical Approval: The study was approved by the Institutional Ethics Committee

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