Effect of parenteral iron sucrose therapy to improve the feto-maternal prognosis related to iron deficiency anemia

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ABSTRACT

Background: The objective was to determine the effect of parenteral iron sucrose therapy to improve the feto-maternal prognosis related to iron deficiency anemia.

Methods: This was a longitudinal study conducted among 205 women admitted in an outpatient clinic of a tertiary care hospital and received iron sucrose. The iron sucrose dose was calculated from the following formula: weight before pregnancy (kg) - (110 g/L – actual hemoglobin [g/L]) X 0.24 + 500 mg. Treatment efficacy was assessed by measuring hemoglobin ferritin and other hematological parameters on the 30 th day, at delivery and at first day of postpartum.

Results: Hemoglobin level was significantly (p<0.001) increased from baseline (8.33±1.13) to 30 th (9.45±1.02), at delivery (11.89±0.89) and at first postpartum day (12.15±1.11). However, TIBC significantly (p=0.01) decreased from baseline to first postpartum day. Significant (p<0.0001) increase was also noted in serum ferritin and serum folate levels from baseline to 30 th day, at delivery and at first postpartum day. MCV and MCH were significantly (p=0.01) increased from baseline to only at delivery and at first postpartum day. Percent change analysis showed that there was higher change in serum ferritin and serum folate levels than Hb, MCV and MCH levels. About one third (34%) of the patients did not complain any complications during supplementation.

Conclusion: With regard to the use of intravenous iron in obstetrics, there is increasing evidence that iron sucrose is safe for the mother and the fetus using the recommended dosages and therapy regimens.

Keywords: Postpartum, Parenteral iron sucrose, Anemia, Hematological parameters

INTRODUCTION

Worldwide, iron deficiency is the most common cause of anemia in pregnancy. 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. Intravenous iron therapy is reserved for a small number of patients in whom oral treatment fails or for whom iron loss exceeds intake that can be met by oral therapy. Iron sucrose is reported to be safe and effective for the management of anemia, and it can be administered without a test dose.¹³

Anemia leads to an increased risk of blood transfusion during the peripartum period. Iron therapy during pregnancy may reduce the transfusion rate for the iron-deficient women¹ (Dickason 1992). However, there may not be enough time for the treatment of anemia until term. Iron dextran does not induce an erythropoietic response more rapidly than oral iron replacement while use of iron requires several weeks after administration of iron dextran. Thus, the rise in hemoglobin concentration is only slightly faster than that after oral iron treatment.
In past, few studies compared intravenous iron sucrose treatment with oral iron treatment during pregnancy.5,6 However, there are some controversies between these studies. One alternative is the parenteral administration of iron sucrose. The high plasma iron concentrations that occur shortly after intravenous administration bypasses the limited release of iron from the reticuloendothelial system and inhibited absorption through the intestinal mucosa, thus delivering sufficient quantities of iron for erythropoiesis. As in pregnancy, we follow an incremental treatment plan using parenteral iron sucrose at Hb levels below 9.5 g/dL.7

The treatment of postpartum anemia depends on the severity of the anemia and/or additional maternal risk factors or co-morbidities. A young, healthy woman can compensate for heavy blood losses far better than a puerpera with a heart defect who may decompensate even after less severe losses. In addition, blood losses need to be viewed in relation to the body mass and the estimated total blood volume. Another consideration is that significant errors can be made particularly when estimating blood loss. Blood loss is often underestimated, which can readily be verified by comparing pre-partum and postpartum Hb levels.

Oral iron supplementation is usually enough for most of the antenatal women. But intolerance to iron, abnormalities in absorption and non-compliance may make oral iron therapy in some women inadequate and these can be benefited from parenteral iron therapy. Iron sucrose is a suitable alternative source of iron. It can be administered by intra venous infusion. It is well tolerated and safe but may cause hypotension, nausea and low back pain.8,9 Intravenous iron, alone or in association with recombinant human erythropoietin (rHuEPO), has been considered as an alternative in the management of iron deficiency in many settings setting.10

The purpose of this study was to determine the effect of parenteral iron sucrose therapy to improve the fetomaternal prognosis related to iron deficiency anemia.

METHODS

The study was a longitudinal cohort study conducted in a tertiary care hospital in northern India. Patients were recruited from the antenatal clinic of the hospital. Eligible participants were pregnant women, between the 26th and 34th weeks of gestation, with established iron deficiency anemia who had hemoglobin levels 9 g/dL and ferritin levels less than 13 μg/ L. Women were excluded when serum folate and vitamin B12 levels were found to be less than 4 pg/mL and 100 pg/mL, respectively. Anemia from causes other than iron deficiency, multiple pregnancy, previous blood transfusion, history of hematological disease, risk of preterm labor, intolerance to iron derivatives, recent administration of iron for the treatment of iron deficiency anemia, or current usage of iron supplement were the reasons for other exclusions. All eligible women who applied to the antenatal clinic of the hospital during the study period were invited to participate in the study; those who gave informed consent were consecutively enrolled.

In the group of patients to whom iron was administered intravenously, the dose for total iron sucrose was calculated from the following formula: weight X (target hemoglobin - actual hemoglobin) X 0.24 + 500 mg, rounded up to the nearest multiple of 100 mg.6 In the formula, weight represented the patient’s weight before pregnancy in kilograms; target hemoglobin in grams per liter was set at 110 g/L. In each infusion, the maximum total dose administered was 200 mg elemental iron in 100 mL 0.9% NaCl, infused in 20-30 minutes. No test dose was given. Total dose was administered over 5 days and maximum daily dose administered was 400 mg elemental iron. Most of the patients received iron sucrose at the rate of 200 mg every other day. Treatment was completed after administration of the calculated dose. Additional oral iron was not administered during the study. Iron-sucrose infusions were administered in the perinatology unit at an outpatient setting, and all patients were observed for 1 hour after the infusions. All adverse events after each infusion of elemental iron were identified by physical examination and direct inquiry of each patient, using standard forms encoded for adverse events. Blood pressure was measured before, during, and after each infusion, and hypotension was recorded as an adverse event if it was clinically significant.

The primary outcome measure was hemoglobin concentration on day 30, at birth and at first postpartum day. Secondary outcome measures included ferritin levels, the recorded adverse effects, and fetal birth weight. Laboratory evaluation was performed at the time of inclusion in the study, at birth and on the first postpartum day. Initial evaluation included complete blood count, total iron binding capacity (TIBC), serum ferritin, folate (Fe), MCV and MCH. We enrolled a total of 246 pregnant women during 6 month study period, of these 205 women get delivered in the hospital. Thus, we analyzed 205 women during pregnancy and after delivery.

Analysis

Data was analysed by using SPSS 16.0 version. The results are presented in mean±SD and percentages. The paired t-test was used to compare the changes in the hematological parameters from baseline to subsequent follow-ups. The p-value<0.05 was considered as significant.

RESULTS

Table 1 depicts the baseline maternal and neonatal profile. On follow-up, 2 patients developed hypertensive disorder of pregnancy. One of them was admitted at the
40th week of gestation with severe preeclampsia. The other patient developed mild gestational hypertension at the 41st week. Both patients delivered vaginally without complications. Table 2 presents the effect of parenteral iron sucrose therapy on hematological parameters. Hemoglobin level was significantly (p<0.001) increased from baseline (8.33±1.13) to 30th (9.45±1.02), at delivery (11.89±0.89) and at first postpartum day (12.15±1.11). However, TIBC significantly (p=0.01) decreased from baseline to first postpartum day. Significant (p<0.0001) increase was also noted in serum ferritin and serum folate levels from baseline to 30th day, at delivery and at first postpartum day. MCV and MCH were significantly (p=0.01) increased from baseline to only at delivery and at first postpartum day.

Table 1: Maternal and neonatal profile.

<table>
<thead>
<tr>
<th>Profile</th>
<th>n=205</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>26.18±5.32</td>
</tr>
<tr>
<td>Weight in kg</td>
<td>56.34±4.34</td>
</tr>
<tr>
<td>Gestational age at enrolment in weeks</td>
<td>30.07±2.73</td>
</tr>
<tr>
<td>Gestational age at delivery in weeks</td>
<td>33.45±3.45</td>
</tr>
<tr>
<td>Neonatal weight (gms)</td>
<td>3356.66±332.45</td>
</tr>
</tbody>
</table>

Table 2: Effect of parenteral iron sucrose therapy on hematological parameters.

<table>
<thead>
<tr>
<th>Hematological parameters</th>
<th>Baseline (n=205)</th>
<th>30th day (n=205)</th>
<th>At delivery (n=205)</th>
<th>At first postpartum day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dl)</td>
<td>8.33±1.13</td>
<td>9.45±1.02</td>
<td>11.89±0.89</td>
<td>12.15±1.11</td>
</tr>
<tr>
<td>TIBC (µg/dl)</td>
<td>154.66±38.84</td>
<td>152.34±39.34</td>
<td>149.12±32.56</td>
<td>145.02±29.87</td>
</tr>
<tr>
<td>Serum ferritin (µg/L)</td>
<td>17.68±2.1</td>
<td>21.34±3.24</td>
<td>28.45±3.27</td>
<td>33.86±21.22</td>
</tr>
<tr>
<td>Serum folate</td>
<td>44.52±19.60</td>
<td>47.56±18.56</td>
<td>66.34±21.45</td>
<td>82.55±49.54</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>76.12±5.41</td>
<td>76.38±5.37</td>
<td>77.29±5.53</td>
<td>80.72±6.75</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>27.10±3.87</td>
<td>27.87±3.68</td>
<td>28.56±3.45</td>
<td>29.24±3.65</td>
</tr>
</tbody>
</table>

Hb-hemoglobin; TIBC- total iron binding capacity, MCV, mean corpuscular volume, MCH- mean corpuscular volume

1p<0.001, 2p=0.01, 3p<0.0001 (p-values are from baseline to subsequent follow-ups, Paired t-test)

Percent change analysis showed that there was higher change in serum ferritin and serum folate levels than Hb, MCV and MCH levels (Figure 1).

About one third (34%) of the patients did not complain any complications during supplementation. However, 22% had metallic taste, 21% constipation and 11% nausea. Less than 10% of the patients had symptom of dizziness and vomiting (Figure 2).
DISCUSSION

Oral iron therapy is the most widely prescribed treatment for iron deficiency anaemia; however, there are many issues that may prevent oral iron supplementation from successfully managing iron deficiency anaemia. For instance, many patients do not respond adequately to oral iron therapy due to difficulties associated with ingestion of the tablets and their side effects. Side effects may play a significant role in rates of compliance.11,12 Furthermore, the presence of bowel disease may affect the absorption of iron and thereby minimize the benefit received from oral iron therapy.13 In the past, intravenous iron had been associated with undesirable and sometimes serious side effects and was therefore limited in use.14 However, in recent years, new type II and III iron complexes have been developed which are better tolerated and can be used for rapid repletion of iron stores.15-17 Despite the increasing evidence of the safety of the newer preparations, both in pregnant and general populations, intravenous iron continues to be underutilised because of previous concerns with tolerability of older intravenous iron preparations.18-19

The present study confirmed that parenterally administered iron-sucrose elevates hemoglobin and restores iron stores during the treatment of mild iron deficiency anemia in pregnancy. The mean hemoglobin and ferritin levels as well as other hematological parameters throughout the treatment were significantly increased in the intravenously administered from baseline to subsequently follow-ups. A significantly higher number of patients achieved the targeted hemoglobin at delivery and at first postpartum day. Intravenous iron sucrose produces a more rapid increase in hemoglobin concentration than oral iron and intramuscular iron dextran.20 Iron sucrose was approved in the treatment of iron deficiency anemia in patients undergoing chronic hemodialysis receiving supplemental erythropoietin therapy. Two studies compared iron sucrose with orally administered iron in the treatment of iron deficiency anemia in pregnancy.5,6

Iron sucrose was well tolerated with no serious adverse effects. It has a lower incidence of adverse allergic reactions, and death from anaphylactic events has not been reported yet.7 Most of the symptoms in the present study were mild, and no patient discontinued the medication. Major disadvantages of intravenous treatments are cost, need for hospitalization or an outpatient setting, and the invasive nature of the procedure. However, it may be considered an alternative to oral iron in the treatment of pregnant women with severe iron deficiency anemia during the third trimester.

CONCLUSION

With regard to the use of intravenous iron in obstetrics, there is increasing evidence that iron sucrose is safe for the mother and the fetus using the recommended dosages and therapy regimens. Iron sucrose is effective in pregnancy and in the postpartum period in patients.

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REFERENCES


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