Parenteral Iron Therapy for Treatment of Moderate to Severe Anemia in Pregnancy

V Gomathi¹, K Kumaresan², K Sivankumar³

ABSTRACT

Introduction: In India, women become pregnant with low baseline hemoglobin levels resulting in high incidence of moderate to severe anemia in pregnancy where oral iron therapy cannot meet the requirement. Pregnant women with moderate to severe anemia are to be treated with parenteral iron therapy. This study was done to evaluate the effect and response of intravenous iron sucrose given to pregnant women with iron deficiency anemia (IDA).

Material and Methods: A prospective observational study was conducted in 90 pregnant women with documented IDA with Hb between 6-9 gms % were given intravenous iron sucrose 200 mg thrice weekly after calculating the dose requirement. Analysis of data was done by using paired T test.

Results: The mean Hb raised from 7.82±0.93 to 11.34 ±0.82 (p<0.0005) after 8 weeks of therapy. There was significant increase in serum ferritin levels from 12.1±5.1 to 67.34±20.5(p<0.0005). Other parameters including serum iron, TIBC, reticulocyte count and MCV were also improved significantly. No major anaphylactic reactions were observed during the study period.

Conclusion: Intravenous iron sucrose therapy was effective in increasing Hb, S.Ferritin and other hematological parameters in pregnant women with moderate anemia.

Keywords: Anemia, IDA, Iron sucrose, serum ferritin, Hb, parenteral iron therapy.

INTRODUCTION

Anemia is one of the most commonly encountered medical disorder during pregnancy. Prevalence of anemia in India is highest in the world. IDA is the most common nutritional anemia in pregnant women. Increased requirement of iron during pregnancy and most of women become pregnant with low Hb level, resulting in higher incidence of moderate to severe anemia in pregnancy. According to WHO, the prevalence of IDA is about 18% in developed countries and 56%(35-75) in developing countries.¹ In India the prevalence ranges from 33-89%.²

Maternal anemia can have serious deleterious effects in mother and fetus such as poor intrauterine growth of fetus, increased risk of preterm birth and low birth weight babies. This intern results in higher perinatal morbidity, mortality and infant mortality rates. In India IDA is directly or indirectly responsible for 40% of maternal deaths.³

WHO defines anemia as Hb<11gms%, 9-11gms% as mild anemia, 7-9 gms% as moderate anemia and severe anemia is < 7 gms%.⁴ The relative prevalence of mild, moderate, severe anemia are 13%, 57% and 12% respectively in India⁵ (ICMR data). In India the ICMR classification of anemia is 10-10.9 gms% as mild, 7-10 gms% as moderate, severe is < 7 and very severe is <4 gms%.⁶ Serum ferritin <12-15μg /l⁷ is considered as iron deficiency.

The treatment of choice for prophylaxis and mild anemia in pregnancy are oral iron therapy. But in patients with moderate to severe anemia, oral therapy takes long time and decreased compliance due to GI side effects, poor bioavailability and malabsorption. So oral iron therapy cannot meet the requirement in moderate to severe anemia in pregnancy. Thus pregnant women with moderate anemia should be better treated with parenteral iron therapy and or blood transfusion depending upon the individual basis (Hemodynamic status and period of gestation).

The parenteral iron preparations available are iron dextran, iron sorbitol citrate, iron sucrose, ferric carboxy maltose, sodium ferric gluconate and sodium isomaltoside. Test dose is necessary before giving intravenous iron dextran as severe anaphylactic reactions were reported with it. Iron sucrose can be given without test dose and it has a favorable safety profile and it is an alternative to other forms of parenteral iron therapy in correction of iron store depletion and correction of anemia during pregnancy.⁸ Hence intravenous iron sucrose is widely used for the treatment of IDA, when oral iron is inappropriate or ineffective or poorly tolerated and blood transfusion is inappropriate.

Therefore a prospective study was conducted in pregnant women with IDA(Hb between 6-9 gms%) to evaluate the response and effect of intra venous iron sucrose in terms of improvement in hemoglobin and other red cell indices.

MATERIAL AND METHODS

This study was conducted in Melmaruvathur Adhiparasakthi Institute of Medical Science and Research from May 2015 to May 2016 after obtaining the ethical clearance from the IRB. 90 pregnant women with documented IDA with Hb between 6-9 gms% were included in this prospective study. Pregnant women with multiple pregnancy, high risk for preterm labour, history of recent blood transfusion and other causes of anemia other than IDA were excluded from this study.

Informed written consent was obtained from all the patients before starting the therapy. All the pregnant women were given antihelminthic therapy with mebendazole 100 mg twice daily for 3 days. Folicacid were given to all women during the therapy. Baseline investigations including blood (LFT, RFT),

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Urinary (routine, microscopy and culture) and stool examination (ova and cyst) were done.

The iron sucrose dose was calculated by using the formula as follows:

Required elemental iron in mg = 2.4 x (normal Hb – patient Hb) x Prepregnancy weight in kg + 1000.

Here, 2.4 is standard co-efficient. Normal Hb is taken as 14 gms.

To the value calculated by above formula 1000 mg is added for replenishment of stores.

The required elemental iron dose varied depending on index Hb and pre pregnancy weight of patients. The dose requirement was 1600 -2200 mg. The duration to complete total therapy was 2.5 to 4.5 weeks.

The iron sucrose was given as outpatient basis, in a dose of 200 mg intravenously, three times a week, in 200 ml of NS over a period of 15-20 minutes.

Patients were observed during transfusion and one hour post transfusion for side effects. FHR was assessed before and after transfusion. Blood samples were collected to measure Hb, serum ferritin and other red cell indices prior to transfusion and again 3, 6 and 8 weeks.

The primary outcome measures were change in Hb concentration and serum ferritin levels after 3, 6 and 8 weeks. Secondary outcome measures were improvement in serum iron level, reticulocyte count, TIBC, MCV, any adverse effects and perinatal outcome (period of gestation at the time of delivery, mode of delivery, fetal birth weight, PPH and need of blood transfusion).

STATISTICAL ANALYSIS

Interpretation and analysis of data was done by using paired T test. \( P < 0.5 \) was taken as significant.

RESULTS

The mean age of women was 25.5 ± 3.4 (19-32 years). The mean period of gestation at the time of diagnosis was 25 ± 5.12 (18-32) weeks. Prior to iron transfusion mean Hb was 7.82 ± 0.93 gms. Out of 90 pregnant women entered into this study 62 women (68.88%) were defined as having moderate anemia and 28 (31.11%) had severe anemia. After completion of therapy mean Hb raised to 11.34 ± 0.82 gms% (Table-1).

Perinatal outcome

Out of 90 pregnant women, 10 (11%) were delivered before 37 weeks (Table-2), the remaining 80 (88.8%) women were delivered at term (> 37 weeks). Of these 58 (64.4%) were delivered vaginally, 22 (24.4%) were delivered by LSCS (elective or emergency). Mean period of gestation at delivery 38.75 ±1.2 (37.2-40.3) weeks. 5 women had PPH (blood loss >500ml) and required packed red blood cell transfusion. The mean birth weight of babies was 2.75 ±430 gms (2.3 -3.2 kg).

Side effects

Six women had low grade fever after first dose which was self limiting. Three women had giddiness and thrombopoeitis. Eight women were complained of nausea. There were no major side effects and no allergic or anaphylactic reactions were observed in our study.

DISCUSSION

Iron requirement are greater in pregnancy than in non pregnant state. Although iron requirements are reduced in the first trimester because of absence of menstruation, they rise steadily thereafter. In the first trimester the daily iron requirement is 0.8 mg, 4-5 mg in second trimester and 6-8 mg in the third trimester. The total iron requirement during pregnancy is about 1000-1200mg. (for growing fetus- 270 mg, Placenta – 90 mg, for expansion of RBC mass – 450 mg and blood loss during delivery – 150 mg). Usually this iron is mobilized from iron stores. However women with poor iron stores become iron deficiency during pregnancy.

Studies have shown that moderate to severe anemia in pregnancy are associated with higher maternal and fetal morbidity, severe anemia is associated with cardiac decompensation and pulmonary edema. Blood loss even 200 ml in third stage of labour can cause shock and death in severe anemia. The stores in Indian women are deficient and they require 100 mg elemental iron per day for prophylaxis. For the treatment of anemia the recommended dose is 200 mg elemental iron per day.

The major challenges in the management of IDA are related to tolerability and side effects of iron therapy in its different forms. Therefore it is crucial to determine the most appropriate form and dose of iron as well as duration of treatment in order to successfully replenish the iron stores.

In a large systematic review and meta analysis involving 75 studies including 10,879 participants in many specialties had shown that intravenous iron was associated with significant increase in standardized mean Hb concentration comp aried with oral iron or no supplementation. 10 Alkakrifiplani, Reetamehay et al, evaluated the effect of intra venous iron sucrose complex in 100 pregnant women with moderate to severe anemia and they found that the mean Hb was raised from 7.63 to 11.20 after 8 weeks of therapy. In our study, 6-9 gms Hb was taken as cut-off, the raise in mean Hb was from 7.82 to 11.34 after intravenous iron sucrose therapy.

### Table-1: Shows the baseline hematological parameters and changes in hematological parameters after intravenous iron sucrose therapy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline Value.</th>
<th>3 weeks</th>
<th>6 weeks</th>
<th>8 weeks</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb, g%</td>
<td>7.82 ± 0.93</td>
<td>8.14 ± 0.84</td>
<td>9.8 ± 0.80</td>
<td>11.34 ± 0.82</td>
<td>( P &lt; 0.0005 )</td>
</tr>
<tr>
<td>S.iron µg/dl</td>
<td>30.8 ± 5.84</td>
<td>39.92 ± 8.96</td>
<td>58.17 ± 13.0</td>
<td>80.45 ± 11.8</td>
<td>( P &lt; 0.0005 )</td>
</tr>
<tr>
<td>TIBC, µg/dl</td>
<td>360.4 ± 39.9</td>
<td>347 ± 16.3</td>
<td>328.8 ± 13.0</td>
<td>311.7 ± 12.0</td>
<td>( P &lt; 0.0005 )</td>
</tr>
<tr>
<td>S.Ferritin µg/l</td>
<td>18.1 ± 5.1</td>
<td>18.6 ± 9.9</td>
<td>20.1 ± 12.4</td>
<td>20.7 ± 12.4</td>
<td>( P &lt; 0.0005 )</td>
</tr>
<tr>
<td>Reticulocyte Count %</td>
<td>1.38 ± 0.54</td>
<td>3.8 ± 0.72</td>
<td>4.5 ± 2.6</td>
<td>5.5 ± 2.0</td>
<td>( P &lt; 0.0005 )</td>
</tr>
<tr>
<td>MCV, fl</td>
<td>65.3 ± 5.8</td>
<td>76.4 ± 5.0</td>
<td>80 ± 5.4</td>
<td>86.6 ± 2.8</td>
<td>( P &lt; 0.0005 )</td>
</tr>
</tbody>
</table>

### Table-2: Shows associated obstetrical complications.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm delivery</td>
<td>10/90</td>
</tr>
<tr>
<td>IUGR</td>
<td>16/90</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>10/90</td>
</tr>
<tr>
<td>PROM</td>
<td>6/90</td>
</tr>
<tr>
<td>GDM</td>
<td>8/90</td>
</tr>
</tbody>
</table>
So the results of our study were similar to their study.11 Several authors have now reported on their experience with use of parenteral iron therapy for IDA in pregnancy with faster increase in Hb and better replenishment of iron stores in comparison with oral iron therapy, particularly demonstrated for iron sucrose.12 Also parenteral iron therapy in pregnancy reduces the need of blood transfusion.13 An observational treatment study was conducted by Wong and smith et al4, of 1000 mg iron dextron administered over one hour for IDA in 189 women in second and third trimester after oral iron failure. All were received a test dose and monitored for adverse effects, about 2% experienced transient infusion reactions. Hb improved by1-1.9 gms% in 82 % and > 2 gms% in 24%. Second trimester was not associated with greater Hb improvement than third trimester treatment. Anemia resolved in 95%. They concluded that administration of single large dose of intravenous iron dextron was safe and convenient. In our study we used iron sucrose and Hb improvement is significant in 2 nd and 3 rd trimester. In a prospective observational study of 65 anemic pregnant women received ferric carboxy maltose upto 15 mg/kg between 24 – 40 weeks of pregnancy and they found that 1 V ferric carboxy maltose infusion significantly increased the Hb above the baseline levels in all women. No serious adverse effects were found, serum ferritin levels increased significantly after the infusion.15 Cristop P et al16, conducted a retrospective analysis of 206 pregnant women who were treated with ferric carboxy maltose or iron sucrose for IDA. They found that ferric carboxy maltose administration in pregnant women was well tolerated and was not associated with relevant clinical safety concern. It has complete safety profile to iron sucrose but offers the advantage of much higher iron dosage at the time reducing the need for repeated transfusion and increasing patients comfort. Breyman17 treated more than 500 antenatal women diagnosed with IDA. Intravenous iron sucrose was given according to calculated dose as either IV push over 5-10 mins or IV infusion over 20-30 mins. All injections were given on outpatient basis without any testdose. This study also emphasizes the safety of iron sucrose injection. In present study all doses of intravenous iron sucrose was given on outpatient basis without any testdose. None of our patient required any emergency care. Bencaiova et al18, conducted a study to assess and compare the efficacy of 2 and 3 doses of iron sucrose with oral iron therapy. There was higher frequency of responders in intravenous group(80%). There was a significant difference in iron stores before delivery in the group with 3 IV iron dose in comparison to oral iron group.(14%, p < 0.001). In their study, no differences were observed in maternal and perinatal outcome. In Indian women, we took 14 as index Hb and 1000 mg for replenishment of iron stores. Even with this, maximin mean ferritin after 8 weeks of therapy was within normal range. The reason could be due to severely depleted iron stores in Indian women.

CONCLUSION

Our results showed that intravenous iron sucrose therapy was effective to treat moderate to severe anemia in pregnancy with negligible side effects. Therefore the use of intravenous iron should be considered as an effective, rapid and safe treatment option in pregnant women with IDA and for effective rapid repletion of iron stores.

REFERENCES


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