EFFICACY AND SAFETY OF INTRAVENOUS IRON SUCROSE FOR TREATING ANEMIA IN PREGNANCY: A PILOT STUDY.

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ABSTRACT: BACKGROUND: Iron deficiency anemia (IDA) is the commonest medical disorder affecting around 80% of the pregnant females. Iron sucrose has better bioavailability, safety profile and patient compliance than oral therapy. **OBJECTIVES:** To determine an alternative iron supplementation with better efficacy, compliance and safety in treatment of iron deficiency anemia during pregnancy. **METHODOLOGY:** Thirty six pregnant women with haemoglobin < 10.0 g/dl and serum ferritin <13µg/l were included. Women received two doses of IV iron sucrose (200 mg). Hemoglobin, reticulocyte count and serum ferritin were estimated at baseline, 14 days and 28 days after treatment. **RESULTS:** There was a significant increase in hemoglobin levels, reticulocyte count and serum ferritin levels on 14 days and 28 days of treatment. Majority of the patients were free of side effects (80.56%). **CONCLUSION:** Iron sucrose therapy results in significant improvement of hemoglobin levels and iron stores. Iron sucrose injection is safe and well tolerated.

INTRODUCTION: Iron deficiency anemia (IDA) is the commonest medical disorder affecting around 80% of the pregnant females. It is a major contributing factor to maternal morbidity, mortality and high perinatal mortality. WHO defines anemia as hemoglobin level <11gm% and hematocrit <33% in pregnancy. According to National Family Health Survey-3(2005-2006), the prevalence of anemia in pregnancy is 57.9% [1]. There is an increased iron requirement of 1240mg during pregnancy (230mg obligate loss, 450mg for expanded RBC volume, 270mg for fetus, 90mg in placental tissue and 200mg lost at delivery). Woman saves 150mg due to amenorrhea and that leaves around 1000mg of iron to be supplemented.

The Iron-Folic Acid (IFA) program was launched in India to provide free iron and folate to pregnant women to eradicate IDA. The reasons for failure of IFA program often cited are partial coverage of the population, inadequate dosing of the iron supplement, defective absorption due to intestinal infestations, diets containing high levels of iron chelators, poor compliance, short supplies at the beneficiary level, and lack of effective health education [2]. Iron sucrose has minimal side-effects, and because it is administered intravenously (IV), it overcomes the problems with oral iron supplementation, including problems of compliance. Unlike intravenous dextran iron, anaphylactic reactions are very rare with iron sucrose. Blood transfusion is limited to those cases with severe anemia at term, established or incipient cardiac failure or infections. It carries the risk of transmission of blood borne infections, besides mismatched transfusion reactions.

OBJECTIVES: To determine an alternative iron supplementation with better efficacy, compliance and safety in treatment of iron deficiency anemia during pregnancy.

METHODOLOGY: The prospective study was conducted in Department of Obstetrics and Gynaecology, Era's Lucknow Medical College Lucknow, UP. Study was conducted over a period of six months (2011).

Thirty six women attending antenatal clinic (Singleton pregnancy of 16 to 38 weeks, no other medical disorder), with haemoglobin of < 10.0 g/dl and serum ferritin <13µg/l were included after taking a written informed consent. Exclusion criteria included patients with known hypersensitivity to iron preparations and medical disorders (diabetes mellitus, hyperthyroidism and hypothyroidism).

Women received two doses of IV iron sucrose of 200 mg per sitting at interval of 3-5 days. Iron sucrose was given as IV bolus dose over 5 min or with 100ml isotonic saline over 30 min. No test dose was given, and patients were monitored for one hour following first injection. Hemoglobin, reticulocyte count and serum ferritin were estimated at baseline, on day14 and 28 after treatment. Rise in hemoglobin levels at the end of the therapy was analyzed on coulter cell counter.

Clinical safety was evaluated based upon the nature and severity of adverse effects if any, recorded at end of 2 hours and 14 days of treatment. The response and tolerability to therapy was recorded on a global assessment of response to therapy on a 5-point rating scale of "1-Excellent, 2=Good, 3=Average, 4=Poor and 5=Very Poor" at the end of study period. This rating was done independently by the patients and the physicians with respect to efficacy and tolerability. After completion of the study, hemoglobin deficit of the patients was corrected.

Statistical Analysis: Results were analyzed by SPSS 17.0 version using Students paired't' test and analysis of variance. P-value ≤0.05 was taken as significant.

RESULTS: Out of 36 women in the study group, six were primigravida and rest was multigravida. Maximum women (72.22%) were in age group of 21-30 years. Before starting the therapy 75% of the patients had Hb levels between 4.0-6.9 g/dl (severe anemia) and rest had moderate anemia (Hb levels 7-9.9 g/dl). Mean Hb in the pretreatment group was 6.38g/dl (range 5.0-8.1 g/dl). Mean reticulocyte count was 0.73cells/cu mm (range 0.3-1.7) and mean serum ferritin levels were 24.7µg/l (range 12.5-43). After 14 days of receiving IV iron therapy, mean Hb levels were 7.61g/dl (range 6.4- 9.2), mean reticulocyte count was 2.24cells/cu mm (range1.3-3.8) and mean serum ferritin levels were 128.9µg/l (range 95.4-179.6).

After 28 days of treatment, mean Hb levels increased to 9.41g/dl (range 7.4- 11), mean reticulocyte count was 3.07cells/cu mm (range1.9-3.9) and mean serum ferritin levels were 167µg/l (range 121.1-202.4). The rise in Hb, reticulocyte count and serum ferritin from pretreatment levels were all statistically significant (P-value <0.001). After 28 days of treatment, 16.7% were in severe anemia group and 83.3% were now having moderate anemia. There was an improvement from the pretreatment value.

Majority of the patients were free of side effects (80.56%). Minor side effects were noted in few cases (19.44%; pain at injection site- one, metallic taste- three, headache- one, warm tingling sensation-two cases).

The response and tolerability to therapy were recorded on 5-point rating scale. Majority of the patients were satisfied with the treatment (33.4% - excellent, 44.4% - good, 13.9% - average and 8.3% - poor).

DISCUSSION: Iron is an essential component of haem and accounts for 70% of hemoglobin. Iron balance in the body depends solely on gastrointestinal absorption and Fe bioavailability in food. Iron deficiency and its consequence, iron deficiency anemia, is the most common nutritional problem in pregnant woman [3]. Iron deficiency state is characterized by decrease in iron stores in body as reflected by serum ferritin levels, with decrease transferring saturation and serum iron levels. If this continues, erythropoiesis is affected and results in microcytic hypochromic anemia.

Efficacy of oral iron therapy depends upon gastrointestinal absorption and patient's compliance. Iron sucrose injection is safe, efficacious and ensures compliance to therapy and irrefutable data is available on it [4,5,6,7]. The rise in hemoglobin levels occurs after 2-3weeks of treatment. Serum ferritin levels rise only after hemoglobin levels normalize [8]. Early response to therapy is an increase reticulocyte count and reticulocyte hemoglobin concentration [9].

In our study, 36 women with singleton pregnancy between 16-38 weeks, with moderate to severe anemia, were given two doses of 200mg of IV iron sucrose (3-5days apart). There was a statistically significant rise in blood hemoglobin levels, reticulocyte count and serum ferritin levels on 14 and 28 days after treatment. Minor side effects were noted in few cases (pain at injection site-one, metallic taste- three, headache- one, warm tingling sensation-two cases). Majority of the patients were free of side effects (80.56%). The results were consistent with other studies. Studies comparing IV iron sucrose and oral iron therapy in pregnancy, have shown significant improvement in hematological parameters, early replenishments of iron stores with no serious adverse effects [4,5,6,7]. IV iron sucrose is safe and more effective than intramuscular iron therapy in treatment of anemia [10]. Dropout rates are higher in intramuscular groups and majority complained of pain in injection site. The blood transfusion rates are also reduced in patients treated with IV iron sucrose [3,10].

IV iron can be considered for postpartum patients with anemia [11,12,13]. It results in rapid recovery of hemoglobin levels; replete iron stores rapidly and does not have major side effects.

Study comparing iron sucrose bolus push with standard iron infusion technique in chronic renal disease patients, reported similar efficacy in both groups and no serious adverse effects in either of the groups. However there was a significant difference in cost analysis, favoring IV bolus push injection over iron infusion [14]. Further studies are required to study the efficacy and safety of IV iron bolus dose/ single total dose infusion in pregnancy. IV bolus push/ single total dose infusion techniques may prove to be a cost effective strategy for large scale prophylaxis and treatment of IDA in low resource countries like India.

CONCLUSIONS: Iron sucrose therapy results in significant improvement of hemoglobin levels and replenishes iron stores rapidly in pregnant women. Iron sucrose injection is a better alternative to oral and intramuscular iron therapy in terms of efficacy, safety and compliance. In our country with frequent IDA found in pregnancy, this type of treatment may be helpful.

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Table No 1: Showing pretreatment and post treatment hemoglobin, reticulocyte count and serum ferritin values.

Investigations Mean and Range	Pre-treatment	Post-treatment-14	Post-treatment-28	P-value
Hb (g/dl)	6.38(5.0-8.1)	7.61(6.4- 9.2)	9.41(7.4-11)	<0.001
Retic. Count (Cells/cu mm)	0.73(0.3-1.7)	2.24(1.3-3.8)	3.07(1.9-3.9)	<0.001
Serum Ferritin (microgram/l)	24.7(12.5-43)	128.9(95.4-179.6)	167(121.1-202.4)	<0.001

Figure 1: Box whisker plots showing mean and range of Pre and Post treatment Hemoglobin levels (Paired t-test, P<0.001)

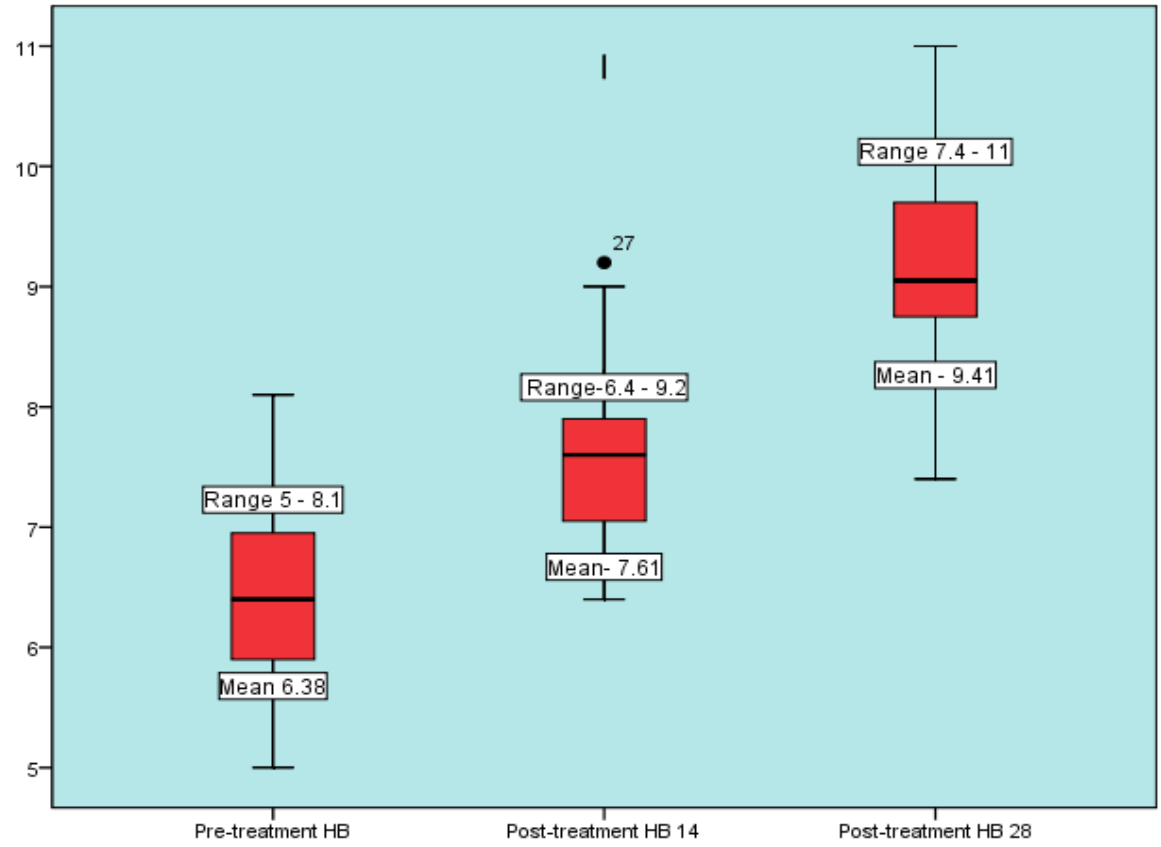


Figure 2: Box whisker plots showing mean and range of Pre and Post treatment Serum Ferritin levels (Paired t-test, P<0.001)

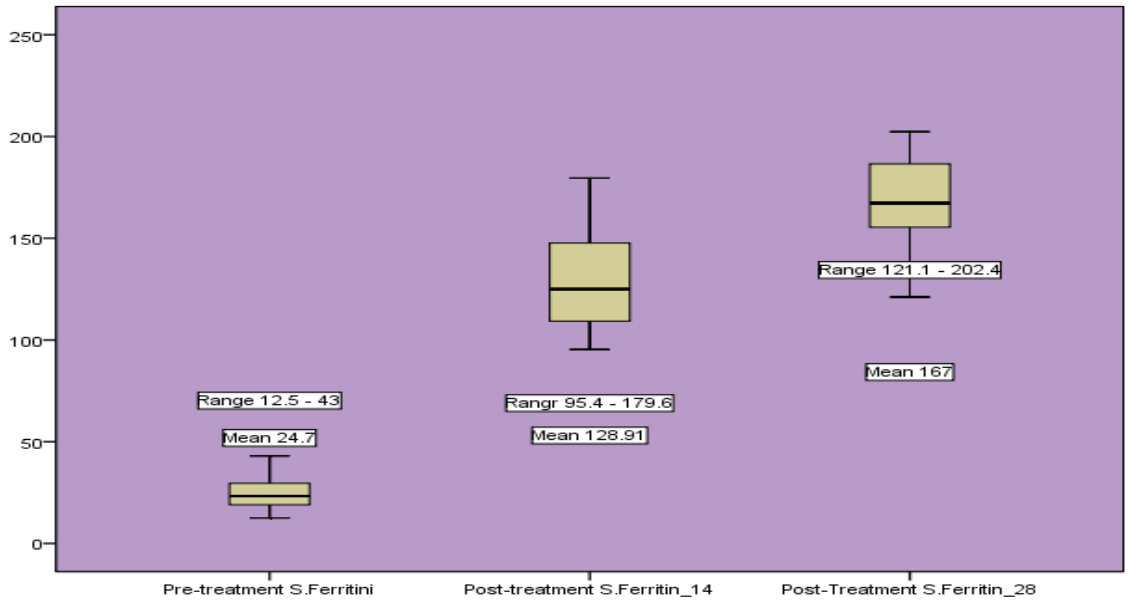


Figure 3: Box whisker plots showing mean and range of Pre and Post treatment Reticulocyte counts (Paired t-test, P<0.001)

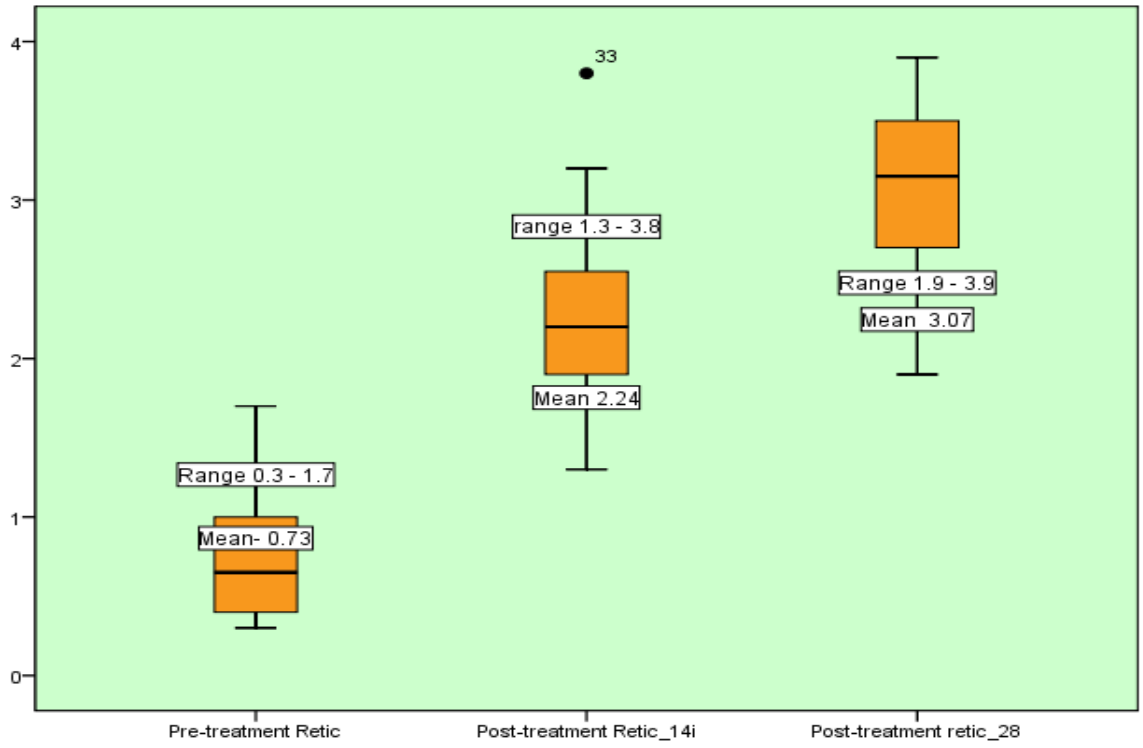
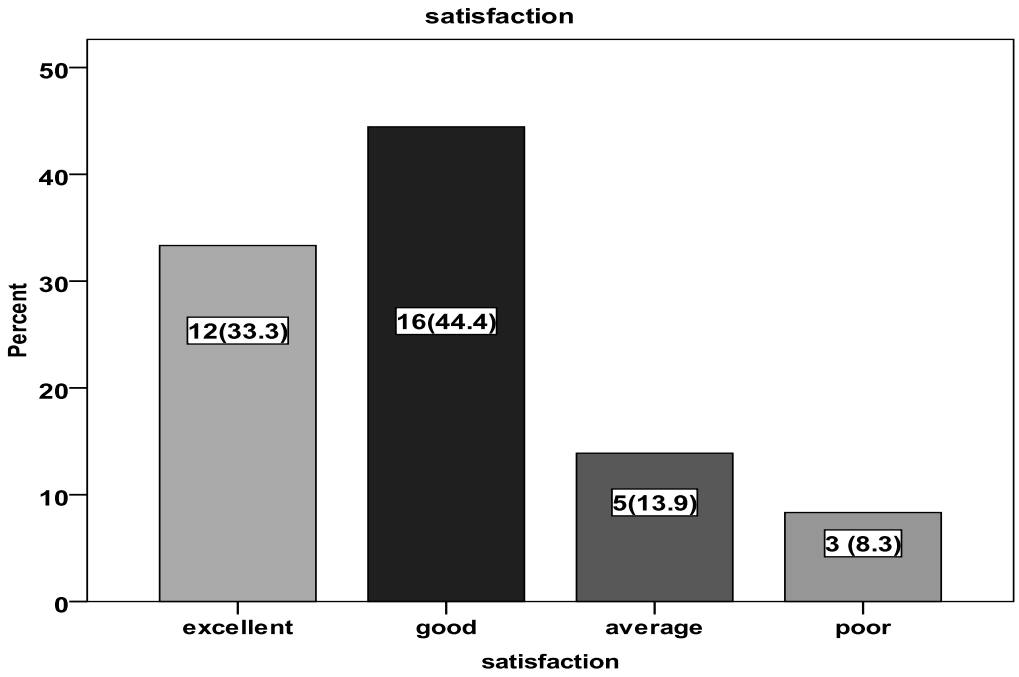


Figure 4: Showing satisfaction by patients on Likert's scale.



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