

Comparison of Efficacy of Treatment with Oral Ferrous Sulfate or Intravenous Iron Sucrose in the Treatment of Mild to Moderate Iron Deficiency Anemia in Pregnancy

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ABSTRACT

Objective: To compare the effect of treatment with either oral ferrous sulphate or intravenous iron sucrose (IVIS) on hematological parameters of women with iron deficiency anemia in pregnancy.

Methods: This prospective randomized study was interventional, conducted from January 2016 to January 2017 in Department of Obstetrics and Gynecology Sree Narayana Institute of Medical sciences.

Pregnant women Singleton pregnancy, Hb < 11 gm in 1st and 3rd trimester Hb < 10gm in 2nd trimester, with hemoglobin level 7-10.9 g/dL ferritin levels less than < 13 microgram/L and peripheral smear hypochromic microcytic anemia were enrolled into intravenous iron and oral iron groups. After detailed history and examination, laboratory investigations performed were hemoglobin, mean corpuscular volume (MCV), serum ferritin and peripheral smear. The dose for IVIS dose is calculated by ganzoni equation. Total iron deficit (mg) = body weight (kg) × [Target Hb (g/L)-actual Hb (g/L)] × 0.24 + depot iron (mg). A maximum IVIS is given as 200 mg in 100 ml normal saline as infusion over 15 to 30 minutes The remaining doses were given on alternate days. Infusions were given as outpatient basis in labor room with facilities for acute emergency care. Oral iron group received ferrous sulphate supplementation.

Results: Target hemoglobin of 11 g/dL was attained by 66 %. Hemoglobin done just prior to delivery showed no statistically significant difference (p value = 0.080) [OI group 11.83 (+11.98) g/dL vs. IVIS group 16.19 (+ 11.35) g/dL]. There was significant increase in serum ferritin levels with IVIS infusion There was no significant difference in antepartum or postpartum hemorrhage, infection, preterm labor, between the two groups.

Conclusion: The study concludes that oral iron increases hemoglobin comparably with IVIS. The replenishment of iron stores was good with IVIS compared with oral ferrous sulphate.

Keywords: Anaemia, Ferrous sulphate, Iron deficiency, Iron sucrose.

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Conflict of interest: None

OBJECTIVES

Anemia affects nearly half of all pregnant women in the world increasing morbidity and mortality if left untreated. According to World Health Organisation (WHO) 2001, 52% of pregnant women are anemic. Twenty to forty percent of maternal deaths in India are due to anemia.¹ The national family health survey statistics suggest that the incidence of married women has increased to 56%.² The prevalence of anemia in Kerala is 23%.³ The commonest type of anemia in pregnancy is iron deficiency anemia.⁴

LITERATURE REVIEW

During pregnancy, there is an increase in plasma volume compared to the increase in red cell mass. The biggest discrepancy between plasma and red cell mass happens in the late second and early third trimester with the lowest hemoglobin found at 28 to 36 weeks (Whittaker et al.).

In singleton pregnancy the average iron requirement is about 1000 mg out of which 500 mg is used for expansion of red blood cells (RBC) mass, 300 mg for fetus and placenta, 200 mg is the basal iron requirement. Between 240 and 480 mg of iron is conserved due to amenorrhea in pregnancy. This leaves an additional requirement of 500 to 600 mg iron/day or 4 to 6 mg/day of absorbed iron (Stoltzfus and Dreyfuss 1998) as the absorption is less than 10%, 40 to 60 mg of iron must be made available Sharma.^{5,6}

Iron deficiency anemia diagnosed as Hb < 11.0 gm/dL in first and third trimester Hb < 10.5 gm in the second trimester, serum ferritin < 13 micrograms/l.⁷ It is further classified as mild 10 to 10.9 moderate 7 to 9.9 gm/dL severe 4 to 6.9 gm/dL and very severe < 4gm/dL. Anemic patients are treated with either oral iron or IVIS. The rise of hemoglobin is up to 1 g per week (Sharma).⁶ Some studies have shown equal effects with the different route of administration.⁸ There were conflicting results regarding the outcome regarding either of drugs.⁹ The protocol based indication for iron sucrose is poor compliance with oral iron.

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Women with established iron deficiency anemia (IDA) will be given 100 to 200 mg elemental iron (Pavord et al.) this would be three tablets 180 mg of ferrous sulfate (ICMR 1992).¹⁰

Intravenous iron sucrose dose is calculated by Ganzoni equation. Total iron deficit (mg) = body weight (kg) X [Target Hb(g/L)-actual Hb (g/L)] × 0.24 + depot iron (mg). IVIS is given as 200 mg in 100 mL normal saline as an infusion over 15 to 30 minutes twice a week (Bayoumeu et al. and Fogsí 2008).¹¹ Iron sucrose confers the benefit of excellent tolerance, minimum adverse reactions, a rapid rise in hemoglobin concentration (Van Wyck et al. 2004, 2000; Fogsí 2008)the complications are life-threatening anaphylaxis occur in 0.002%, hypersensitivity reactions in 0.005% and mild adverse reactions in 35%.¹²

METHODS

The study compared the effectiveness of IVIS therapy with oral ferrous sulfate (OI) therapy in pregnant women with mild to moderate iron deficiency anemia. This prospective randomized study was carried out from January 2016 to January 2017 in the Department of Obstetrics and Gynecology Sree Narayana Institute of Medical Sciences. Ethical committee clearance was obtained from the institutional ethical committee. Pregnant women singleton pregnancy, Hb < 11gm in 1st and 3rd trimester Hb < 10 gm in the 2nd trimester, with hemoglobin level 7 to 10.9 g/dL ferritin levels less than < 13 micrograms/L and peripheral smear hypochromic microcytic anemia were enrolled after taking informed consent. Women with severe anemia requiring blood transfusion any preexisting chronic medical illness like diabetes, hypertension, preeclampsia, hemoglobinopathies, malabsorption syndromes, chronic liver and renal diseases, anemia due to other causes were excluded from the study.

Patients were assigned to either the IVIS or the OI group using randomization by lottery method. Target hemoglobin in g/dL was set at 11 g/dL based on the WHO definition for anemia in pregnancy. After detailed history and examination, laboratory investigations performed were hemoglobin, mean corpuscular volume

(MCV), serum ferritin and peripheral smear. Investigations were repeated after 1 month. The dose for IVIS dose is calculated by Ganzoni equation. Total iron deficit (mg) = body weight (kg) × [Target Hb(g/L)-actual Hb(g/L)] × 0.24 + depot iron (mg).

Dose thus calculated was rounded up to the nearest multiple of 100 mg. Maximum IVIS is given as 200 mg in 100 mL normal saline as an infusion over 15 to 30 minutes twice a week Bayoumeu et al.¹¹ Oral ferrous sulfate was withheld during IVIS therapy. The total dose was completed by giving infusions on alternate days as an outpatient basis in the labor room with facilities for managing anaphylaxis.

Ferrous sulfate 100 mg was used for oral therapy. Compliance was checked with weekly telephonic calls. At each visit, enquiring was detailed regarding the occurrence of adverse effects.

Statistical compilation and analysis were done with the Statistical package for social science (SPSS-17). Difference between groups was analyzed using independent sample t-test, Chi-square test or analysis of covariance appropriately. The p < 0.05 was taken as statistically significant.

There was no significant difference in baseline demographic and clinical characteristics between two groups (Table 1). The groups were comparable with regard to gravidity and parity (Table 2).

Sixty-six percent of the study population achieved the target hemoglobin of 11 g/dL.

Hemoglobin done just prior to delivery showed no statistically significant difference (p-value = 0.080) (Table 3). (OI group 11.83 (+11.98) g/dL vs. IVIS group 16.19 (+ 11.35) g/dL). There was significant increase in serum ferritin levels (Table 4) with IVIS infusion as seen in Graph 1. There was no significant difference in antepartum or postpartum hemorrhage, infection, preterm labor, between the two groups.

DISCUSSION

The current study compares the efficacy of IVIS to oral ferrous sulfate in treating iron deficiency anemia in pregnancy. Most of the studies observed safety and speedy correction of anemia with the use of iron sucrose

Table 1: Comparison of demographic characteristics in the two groups

Parameters	Oral iron group (n = 46)	Intravenous iron group (n = 44)	p-value
Age (years)	26.58 (+ 4.24) (21–35)	26.09 (+ 4.47) (19–40)	0.591
Maternal weight (kg)	54.15 (+ 9.85) (40–78)	53.72 (+ 8.86) (40–72)	0.830
Total iron deficit	518.21 (+ 16.1) (503.30–576.20)	520.59 (+ 17.8) (504–591.20)	509

*p-value < 0.05 significant, unpaired t-test, values are given as mean (standard deviation) and range

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Table 2: Comparison of gravidity and parity in the two groups

Parameters	Oral iron group (n = 46)	Intravenous iron group (n = 44)
<i>Gravidity (n = 90)</i>		
Gravidity 1	23 (50%)	17 (38.6%)
Gravidity 2	18 (39.1%)	17 (38.6%)
Gravidity 3	5 (10.9%)	5 (11.4%)
Gravidity 4	0	5 (11.4%)
<i>Parity (n = 38)</i>		
Parity 1	17 (89.5%)	16 (84.2%)
Parity 2	2 (10.5%)	3 (15.8%)

Table 3: Percentage increase in various parameters after treatment in the two groups

Percentage increase (value%)	Oral iron group (n = 46)	Intravenous iron group (n = 44)	p-value
Hemoglobin	11.83 (+ 11.98)	16.19 (+ 11.35)	0.080
Ferritin	21.62 (+ 25.62)	54.80 (+ 70.49)	0.005*
Mean corpuscular volume	1.81 (+ 4.96)	5.50 (+ 7.39)	0.007*

*p-value <0.05 significant, Unpaired t-test, Values are given as mean (standard deviation)

Table 4: Laboratory parameters before and after treatment in the two groups

Parameters	Before treatment			After treatment		
	Oral iron (n=46)	Intravenous iron (n=44)	p-value	Oral iron (n=46)	Intravenous iron (n=44)	p-value
Hemoglobin	9.79 (+ 0.88)	9.65 (+ 0.75)	0.398	10.88 (+ 0.85)	11.14 (+ 0.67)	0.105
Ferritin	11.57 (+3.66)	12.17 (+ 7.15)	0.617	13.5 (+ 3.06)	15.5 (+ 3.42)	0.004*
Mean corpuscular volume	83.12 (+7.02)	79.52 (+ 8.81)	0.035*	84.39 (+ 5.31)	83.45 (+ 6.57)	0.458

*P value <0.05 significant, Unpaired t test, Values are given as mean (standard deviation)

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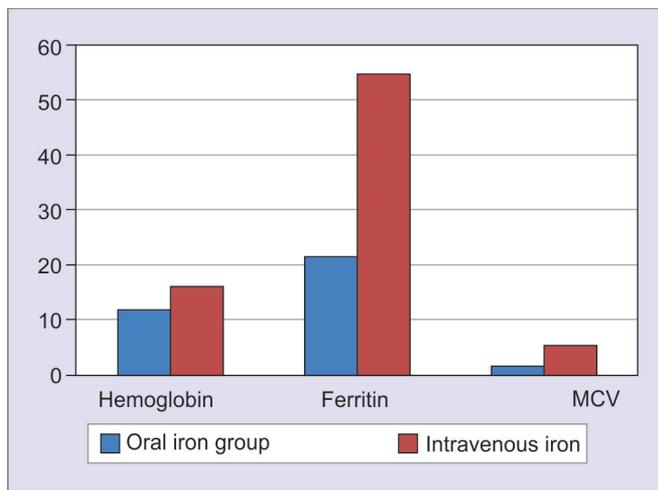
Name	Age				Hospital Number			
Obstetric Score								
Total Iron Deficit								
Iron Replacement	Oral				Intravenous			
Weeks	20	24	28	32	36	40	4	
Hb								
Ferritin								
MCV								
Peripheral smear								
APH/PPH								
Infection								
Preterm labour								
Wound healing								
Cord blood								
Hb								
Ferritin								
Peripheral smear								

in pregnancy. IVIS also replenished iron sucrose better than oral ferrous sulfate.¹³⁻¹⁶

As different lab parameters were used, comparison with other studies was not possible. There was a significant difference in ferritin level between the two study groups. The conclusion we could derive from it was that although anemia was corrected in either group iron stores were replenished in the intravenous iron sucrose

group. Similar findings were observed by Bayoumeu et al.¹³

The target hemoglobin was reached in both the groups. Both groups showed a significant increase in Hemoglobin levels at 1 month when compared to the initial value. Because of physiological hemodilution and blunted erythropoietin response of second trimester significantly higher response was observed after 28 weeks.¹⁴



Graph 1: Percentage increase in various parameters after treatment in the two groups

So IVIS is the preferable treatment of moderate anemia in the third trimester.

An oral iron therapy group had 23% of gastrointestinal side effects in comparison to 31% in other studies.^{15,16} Adverse drug reactions noted in intravenous therapy were giddiness, vomiting, and rashes. There were no episodes of anaphylaxis supporting the safety in pregnancy.

Intravenous iron sucrose complex releases iron rapidly to endogenous iron-binding proteins. It has a half-life of about 6 hours.¹⁷ It does not get deposited in the parenchymal tissue hence increasing ferritin levels.

On comparison of the cost factor, oral iron therapy was found cheaper and easy for administration. A back upsetting for treatment for anaphylaxis was mandatory for IVIS.

The limitations of this study were small study sample size and absence of follow-up in the postnatal period to determine whether hemoglobin levels were maintained during lactation because of higher stores after intravenous iron therapy.

The study concludes that oral iron increases hemoglobin comparably with IVIS. The replenishment of iron stores was good with IVIS compared with oral ferrous sulfate.

Women may become anemic again during lactation if their iron stores are not replenished. Hence replenishing stores is significant in our country where ongoing postnatal follow-up is often absent.

The absence of major adverse events with iron sucrose proves it a safe, efficacious treatment of mild to moderate IDA in pregnant women.

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