

A prospective study to assess the efficacy and safety of iron sucrose in pregnant women with iron deficiency anemia in a tertiary care hospital

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ABSTRACT

Background: Prevalence of iron deficiency anemia (IDA) is 58% among pregnant women in India. Oral iron therapy is recommended as first-line therapy in mild anemia. Moderate anemia in pregnancy results in high maternal morbidity and mortality. In India, women become pregnant with low iron stores, where oral iron therapy cannot meet the requirement and need parenteral iron therapy. This study was undertaken to evaluate the efficacy and safety of iron sucrose complex (ISC) in pregnant women with IDA.

Methods: A prospective study was conducted between June 2014 and June 2015 in the Department of Obstetrics and Gynaecology, Bangalore medical college and research institute. 60 pregnant women having hemoglobin (Hb) between 7 and 9 g/dl with diagnosed IDA were given intravenous ISC in a dose of 200 mg on alternate days after calculating the dose requirement. The efficacy of the therapy was assessed by hematological parameters measured at 4 weeks and 8 weeks of treatment. To assess the safety, adverse drug effects were recorded.

Results: The mean Hb increased from 8.02±0.56 to 11.38±0.5 g% (p<0.0001) after eight weeks of therapy. There was a significant rise in serum ferritin levels (from 15.12±1.8 to 31.4±4.9 µg/l) (p<0.0001) at the end of the study. Other parameters including mean corpuscular volume, mean corpuscular Hb, mean corpuscular Hb concentration, and serum reticulocyte count were also improved significantly. There were no allergic reactions.

Conclusion: Parenteral iron therapy was effective in increasing Hb, serum ferritin, and other hematological parameters in pregnant women with moderate anemia. Intravenous iron sucrose complex can be used in tertiary care hospitals where it can replace conventional parenteral iron therapy due to injection-related side effects.

Keywords: Hematological parameters, Iron deficiency anemia, Iron sucrose, Pregnant women

INTRODUCTION

Iron deficiency anemia (IDA) is the most widespread micronutrient deficiency in the world leading to an epidemic public health crisis. According to a study done by Indian Council of Medical Research (ICMR), the prevalence of anemia in pregnant women in India ranges between 50% and 90% and that of moderate anemia (<8 g%) and severe anemia (<5 g%) was persistently high.¹ The factors responsible for higher incidence of IDA are low iron and folic acid intake, phytate rich Indian diet, parasitic infestation, early marriage, teenage pregnancy, multiple pregnancies, and less birth spacing in the Indian population.² IDA is the

major contributor to high maternal morbidity and mortality as it predisposes to postpartum hemorrhage, sepsis, and pre-eclampsia and accounts for 20-40% of maternal deaths. Maternal anemia is associated with intrauterine growth retardation, preterm birth, and low birth weight babies.^{3,4} Thus, in developing countries like India, IDA is a major public health problem which needs to be corrected urgently.

The WHO defines IDA as hemoglobin (Hb) <11 g% and serum ferritin levels <12-15 µg/L. In India, the ICMR classification of IDA is graded as mild, moderate, and severe with 8-11 g%, 5-8 g%, and <5 g% of Hb, respectively.^{1,4} The treatment of anemia depends on its severity and added

maternal risk factors or co-morbidities. The first choice for prophylaxis and treatment of mild IDA in pregnancy is oral iron therapy. In the majority of cases, oral iron is not adequate to treat moderate to severe anemia, since the endogenous iron stores are usually depleted, and less iron is provided for erythropoiesis. Therefore, as per WHO guidelines, moderate to severe anemia requires parenteral iron therapy.⁵ Conventional parenteral iron preparations such as iron dextran and iron sorbitol citrate require test dose, as these are reported to cause anaphylactic reactions. Iron sucrose, a novel, safe intravenous iron preparation, is widely used to prevent functional IDA.^{6,7}

A prospective study, therefore, was conducted to evaluate the efficacy and safety of intravenous iron sucrose therapy in pregnant women with moderate IDA.

METHODS

It was a prospective study conducted at the Department of Obstetrics and Gynaecology, VaniVilas hospital attached to Bangalore Medical College and Research Institute, from November 2013 to June 2015. After obtaining Ethics committee clearance and written informed consent, 60 pregnant women were included in the study as per selection criteria.

Inclusion criteria: women aged 18-45 years, singleton pregnancy between 12 and 32 weeks on folic acid, Hb level between 7 and 9 g/dl, and patients willing to give written informed consent. Exclusion criteria: anemia due to other causes, known hypersensitivity to parenteral iron preparation, recent blood transfusion, associated cardiovascular, renal, hepatic dysfunction, and infections including malaria, hookworm infestation, schistosomiasis, hereditary defects such as sickle cell anemia, thalassemia, G6PD deficiency, and previous history of any bleeding tendency.

All the enrolled subjects were given intravenous iron sucrose therapy. Demographic data, history, clinical examination, hematological parameters, and details of drug prescription were recorded. The target Hb to be achieved was 11gm/dl. Total iron requirement was calculated as per the formula.⁸

Total iron deficit (mg) = Body wt (kg) × (Target Hb - Actual Hb [g/dl]) × 0.24 + 1000

At the initiation of therapy, one ampoule of 5 ml iron sucrose (100 mg elemental iron) inj. is added to 100 ml of sterile normal saline and first 25 ml will be infused over a period of 15-min. This worked as a test dose. Subjects were monitored for any adverse reactions during this period. The remaining portion of the infusion is administered over next 15 mins. The total calculated dose of iron is given in divided doses on alternate days until the target Hb level was achieved.

Evaluation of efficacy parameters, such as Hb, mean corpuscular volume (MCV), mean corpuscular Hb (MCH),

MCH concentration, serum ferritin, and serum reticulocyte count, were recorded at baseline, at the end of 4 weeks, and at the end of 8 weeks. Safety and tolerability were assessed by recording the adverse events and by Likert's scale during the study period.⁹ Once the target Hb was achieved, all the pregnant women continued to receive oral iron therapy until delivery. Data were analyzed using percentage, mean, standard deviation, ANOVA test. The level of significance was taken as 5%. The power of the study was taken as 80% and confidence interval 95%.

RESULTS

The mean age of pregnant women was 23.4±1.76 (range 19-32) years. 54% and 46% of the pregnant women were in middle and lower class according to modified Kuppuswamy scale. The regional distribution of the study population from the rural and urban area was 52% and 48%, respectively. 40% of the pregnant women were found to be primigravida while 60% were multigravida.

Efficacy parameters

At the baseline, the mean Hb was 8.02±0.56 g%. After completion of therapy, mean Hb increased to 11.38±0.54 g%. Table 1 shows the baseline hematological parameters and effect of iron sucrose therapy on all the parameters.

Side effect and tolerability

Pregnant women treated with iron sucrose had no allergic or anaphylactic reaction. Local reactions at the injection site were common than systemic adverse effects as summarized in Table 2.

Patient's tolerability was analyzed by Likert's scale. As depicted in Figure 1, a high percentage of pregnant women treated with iron sucrose reported excellent tolerability.

DISCUSSION

Anemia is widely prevalent in developing countries like India and is responsible for 95% of anemia during pregnancy.¹⁰

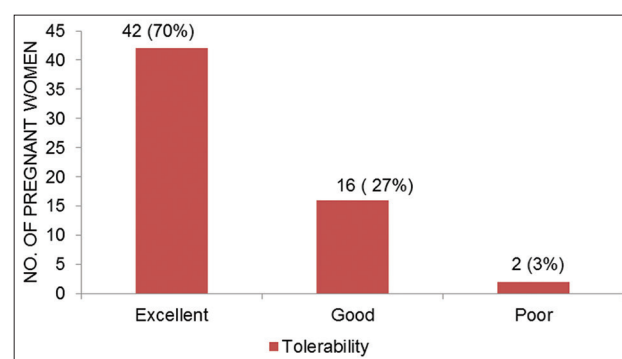


Figure 1: Overall tolerability with iron sucrose.

Table 1: Baseline hematological parameters and effect of iron sucrose therapy.

Parameters	Baseline	4 weeks	8 weeks	p value*
Hb (g/dl)	8.02±0.56	9.48±0.7	11.38±0.5	0.0001
MCV (fl)	79.67±6.03	84.1±5.9	89.6±5.7	0.0001
MCH (pg)	27.09±3.67	30.1±3.9	35.3±4.2	0.0001
MCHC (g/dl)	36.07±3.5	39.5±3.7	42.7±4.2	0.0001
Serum ferritin (µg/l)	15.12±1.80	-	31.4±4.9	0.0001
Serum reticulocyte count (%)	1.3±0.5	3.8±0.3	5.1±0.37	0.0001

*Significant ($p < 0.0001$), values are mean±SD (n=60), SD: Standard deviation, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, Hb: Hemoglobin

Table 2: Adverse effects of iron sucrose therapy.

Side effects	N (%)
Injection site pain	5 (8)
Injection site burning	6 (10)
Itching at injection site	3 (5)
Nausea/vomiting	2 (3)
Headache	3 (5)
Fever	2 (3)

The total amount of extra iron requirement during pregnancy ranges from 700 to 1400 mg with an average of 1000 mg. This is implausible to be provided by dietary iron, thus warrants the use of iron supplementation.¹¹

In the present study, the pregnant women were between 19 and 32 years and the youngest being 19 years which is similar to a hospital based cohort study done in West Bengal¹² that showed that the teenage mothers between 15 and 19 years who were prone for anemia, preterm delivery, and low birth weight. Anemia in pregnant women is a major contributing factor to maternal morbidity and mortality in developing countries. In this study, 46% of the pregnant women belonged to a lower socioeconomic group which could attribute to inadequate antenatal care.

A study done in Malaysia by Rosmawati et al.,¹³ the proportion of anemia was high in multigravidas than primigravidas (33% vs. 14%). In the present study, 60% of anemic women were multigravida, while 40% were primigravida. The reasons being frequent births inadequate spacing between childbirth and delayed antenatal booking giving insufficient time for correction of anemia. Additional causes include poor socioeconomic status, worm infestation. This is inconsistent with the study done in Nigeria and Ethiopia that showed the higher prevalence of anemia in primigravida (69.7%).¹⁴

For prophylaxis of anemia daily requirement of elemental iron is 30-40 mg in western women as they have sufficient iron stores. In Indian women, the requirement is 100 mg/day. The high requirement is because of inadequate antenatal care, lack of knowledge of dietary needs of pregnant women leading to insufficient iron stores and anemia. For the

treatment of anemia, dose recommended is 200 mg elemental iron per day in Indian women.^{15,16}

Treatment of moderate IDA (Hb levels < 8 g%) in pregnancy is associated with higher maternal and perinatal morbidity and mortality. Therefore, as per WHO guidelines, the treatment of moderate anemia requires parenteral iron therapy.

In the present study, there was a gradual rise in Hb% from baseline throughout the study period. The mean rise of Hb was 1.38 g/dl at the end of 4 weeks and 3.28 g/dl at the end of 8 weeks. The study done by Perewsky et al. found that accumulation of iron sucrose complex in parenchyma of organs is low while incorporation into bone marrow for erythropoiesis is rapid.¹⁷

This is also comparable to a study done in Pakistan by Walli et al. showing a mean increase of 2.6 g/dl Hb level at the end of 3.6 weeks of iron sucrose therapy emphasizing the superiority of intravenous iron therapy.¹⁸ In a study conducted by Breymann et al.,¹⁷ the mean rise in the Hb level was 1.7 g/dl after 3 weeks of iron sucrose therapy.

The mean increase in serum ferritin was 31.4±4.9 µg/l at the end of 8 weeks ($p < 0.0001$). This could be explained by the immediate availability of iron sucrose for erythropoiesis and faster replenishment of iron stores. The study done at AIIMS, New Delhi by Kriplani et al.¹⁹ showed the rise in serum ferritin at the end of 8 weeks to be 69±23.1 µg/l, from a baseline of 11.2±4.7 µg/l. In the present study, ferritin level showed a lesser increase which could be explained by severely depleted iron stores in Indian women.

The mean increase in MCV from baseline was 89.6±5.71 fL at the end of therapy. The mean rise of MCV in iron sucrose group was 9.97 fL at 8 weeks as compared to baseline, which was similar to study by Al-Momen et al.²⁰ and Halimi et al.,²¹ which showed that the mean rise was 10 fL. The rise in MCV was higher in the present study unlike the study done by Khurshid Shabir in Pakistan, which showed a minimal rise.²² The mean increase in serum Reticulocyte count was 3.83% at 8 weeks as compared to baseline, which is akin to the study done by Shaik et al.,²³

which showed that the rise in serum Reticulocyte count was 3.27%.

Safety and tolerability

Iron sucrose therapy was well-tolerated with very few local side effects such as pain and burning at the injection site. There was no treatment-related serious adverse events. There was no incidence of anaphylactic or anaphylactoid reaction. None of the adverse events required further medical intervention. This is consistent with the studies done by Perewunsky et al.,¹⁷ Breyman et al.²⁴ and Shaik et al.,²³ showed among the patients who received iron sucrose, 53% reported excellent tolerability while 20% had good tolerability which in comparison to the present study, 70% and 27% of the patients reported excellent and good tolerability, respectively. High tolerance to this preparation is due to low allergic effect of the sucrose, slow release of elementary iron from the complex, less tissue accumulation and fewer chances of toxicity.²⁵

Limitations of the present study include that it was a non-randomized trial with the lack of control group and small sample size.

CONCLUSION

Our results showed that intravenous iron sucrose therapy was effective in raising the hematological parameters, as it caused a rapid rise in Hb level and faster replenishment of iron stores with negligible side effects. Hence, iron sucrose can be an effective agent for the treatment of IDA in pregnancy.

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Conflict of interest: None declared

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

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