

## Iron Deficiency Anemia in Pregnancy Intravenous versus Oral Route

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**Abstract:** In India the prevalence of IDA in pregnancy has been reported to be 57.9% (54.6% urban and 59% in rural) by National Family Health Survey-3 (NFHS) with a wide variation of Incidence from state to state. The world health Organization (WHO) presented data at Federation of International Obstetrics and Gynecology (FIGO) meeting in 2003 in chile around 500,000 Maternal deaths and 20,000,000 maternal morbidity cases per year are related to iron deficiency anemia. Aim: The Aim of this prospective, randomized, controlled study was to compare the efficacy of Intravenous iron sucrose versus Oral iron in the treatment of Iron deficiency anemia. Materials & Methods: This study was conducted in the department of Obstetrics and Gynecology, Gayatri Vidya Parishad Institute of health care & Medical Technology, Marikivalasa, Visakhapatnam. 200 pregnant women with gestational age between 24 to 34 weeks attending the Ante Natal Clinic from January 2018 to February 2019 were included in the study and they were randomized into two groups of 100 each. **Group A:** Intravenous iron sucrose 200 mg in 200 ml normal saline given by IV infusion. **Group B:** Oral iron group received ferrous ascorbate oral tablets, each containing 100 mg elemental iron twice daily during pregnancy as per the recommendation of World Health Organization. Results: The significant rise in the Hemoglobin from 6.58 to 11.14 in intravenous group as compared to Oral group from 6.98 to 10.58 was noticed. Intravenous group did not have any significant adverse drug reactions and Oral group experienced adverse effects mainly gastro intestinal symptoms. Conclusion: Intravenous Iron Sucrose is a safe and more effective alternative to Oral Iron therapy for the treatment of Iron deficiency anemia in pregnancy. It also improves Hemoglobin level faster than Oral Iron

**Key Words:** Anemia, Iron Deficiency anemia, Oral Iron, Iron Sucrose

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### I. Introduction

Iron deficiency anemia is the most common nutritional disorder in the world, affecting approximately 25% of the world's population. The prevalence of iron deficiency anemia in pregnant women is estimated to be 35% - 75% (average 56%) in developing countries where as in industrialized countries the average prevalence is 18%. Anemia during pregnancy has been shown to be associated with two fold risk of preterm delivery and three fold risk for low birth weight as well as maternal mortality.<sup>1,2</sup>

The world health Organization (WHO) presented data at Federation of International Obstetrics and Gynecology (FIGO) meeting in 2003 in chile around 500,000 Maternal deaths and 20,000,000 maternal morbidity cases per year are related to iron deficiency anemia. FOGSI-who study on maternal morbidity revealed 64.4% of women who died, had hemoglobin less than 8gm% and 21.6% had hemoglobin 5gm%

In India the prevalence of IDA in pregnancy has been reported to be 57.9% (54.6% urban and 59% in rural) by National Family Health Survey-3 (NFHS) with a wide variation of Incidence from state to state.<sup>3,4</sup>

According to recent studies, the prevalence of iron deficiency anemia in the first trimester ranges from 3.5% - 7.4% and increases to 15.6% -55% in the third trimester. With adequate iron stores, daily requirement increases from an average of 2mg-3mg/day in early trimester to 6mg-8mg / day in last trimester which is explained by hemodilution phenomenon.

Oral iron is the treatment of choice because of its effectiveness, safety and low cost. Parental iron is reserved for those in whom oral treatment fails due side effects, noncompliance, decreased absorption like ulcerative colitis and last trimester of pregnancy when rapid correction of anemia is needed.

As compared with oral iron, IM iron dextran injections are painful with risk of skin staining. However, intravenous iron dextran induces similar or slightly more rapid erythropoietic response than oral iron. The advantage of IM iron dextran is that, it can be administered in primary care after test dose, although facilities for resuscitation should be available as there is a small risk of allergic and anaphylaxis reaction.<sup>5,6</sup>

Iron sucrose is a complex of poly nuclear iron III – hydroxide in sucrose for intravenous use. The polynuclear iron III – hydroxide cores are superficially surrounded by a large number of non covalently bound sucrose molecules resulting in a complex with a molecular weight of approximately 60000 Daltons. The Iron in the polynuclear cores is bound in a similar structure to that of physiological condition. 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. The short half life of 5-6 hrs is responsible for rapid erythropoiesis as compared to iron dextran; which has serum half-life of 3-4 days. Rate of iron delivery is a major factor in the regulation of marrow proliferation so it produces a more rapid increase in hemoglobin concentration than oral iron and iron dextran. It is administered without a test dose and have lower incidence of allergic reactions. Death from anaphylactic reactions has not been reported till date with its use.<sup>5,6</sup>

## II. Materials & Methods

This study was conducted in the department of Obstetrics and Gynecology, Gayatri Vidya Parishad Institute of health care & Medical Technology, Marikivalasa, Visakhapatnam.

Pregnant women with gestational age less than 35 weeks with moderate to severe Iron deficiency anemia (Hb less than 8g/dl) were selected from the Ante Natal clinic were Screened in the Laboratory attached to the clinic. Iron deficiency anemia was diagnosed on the basis of automated red cell counts, peripheral blood smear, serum ferritin level and serum iron parameters. Hb electrophoresis and HbA2 quantification was done when it indicated, to exclude beta Thalassemia trait 200 women were included in the study who fulfills the Inclusion Criteria.

### Eligible criteria included were:

Hemoglobin level between 7-9g/dl, Singleton live pregnancy, Gestation Age 20-35 weeks, Microcytic Hypochromic anemia, Serum Ferritin level <15ng/ml.

### Exclusion Criteria included were:

Anemia other than Iron deficiency, History of hematological disease, blood Transfusion during current Pregnancy, Medical disorders, Chronic blood loss, Placenta previa

**Group A:** Intravenous iron sucrose 200 mg in 200 ml normal saline given by IV infusion (first dose, initial 12.5ml was infused over 15 minutes i.e. 50 ml per hour) over a period of 2 hours on alternate days for 3 days a week up to a maximum of 600 mg/week was administered. The following formula was used: Body weight in Kg x (target Hb-initial Hb) gm/dl x 2.4 plus 500 mg to calculate the total iron requirement of the patient to fulfil the deficit as well as to replenish the iron stores to make it 11g/dl

**Group B:** Oral iron group received ferrous ascorbate oral tablets, each containing 100 mg elemental iron twice daily during pregnancy as per the recommendation of World Health Organization for the treatment of iron deficiency anemia. The Target Hemoglobin was 11g/dl. All the subjects received folic acid tablet once daily. Statistical Analysis was done applying Students't' test and Chi Square test. Value of <0.05 was taken as significant and <0.001 as highly significant.

## III. Results

**Table: 1** Demographic and Clinical Characteristic

Characteristics	IV groups (A) (n=100)	Oral groups (B) (n=100)
Age( mean + SD ) years	25.18 ± 3.12	25.22 ± 3.17
<20 yrs	08	09
21-30 yrs	62	71
>30 yrs	30	20
Low socioeconomic group	60%	65%
Education up to primary or below	72%	84%
Parity of women		
Nullipara	52	46

Multipara	48	54
BMI ( kg/sq.m)	22.18 ± 2.12	22.13 ± 2.14

**Table-2:** Hemoglobin Level before and After Treatment.

Group	Hb level (g/dl)		Difference (g/dl)
	Before treatment	After treatment	
Group A (n= 100)	6.58	11.14	4.56
Group B (n=100)	6.98	10.58	3.60

**Table-3:** Side effects

Side Effects	Group A	Group B
Epigastric discomfort / Nausea / Vomiting	0	18 (18%)
Constipation / diarrhea	0	17 (17%)
Metallic taste	0	12 (12%)
Pain at injection site	28 (28%)	0
Phlebitis	8 (8%)	0
Fever	6 (6%)	0

#### IV. Discussion

The rapid rise in hemoglobin and iron stores is due to the different pharmacokinetics of iron sucrose. In case of Oral iron therapy iron absorption is far below the iron requirement of iron deficient pregnant women.

The safety and effectiveness of iron sucrose has been demonstrated in several clinical trials of patients with chronic kidney disease with refractory anemia. In anemic pregnant women, Goven and Scott reported a case series as early as 1949 demonstrating the benefits of intravenous iron. Subsequently, small observational studies, quasi- experimental studies, and small randomized clinical trials have shown improvement in haematological indices with intravenous iron sucrose in pregnant women.<sup>7,8</sup>

Iron sucrose is a type II Fe complex that releases iron to endogenous iron binding protein with half – life of 6 hours, are not only effective but carry a minimum risk of allergic accident or overload. Sucrose iron is directly delivered to the haemopoietic system. It is more bioavailable than other preparations. Unlubilgin et al conducted a randomized open label study with the aim to compare the efficacy of intravenous iron to oral iron in treatment of anemia in pregnancy. They concluded that intravenous iron, treated iron deficiency anemia of pregnancy and restored iron stores faster and more effectively than oral iron, with no serious adverse reactions.<sup>9,10,11,12</sup>

Al Momen et al., observed that the IVIS group achieved significantly higher hemoglobin level ( P value < 0.001) in a shorter period ( P value < 0.001). In a study done by Al et al., hemoglobin was different for patients in the OI and IVIS groups across time in each individual group as well as at any given point of time. The hemoglobin level was significantly higher in the IVIS group. In the present study, hemoglobin within an individual group was significantly higher across time, with no difference in between both groups at any point of time.<sup>13,17,18,19</sup>

After treatment, the IVIS group maintained hemoglobin with routine supplementation of OI in the present study, unlike in Bayoumeu et al.'s study, where no additional oral supplementation was given. Because of the prevalence of anemia (57.9%) in pregnant women as per National Family Health Survey -3, oral supplementation even with normal iron stores is essential in India. Unlike in the parenteral iron-treated group, once the anemia is corrected with OI, absorption slows down. This is responsible for the iron stores not being replenished with OI, unlike intravenous iron.<sup>14,15,16,20</sup>

Many Indian studies have used the intramuscular route for parenteral iron and reported side-effects such as pain, staining at the injection site and arthralgia. IVIS cannot be given intramuscularly and does not have these side-effects.

Gastrointestinal side-effects were about 18% in the OI group, while the reported incidence varied from negligible to 31% in other studies. Mild adverse events noted in the IVIS group were vomiting, rashes and giddiness following first dose of iron sucrose. Other studies reported unpleasant state and fever, which were not observed in the present study. Because there were no serious adverse drug reactions and no episodes of anaphylaxis, we feel that it is safe for anemia in pregnancy.

#### V. Conclusion

Intravenous Iron Sucrose is a safe and more effective alternative to Oral Iron therapy for the treatment of Iron deficiency anemia in pregnancy. It also improves Hemoglobin level faster than Oral Iron which helps to cope up easily with excessive bleeding during delivery. Hence, it may help to reduce the need for the blood transfusion and the associated risks.

The Major Advantages are safety, Efficacy, Good Compliance, Simple mode of Administration and cost effectiveness because admission is not required.

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