Iron Deficiency Anemia In Pregnancy: Pre And Post Iron Sucrose Therapy In A Tertiary Referral Centre

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Abstract:
Introduction: Iron deficiency is commonly prevalent in women of reproductive age group. Early detection of iron stores before the development of anemia is beneficial. The maternal iron level is important for the growth of fetus and is always advantageous to have parameters which can detect iron deficiency at an early stage. The timely implementation of intervention to correct maternal iron status will improve the fetal outcome.

Objectives: To study levels of serum transferrin, iron and serum ferritin during pregnancy, pre and post intravenous Iron sucrose therapy in iron deficiency anemia.

Materials and Methods: Case control study was conducted on 60 pregnant women reporting to antenatal clinic between 18-34 weeks gestational age. Samples were collected and analysed from diagnosed cases of Iron deficiency anemia for Serum Iron, Ferritin and Transferrin before and after intravenous iron sucrose therapy and were compared with that of normal pregnant ladies.

Result: The hemoglobin levels were 11.97±1.09% in controls and 8.21±1.1% and 10.64±1.5% in cases on Day 1 and day 28. The Serum iron was 133.83±32.4µg/dl in controls and 20.66±10.01µg/dl and 79.97±40.32µg/dl in cases on day 1 and 28. Similarly serum ferritin was 35.6±7.85 µg/L, 13.25±10.7 µg/L and 40.2±62 µg/L respectively in normal pregnant women and iron deficient women pre and post iron sucrose therapy. The serum transferrin in controls was 271.31±35.13mg/dl and in cases were 471.05±70.6mg/dl on day 1 and 427.6±83.51mg/dl on day 28. All were statistically significant.

Conclusion: The finding of the present study suggests that serum iron, ferritin and transferrin levels measurement could be a better parameter for predicting iron deficiency in pregnancy and can be advised along with other routine hematological investigations.

Key Words: Anemia, Pregnancy, intravenous Iron sucrose, Serum Iron, Ferritin, Transferrin.
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II. Materials And Methods

The study was conducted at Bangalore Medical College and Research Institute, Department of Clinical Biochemistry, Victoria hospital, and the study groups were from Vani vilas hospital, Bangalore. The ethical committee clearance was taken from the Institution. The project was funded by National Rural Health Mission (NRHM). The samples were collected from 30 normal pregnant females aged 20 to 40 years of age, between 18 to 34 weeks gestational age, who had complaints of generalized weakness, but the cases who had history of pregnancy induced hypertension, gestational diabetes, epilepsy, thyroid or psychiatric disorders were excluded from the study. Selection of the cases were made on basis of history given, clinical examination, hemoglobin and peripheral smear done.

7ml of venous blood was collected from both cases and controls into plain and edta vacutainers under aseptic precautions after obtaining informed consent. The investigations done in the collected sample included Hemoglobin, reticulocyte count, peripheral smear in the whole blood and iron, ferritin, transferrin in the serum. Iron, Ferritin and transferrin were considered as indicators of iron deficiency anemia. The hemoglobin levels less than 10gm%, and PBS with microcytic and hypochromic blood picture were diagnosed as anemic. These patients were administered with intravenous infusion of 200mg iron sucrose diluted in 100ml normal saline over a period of 30minutes; was repeated up to three times a week. [The required dose of injection was calculated according to the formula (2.4xpregnancy weight in kg x Hb%deficit(11-actual Hb% of patient) in mg]. All participants were given protein powder as part of therapy. The repeat analysis of the samples for the same parameters was also done on day 28 of the start of the therapy. Biochemical analysis of the samples was done in fully automated random access chemistry analyzer Cobas Integra 400 plus, Roche make.

III. Results

Data was analysed with Microsoft excel and Statistical software using Unpaired ‘T’ test

**Table 1** showing Mean,S.D,SEM, t value, p value of Controls and cases on Day 1 (Pre Iron sucrose therapy)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Groups</th>
<th>Mean±S.D</th>
<th>SEM</th>
<th>t1 value</th>
<th>p1 value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>Controls Cases-Day 1</td>
<td>11.97±1.09</td>
<td>2.03</td>
<td>14.41</td>
<td>p1&lt;0.0001</td>
<td>Very highly significant</td>
</tr>
<tr>
<td>Serum Iron</td>
<td>Controls Cases-Day 1</td>
<td>13.3±3.2</td>
<td>20.66</td>
<td>14.86</td>
<td>p1&lt;0.0001</td>
<td>Highly significant</td>
</tr>
<tr>
<td>Serum Ferritin</td>
<td>Controls Cases-Day 1</td>
<td>35.6±7.85</td>
<td>13.25</td>
<td>6.33</td>
<td>p1-0.4206</td>
<td>Not Significant</td>
</tr>
<tr>
<td>Serum Transferrin</td>
<td>Controls Cases-Day 1</td>
<td>271.3±55.13</td>
<td>471.67</td>
<td>20.01</td>
<td>9.50</td>
<td>p1&lt;0.0001</td>
</tr>
</tbody>
</table>

S.D – Standard deviation
SEM – Standard error of mean
t1 – t value between Controls and Day 1
t2 – t value between Day 1 and day 28
p1 – p value between Controls and Day 1
p2 - p value between Controls and Day 28

Data was analysed with Microsoft excel and Statistical software using Paired ‘T’ test

**Table 2** showing Mean,S.D,SEM, t value, p value of cases (Day 1 and Day 28) Pre and post iron sucrose therapy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Groups</th>
<th>Mean±S.D</th>
<th>SEM</th>
<th>t1 value</th>
<th>p1 value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>Cases-Day 1 Cases-Day 28</td>
<td>8.2±1.14</td>
<td>10.64</td>
<td>9.33</td>
<td>P2&lt;0.0001</td>
<td>Extremely statistically significant</td>
</tr>
<tr>
<td>Serum Iron</td>
<td>Cases-Day 1 Cases-Day 28</td>
<td>20.66±10.01</td>
<td>79±40.32</td>
<td>7.81</td>
<td>P2&lt;0.0001</td>
<td>Extremely statistically significant</td>
</tr>
<tr>
<td>Serum Ferritin</td>
<td>Cases-Day 1 Cases-Day 28</td>
<td>13.25±10.7</td>
<td>40.2±60.5</td>
<td>2.28</td>
<td>P2&lt;0.0302</td>
<td>Statistically significant</td>
</tr>
</tbody>
</table>

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The pregnancy itself contributes to an oxidative stress condition. It has been demonstrated that hypoxia and the resultant decrease in the oxygenation of RBC-hemoglobin destabilizes hemoglobin increasing the rate of hemoglobin autoxidation. This relationship between hypoxia and red cell oxidative stress explains how anemia generates redcell oxidative stress. With fewer RBCs and less hemoglobin available the consumption of oxygen by the tissues lowers the partial pressure of oxygen and a greater fraction of the RBC oxygen is transferred to the tissues. The increase in partially oxygenated hemoglobin increases autoxidation generating metHb and superoxide. Most of the metHb formed during autoxidation is reduced back to functional Fe(II) hemoglobin by cytochrome b5 reductase. However, the excessive autoxidation of hemoglobin that results from anemia is not fully reduced and an increase in methemoglobin is observed. Iron-deficiency anemia is considered the most widespread pregnancy-associated pathological condition.

The release of oxygen from maternal hemoglobin (Hb) is favored by the lower partial pressure of oxygen in the placental cellular structure and fetal circulation (rich in fetal hemoglobin), which has a greater affinity for oxygen, and by the release of fetal and placental metabolites (the placenta produces abundant lactic acid), which lower blood pH causing a displacement of the Hb dissociation curve favoring oxygen delivery. Initially the placenta, has a hypoxic environment. As it matures and its vascularization develops, it changes to an oxygen-rich environment and its abundant mitochondrial mass favors the production of reactive oxygen species (ROS), which increases free iron liberated from iron-sulfur clusters.

In the present study there was a significant decrease in Hb in the anemic group as compared to the control group. But after the iron sucrose therapy there was an increase in the Hemoglobin level of the anemic patients on day 28. An elevated hemoglobin concentration is usually the result of 2 mechanisms: increased red blood cell production as a compensatory mechanism when blood oxygen carrying capacity is compromised to meet the demand of tissue (with a net increase in red cell mass), or contracted plasma volume resulting in an appearance of greater red cell volume (without a net increase in red cell mass).

Authoritative international groups, such as the International Nutritional Anemia Consultative Group and the World Health Organization, have recommended universal supplementation of iron from the second trimester onwards. Oral iron therapy has been effective in correcting IDA in most cases. Its efficacy however is limited in many women especially in pregnancy because of dose-dependent side effects, poor compliance and insufficient absorption. Considering inadequate effects of oral iron therapy, particularly in later months of pregnancy, it was pertinent to try an alternative treatment for IDA to achieve optimum health of mothers without risk various parenteral iron preparations like sodium ferric gluconate are considered safer than iron dextran but study reported 74 adverse events attributed to ferric gluconate complex and was reported to WHO. Therefore, considering significant adverse reaction to iron dextran and other similar molecules iron sucrose has been considered as an effective alternative in the management of IDA.

Iron sucrose molecule is a type II iron complex of intermediate stability and unique iron distribution profile makes iron sucrose clinically safe. Moreover, as complexes contain no biological polymers, anaphylactic reactions are unlikely and makes these preparations safe to use in pregnancy. Iron sucrose is favored by the lower partial pressure of oxygen and a greater fraction of Hb dissociation curve favoring oxygen delivery.

IV. Discussion

The serum iron levels and ferritin levels were also increased as compared to the normals in day 1 as well as day 28 after administration of iron sucrose. Parenteral iron sucrose complex has several advantages because it has a low allergenic properties with an extremely low incidence of severe side effects such as anaphylactic reactions. Modern intravenous iron formulations have emerged as safe and effective alternatives for anemia management, as they present several advantages over oral supplementation. The administration of intravenous ironables a fivefold erythropoiesis response to significant bloodloss anaemia in normal individuals. Hb starts to rise after a few days. Each iron product is taken up into the RES, where the shell is degraded for iron to become bioavailable.
The serum transferrin level in controls was 271.31±35.13, in day 1 was 464.05±67.72 and decreased on day 28 (429.9±83.83). Transferrin is the glycoprotein responsible for the transport of iron and is upregulated in serum during iron deficiency to maximize the efficiency of iron transport from the intestine to tissues [24, 25].

The serum transferrin raise in cases is in accordance with the studies made by Shailesh et al and chaudhari et al[25, 26, 27] except for that their studies were based on LII and III trimesters. Serum transferrin carries iron from the maternal circulation to transferrin receptors located on the apical surface of the placental syncytiotrophoblast, holotransferrin is endocytosed, iron is released, and apotransferrin is returned to the maternal circulation. The free iron then binds to ferritin in placental cells where it is transferred to apotransferrin, which enters from the fetal side of the placenta and exits as holotransferrin into the fetal circulation. This placental iron transfer system regulates iron transport to the fetus. When maternal iron status is poor, the number of placental transferrin receptors increases so that more iron is taken up by the placenta. Excessive iron transport to the fetus may be prevented by the placental synthesis of ferritin[28].

There are various investigations available nowadays which can diagnose and describe anemia accurately. Although, there could not be a single parameter for solving this problem. The finding of the present study suggests that serum transferrin level measurements could be a better parameter which can be advised along with other routine hematological investigations. At tertiary level health institution there is still more possibilities available for research to be done in this field. The drop out of subjects during follow up antenatal visits and at the time of delivery limits the number of subjects included in the study. Considering the cost for serum ferritin and transferrin estimation during entire duration of pregnancy effort should be undertaken to reduce cost of tests so that benefits of medical advancement can be afforded.

V. Conclusion

Iron deficiency Anemia is the most widespread pregnancy associated pathological condition. It is associated with preterm delivery and small for gestational age fetus. Pregnancy itself is known to induce oxidative stress. Anemia is known to promote oxidative stress due to inadequate tissue oxygen supply. This paper explores potential biological mechanisms that might explain how iron deficiency anemia related parameters can assess the outcome of storage parameters of iron in relation to intravenous iron sucrose therapy.

References

[4]. Ferrous iron administration during pregnancy and adaptational oxidative stress (Pilot study) Aune Rehema, Kersti Zilmer, Ursula Klaar1, Helle Karro1, Tiu Kullisaar, Mikhail Zilmer,Medicina (Kaunas) 2004; 40(6):547-552.

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