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# Effectiveness and Safety of Intravenous Iron Sucrose Therapy in Moderately Anaemic Pregnant Women in Third Trimester

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**Abstract:** ***Background- Anaemia is the commonest medical disorder encountered during pregnancy and is an important cause of maternal mortality and morbidity. According to WHO the prevalence of iron deficiency anaemia is about 18% in developed countries and 35-75 per cent (average 56%) in developing countries. Many pregnant ladies in developing countries have low iron stores and their baseline Hb is low before pregnancy. As such oral iron supplements fail to raise the Hb and also compliance and absorption is low because of various factors.*** **Aims and Objectives:** ***1. Estimation of Hb and serum ferritin levels in anaemic pregnant women in third trimester. 2. Evaluate the response to intravenous iron sucrose in such ladies. Methods and materials: 100 anaemic pregnant women with Hb level between 7-9.9g/dl and gestational age between 32-35 weeks and S. ferritin level less than 12 ng/ml are given injection iron sucrose after calculating the iron deficit. Hb and serum ferritin rise were noted after 4 weeks. Patients were also observed for any adverse effects and demographic factors affecting anaemia were also noted. Results: The mean rise of Hb after treatment with intravenous iron sucrose was from 8.0±0.59 to 10.9±0.73g/dl which is statistically significant (p<0.0001). The serum ferritin level increased from a mean of 8.6±1.6 to 31.9±7.7ng/ml which was found to be statistically significant (<0.0001). Minor adverse effects were noted in 7% of cases. Target haemoglobin of 11g/dl was achieved by 68% patients. Conclusion: Intravenous iron can be effectively and safely used among anaemic pregnant women. It caused significant rise in Hb and iron stores, which is depicted by improvement of serum ferritin level within a short time which helps to cope up easily with excessive bleeding during delivery. Hence, it may help to reduce the need for blood transfusion and the associated risks.***

**Keywords:** iron deficiency _ pregnancy _ serum ferritin, Hb: Haemoglobin _ iron sucrose

## 1. Introduction

Anaemia is the commonest medical disorder encountered during pregnancy and is an important cause of maternal mortality and morbidity. According to the FOGSI-WHO study (1997), anaemia is responsible for 64.4% of maternal deaths in India and is the second most common cause of maternal mortality in India. WHO defines anaemia in pregnancy as Hb concentration of less than 11gm/dl and a haematocrit of less than 33% [1].The centre for disease control and prevention (CDC) (1998) defines- anemia in iron supplemented women using a cut-off of the 5$^{th}$ percentile-11g/dl in the first and third trimesters, and 10.5g/dl in the second trimesters of pregnancy [2]. Using 11gm/dl as cut-off for definition of anaemia is probably too high for India and hence Federation of Obstetrics and Gynaecological Societies of India (FOGSI) has suggested a cut off of haemoglobin of 10gm/dl for India [3].

The best parameter of maternal iron status currently available is serum ferritin concentration. Iron deficiency in pregnancy has been defined by the National Academy of Sciences Panel On Nutrition and Pregnancy as serum ferritin levels lower than 12 ng per ml [4]. The first choice for prophylaxis and treatment of mild iron deficiency anaemia in pregnancy is oral iron therapy. But in patients with moderate and severe anaemia, oral therapy takes long time and compliance is an issue. Thus, pregnant women with moderate anaemia should be better treated with parentral iron therapy and/or blood transfusion depending upon degree of anaemia, hemodynamic status, period of gestation, *etc*. Initially, iron dextran and iron sorbitol citrate was started but severe anaphylactic reactions were reported with intravenous iron dextran and test dose was required before giving it. Iron sucrose is a complex of polynuclear iron III – hydroxide in sucrose for intravenous use. Its i.v. route makes availability of elemental iron for incorporation at the pro-erythroblast stage and hence it can provide quick rise in Hb within 5 to 7 days. Iron sucrose has been reported to be safe and effective during pregnancy [5] and can be given without test dose [6]. It has showed to be effective in achieving target Hb of 11g/dl in upto 80% of patients [7]. The early rise in Hb levels is crucially important during final period of pregnancy, as there is reduction in the risk of blood transfusion during peripartum period which thereby decreases the rate of maternal mortality.

## 2. Materials and Methods

This study is a hospital based prospective study which was carried out for twelve months from 1$^{st}$ June 2015 to 31$^{st}$ May 2016 in the Department of Obstetrics & Gynaecology, Gauhati Medical College and Hospital, Guwahati, Assam. The study population consisted of 100 anaemic pregnant patients attending the antenatal outpatient department or admitted in ante natal ward in Gauhati Medical College and Hospital, Guwahati, Assam and who fulfilled the Inclusion criteria of Pregnancy with period of gestation from 32 to 35

weeks having iron deficiency anaemia with Hb levels between 7 to 9.9 g/dl and serum ferritin levels less than 12 ng/ml. Exclusion criteria were pregnant women with Hb level above 10g/dl, gestational age below 32 weeks and above 35 weeks, medical disease like chronic liver disease, renal disease, heart disease, malaria, tuberculosis etc, hypersensitivity to iron, high risk of preterm labour, history of recent blood transfusion, haemoglobinopathies, haemolytic anaemia. The study protocol was approved by the institutional ethics committee. Written & Informed consent was obtained from each subject.

After taking detailed history and doing the general, systemic and obstetrics examination and routine investigation, 100 patients were randomly selected. Special investigation required for the study was advised. Iron deficiency anaemia was diagnosed on the basis of red cell indices by automated cell counter and peripheral blood examination by pathologists at pathology department of our institute, serum iron and serum ferritin level. Hb electrophoresis and HbA2 estimation was done by HPLC, when it was indicated, to exclude beta thalassemia trait.

100 anaemic patients were given injection iron sucrose after calculating the iron deficit. Total iron deficit = body weight (in kg) x (target Hb-actual Hb) x 2.4 +500 mg if weight >35 kg or 15 mg/kg body weight if weight <35 kg, W = Weight; taken was pre-pregnancy weight or at the time of first visit. Target Hb was taken as 11 gm /dl. Patients received divided doses of 200 mg each on alternate days. Dose of 200 mg was diluted in 200 mL of normal saline & administered as intravenous infusion. Patients were observed for adverse effects or anaphylactic reactions.

The primary outcome of the study was increase in Hb & serum ferritin levels over 4 weeks. Secondary outcome measures were to observe for any adverse effects, demographic factors affecting anaemia in pregnancy, maximum and minimum dose of injection iron sucrose required, percentage of patients achieving target haemoglobin, and need of blood transfusion. Data was entered in the predesigned proforma. Entire data was expressed by the descriptive statistics i.e. mean and standard deviation. For quantitative data, difference between means was measured by student's paired t test. If p value was less than 0.001, the difference was considered to be statistically significant. The qualitative variables like economic class (lower, middle, upper) and efficacy of drug was presented by calculating the percentage.

## 3. Results and Observations

In our study, 47 patients had Hb level between 7-7.9g/dl, 46 patients between 8-8.9g/dl and only 7 patients had Hb between 9-9.9g/dl.13 patients had serum ferritin level between 4-6.9ng/ml, 64 patients had level between 7-9.9ng/ml and 23 patients had level between 10-11.9ng/ml. The Hb level increased significantly ($p<0.0001$) from 8.0±0.59 to 10.9±0.73g/dl after 4 weeks of treatment with iron sucrose injection (Table 1). The target haemoglobin of 11g/dl was achieved by 68% patients (Table 2). Minimum and maximum dose of injection Iron sucrose dose required was 735mg & 1124mg respectively. The serum ferritin value increased from a mean of 8.6±1.6 to 31.9±7.7ng/ml which was found to be statistically significant (<0.0001) (Table3). Out of 100 anaemic pregnant patients it was noted that 80% of the study population belonged to the age group of 20-30 years. The mean age and standard deviation of the study population was found to be 23.9±4.1 years respectively. Anaemia was more common in the low socio-economic class of people of which 70% belonged to class IV and 20% belonged to class V according to B.G.Prasad's Socio-economic status classification for 2013.Majority of the patients(72%) were illiterate, 91% of anaemic patients had less than 4 ante-natal check-up, anaemia was more common in patients who had inter-pregnancy interval of <1 years (45%), 91% of the patients had taken iron supplements prior to their first visit, 52% of the anaemic patients were multigravida and 48% were primigravida, (69%) of the patient belonged to Hindu religion, 95% of the anaemic patients consumed non –vegetarian diet and only 5 % consumed vegetarian diet, (68%) of the anaemic patients were from rural area and 32% from urban area. In our study majority of the patients (69%) were asymptomatic at the time of first visit. Mild adverse reactions were seen in 7 patients (3 had swelling at injection site, 3 had pain at injection site and 1 had low grade fever). This symptom was treated symptomatically and no serious side effects were noted.

**Table 1:** Showing means of pre-treatment and post treatment haemoglobin levels

| *Haemoglobin level(g/dl)* | *Mean* | *SD* |
|---|---|---|
| Before therapy | 8.0 | ±0.59 |
| After therapy | 10.9 | ±0.73 |

**Table 2:**. Showing patients achieving target haemoglobin

| *Haemoglobin(g/dl)* | *No. of cases(n=100)* | *Percentage (%)* |
|---|---|---|
| <11 | 32 | 32 |
| >11 | 68 | 68 |
| Total | 100 | 100 |

**Table 3:** Showing means value of pre-treatment and post treatment serum ferritin values

| *Serum ferritin(ng/ml)* | *Mean* | *SD* |
|---|---|---|
| Before therapy | 8.6 | ±1.6 |
| After therapy | 31.9 | ±7.7 |

**Table 4:** Showing adverse effects of iron sucrose injection

| *Adverse effects* | *No. of cases (n=100)* | *Percentage (%)* |
|---|---|---|
| Swelling at injection site | 3 | 3 |
| Pain at injection site | 3 | 3 |
| Low grade fever | 1 | 1 |
| None | 93 | 93 |
| TOTAL | 100 | 100 |

## 4. Discussion

In our study 80% of patients belong to the age group of 20 to 30 years, having a mean age of 23.9 ±4.1 years which was comparable with study of Swami M.B.et al [8], Dipti A. et al [9], DK Singh et al [10], Prassana B et al [11], Sunita D et al [12]. The probable explanation of higher occurrence of anaemia in this age group is that, in India most women get married at this age group. Mean rise in Hb levels from the

baseline to day 30 was 2.9±0.6g/dl ($p<0.0001$) which is statistically significant. Ragip et al [13] observed a rise of 1.2g/dl on day 28, Kriplani et al [14] observed a rise of 2.27g/dl on day 28 and Gupta et al [15] observed a rise in 2g/dl on day 28.The observed finding was almost correlated with the findings of the studies of Dewan Bhupesh et al (2.2g/dl) [16], Dipti A et al (3.5 g/dl), Lakshmi et al ( 2g/dl) [18] ,Hallak M et al (2.3g/dl) [19] and Wali Aet al (2.8g/dl) [20]. 68% of patient achieved the target Hb of 11g/dl and above which is comparable with the study of Sunita D et al, Kriplani et al, Gupta et al, Dipti A.et al(Table 6). Mean rise in ferritin level was found to be from 8.6±1.69 to31.9±7.7ng/ml ($p<0.0001$) which is statistically significant and comparable to the studies of Ragip et al, Al-Momen et al [17], Kriplani et al and Gupta et al. In the present study maximum dose of injection iron sucrose required was 1124mg and minimum was 735mg (Table 6 ).In the present study minor side effects like pain, swelling and soreness at injection site were reported in 7% of cases which was treated symptomatically. No serious side effects like anaphylactic reaction were reported in the study which is comparable to the findings of Dipti A et al (1.4%), Bhupesh et al (4.19%), Sunita D.et al (6%) and Kriplani et al (5%) (Table 7). Iron Sucrose is thus safe in pregnancy. 4% patient had post-partum haemorrhage and required blood transfusion at the time of delivery. Kriplani et al observed in their study to be 2.2%. In the study of Gupta et al no patients required blood transfusion.

**Table 5:** Showing percentage of patient achieving target haemoglobin in different studies

| Studies | Achieved target haemoglobin in percentage |
|---|---|
| Sunita D et al | 62% |
| Kriplani et al | 67% |
| Gupta et al | 76% |
| Dipti A et al | 52% |
| Present study | 68% |

**Table 6:** Showing maximum and minimum dose of injection iron sucrose required in different studies

| *Studies* | *Maximum dose of injection iron sucrose required* | *Minimum dose of injection iron sucrose required* |
|---|---|---|
| Dewan et al | 1050mg | 100mg |
| Christopher et al | 1200mg | 300mg |
| Breyman et al | 1600mg | 400mg |
| Present study | 1124mg | 735mg |

**Table 7:** Showing percentage of adverse effects of iron sucrose in different studies

| Studies | Adverse effects in percentage (%) |
|---|---|
| Dipti A et al | 1.4% |
| Sunita D et al | 6% |
| Bhupesh et al | 4.19% |
| Kriplani et al | 5% |
| Present study | 7% |

## 5. Conclusion

Intravenous iron sucrose can be effectively and safely used among anemic pregnant women. It caused significant rise in Hb and iron stores, which is depicted by improvement of setrum ferritin level within a short time , which helps to cope up easily with excessive bleeding during delivery. Hence, it may help to reduce the need for blood transfusion and the associated risks.

It can be used as an alternative to oral iron therapy in pregnant women in the late second trimester of pregnancy whose Hb are low even after taking iron supplements and thus prepare her for a safer delivery.

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