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**INTRAVENOUS IRON SUCROSE VS ORAL IRON THERAPY IN  
TREATMENT OF PREGNANCY WITH MODERATE ANAEMIA: A  
PROSPECTIVE STUDY IN A TERTIARY CARE CENTRE**

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**ABSTRACT**

A high proportion of women in both industrialized and developing countries become anaemic during pregnancy. Anaemia is associated with adverse fetomaternal outcome and is estimated to contribute 20% of all maternal deaths. Oral iron supplementation is commonly being promoted for correction of anaemia; however, the major problems faced are gastrointestinal side effects and slow rate of action in correcting anaemia. Intravenous iron supplementation using iron sucrose, besides having less gastrointestinal side effects, is more efficacious in correcting anaemia and replenishing the iron stores. This prospective study was conducted to compare the efficacy of intravenous Iron sucrose to oral iron in the treatment of moderate anaemia in 200 pregnant women who fulfilled the inclusion criteria in the Postgraduate Department of Obstetrics and Gynaecology, GMC Srinagar (tertiary care hospital). Both the groups showed significant improvement in all the parameters; however, the intravenous group showed achievement of target haemoglobin in 58% against 40% in the oral group, and ferritin levels increased significantly much more in the intravenous group than the oral group with  $p$  value  $< 0.0001$ . Only 1 patient needed blood transfusion in the intravenous group compared to 3 patients in the oral group. Iron sucrose is more effective in achieving target haemoglobin levels and replenishing iron stores in anaemic patients, and if given in time, intravenous iron therapy will help to reduce the risk of anaemia and subsequent maternal and fetal complications, as well as the risk of blood transfusion during pregnancy and at the time of delivery.

**Keywords:** *Haemoglobin, Anaemia, Serum Ferritin*

**INTRODUCTION**

Anaemia is estimated to affect about 2 billion people, mostly in developing countries (Viteri, 1998). A high proportion of women in both industrialized and developing countries become anaemic during pregnancy, as estimated from the World Health Organization report that from 35% to 75% (56% on average) of the pregnant women in developing countries and 18% of women in industrialized countries are anaemic (World Health Organization, 1992). Anaemia is estimated to contribute 20% of all maternal deaths and nine times higher risk of perinatal mortality (Morbidity Mortality Weekly Report, 1998). Fetal consequences are increased risk of growth restriction, prematurity, intrauterine fetal death, rupture of membranes, and infections (Allen, 1997). Anaemia leads to an increased risk of blood transfusion during the peripartum period. Iron therapy before delivery may reduce the transfusion rate for the iron-deficient women. Internationally, oral iron supplementation is the most common way of treatment, and dose depends on severity of condition. Severe systemic adverse effects associated with iron dextran and iron gluconate limited the use of intravenous iron. Iron sucrose can be given as total dose intravenous infusion. It is more effective, convenient, well tolerated, with no serious side effects. Blood transfusion is rarely used to treat iron deficiency anaemia in pregnancy. It may be considered where there is an inadequate amount of time to treat severe anaemia prior to birth. We sought to compare the efficacy of intravenous Iron sucrose to oral iron in the treatment of moderate anaemia in pregnancy.

## **Research Article**

### **MATERIALS AND METHODS**

This prospective study was conducted in the Postgraduate Department of Obstetrics and Gynaecology, Lalla Ded Hospital (tertiary care hospital) of Government Medical College Srinagar and was completed within one and half year with pregnant women attending the antenatal clinic. The study was approved by the ethical committee and the review board of the institution.

Anaemia during pregnancy was diagnosed as haemoglobin (Hb) concentration of less than 11g%.

#### **Inclusion Criteria**

- Singleton pregnancy
- Moderate anaemia in pregnancy (7-10.9g%).

#### **Exclusion Criteria**

- Anaemia due to haemoglobinopathies, chronic bleeding, diseases of liver, cardiovascular system and kidney.
- Medical disorders like tuberculosis and diabetes mellitus with anaemia.
- Women who have taken any form of parenteral iron therapy for anaemia during the present pregnancy.
- Patients with antepartum haemorrhage.
- Intolerance to iron or any allergic reaction to iron.
- History of any allergic reaction to iron in past

#### **Study Design**

A total of 200 women who fulfil the inclusion criteria and consented to participate were recruited for the study. They were randomly allocated in two groups. A detailed history was taken and a complete clinical examination was performed at the time of enrolment. The participants of group A was given oral tablets of 100mg elemental iron (Ferrous Sulphate) and 500 µg of folic acid daily as recommended by National Nutritional Anaemia Prophylaxis Programme (NNAPP). Tablets were provided for one month and women were asked to bring back empty packs after 15 days and were also asked about the intake of their tablets and the color of their stools to ensure that they had consumed the tablets.

In group B the women were be given two doses of IV iron sucrose of 200mg per sitting, 3-5 days apart, on an outpatient basis and 500 µg of folic acid daily orally. The iron was administered in short infusion with 100ml of normal saline over 30 minutes. We observed the response to a uniform dose over a range of pre-treatment haemoglobin. A 5ml of venous blood was taken before start of iron therapy and four weeks after therapy and divided into two parts.

*Part 1 (2ml in EDTA Vial):* For Haemoglobin, Haematocrit (PCV) (normal range 0.36-0.45) and red cell count. MCH, MCHC and MCV was derived from above parameters.

*Part 2 (3ml):* The other part of sample was evaluated for serum ferritin, serum iron and serum total iron binding capacity.

#### **Follow up**

Patients in both the groups were followed in the antenatal clinic till delivery. Routine investigations were performed. Patients on oral iron therapy were asked regarding side effects and tolerance to iron therapy. The blood indices were re-evaluated at 4 weeks to see the effect after iron supplementation. The mode of delivery, preterm delivery, birth weight of the new born and any transfusion required to mother during delivery were noted in all patients.

#### **Statistical analysis**

Data was described as Mean±S.D and Percentage. Intergroup comparison for measuring least significant difference of metric data was done by student 't' test at 95% confidence level. Intergroup variance of non-metric data was compared by chi-square test and Mann-Whitney 'U' test. Statistical package for social sciences (SPSS), MS Excel and Java Stat software were used for data analysis.

### **RESULTS**

Majority of the patients were in the age group of 25 to 29 years in both oral and intravenous group. Mean age of the patients in oral group was 26.2±3.8 and in the intravenous group it was 25.8±3.3 years. 73% patients in oral group and 74% in the intravenous group were primigravida. In oral group, 90.5% of the cases and in the intravenous group 87.5% of the cases had previous delivery more than 18 months back.

### Research Article

In oral group, 75% of subjects were Rh positive and 25% were Rh negative while in intravenous group 76% were Rh positive and 24% were Rh negative. The difference between the two groups was not statistically significant.

**Table 1: Haemoglobin status of the studied subjects**

Parameter		Oral	Intravenous	p value
Haemoglobin	Initial	9.5 ± 0.6 (8.3, 10.6)	9.3 ± 0.7 (8, 10.6)	0.130 (NS)
	Follow Up	10.8 ± 0.6 (9.4, 11.8)	11.0 ± 0.8 (9.0, 12.2)	0.007 (Sig)

As shown in above table, mean haemoglobin (g/dl) value of the oral and intravenous group before initiation of therapy was 9.5±0.6 and 9.3±0.7g/dl respectively whereas four weeks after the iron therapy, it was 10.8±0.6 and 11.0±0.8 in the oral and intravenous group respectively, there was significant improvement in both groups and the improvement in intravenous group was significantly more than oral group with p value of 0.007.

**Table 2: Haemoglobin Status at Follow up**

FU_Haemoglobin	Oral		Intravenous		p value
	N	%	n	%	
<11.0	60	60	42	42	0.016 (Sig)
≥ 11.0	40	40	58	58	

On follow up, 60% and 42% were having <11g% haemoglobin in oral and intravenous group. 40% of patients in oral and 58% in intravenous group were having ≥11g% respectively. In attaining the target haemoglobin levels, the difference between the two groups was statistically significant with p value of 0.016.

**Table 3: Parameters of the studied subjects**

Parameters		Oral	Intravenous	p value
Haematocrit (PCV)	Initial	29.1 ± 1.7	28.6 ± 2.7	0.095 (NS)
	Follow Up	32.6 ± 4.2	33.1 ± 2.4	0.704 (NS)
MCH	Initial	25.5 ± 3.4	26.1 ± 3.2	0.222 (NS)
	Follow Up	30.5 ± 2.7	30.0 ± 3.1	0.165 (NS)
MCHC	Initial	30.6 ± 3.2	30.1 ± 3.0	0.253 (NS)
	Follow Up	34.5 ± 3.0	34.7 ± 2.9	0.615 (NS)
MCV	Initial	79.8 ± 6.0	79.4 ± 6.4	0.638 (NS)
	Follow Up	87.0 ± 5.6	87.0 ± 6.7	0.950 (NS)
Serum Iron	Initial	55.5 ± 4.0	56.5 ± 7.3	0.539 (NS)
	Follow Up	71.6 ± 4.7	73.8 ± 5.1	0.121 (NS)
TIBC	Initial	449.6 ± 48.9	434.9 ± 69.8	0.394 (NS)
	Follow Up	350.0 ± 51.8	345.4 ± 46.0	0.741 (NS)
Serum Ferritin	Initial	11.0 ± 1.8	11.8 ± 2.0	0.153 (NS)
	Follow Up	16.5 ± 3.7	26.2 ± 6.3	<0.001 (Sig)

There was significant improvement of these parameters (table 3) in both the groups but the difference between the groups was insignificant except in increase in ferritin levels which showed significant increase in levels in intravenous group compared to oral group.

## Research Article

**Table 4: Perinatal Outcome**

Parameter		Oral		Intravenous		p value
		n	%	n	%	
Delivery Status	Preterm	13	13.0	8	8.0	0.250 (NS)
	Term	87	87.0	92	92.0	
Type of delivery	Normal Vaginal	58	58.0	65	65.0	0.325 (NS)
	Instrumental	4	4.0	3	3.0	
	Caesarean	38	38.0	32	32.0	
Blood Transfusion (if required)	Yes	3	3.0	1	1.0	0.314 (NS)
	No	97	97.0	99	99.0	
Birth Weight (gm)	mean±SD	2816±544 (1950, 3900)		2916±546 (2000, 3950)		0.177 (NS)

In the present study, there was no significant difference between the groups in terms of mode of delivery. Difference in birth weight and incidence of blood transfusion was not statistically significant but only 1 patient in the intravenous group needed blood transfusion against 3 in oral group.

## DISCUSSION

Iron deficiency anaemia remains the commonest medical disorder in pregnancy in developing world (Bernard *et al.*, 2001; Bhatt, 1997; Lopez and Murray, 1994). Iron is an essential component of haemoglobin, the oxygen-carrying pigment in the blood. It is estimated that a median amount of 840-1210 mg of iron needs to be absorbed over the course of the pregnancy (Beard, 2000). Measurements of serum haemoglobin concentration or haematocrit are the primary screening tests for identifying anaemia but are nonspecific for identifying iron deficiency. Measurement of ferritin levels has the highest sensitivity and specificity for diagnosing iron deficiency in anaemic patients. Levels of less than 10–15 micrograms/L confirm iron-deficiency anaemia.. Oral iron preparations consist of one of the iron salts, either alone or in combination with folic acid. Common iron preparation includes ferrous sulphate, and ferrous gluconate. The initial dose is usually 60-120mg elemental iron/day and in severe cases doses may be increase depending on each case. Intra-muscular iron is given in the form of iron sorbitol. Side effects are pain, pigmentation and sterile abscess at injection site, flushing, palpitations, headache and anaphylaxis. Intravenous iron therapy can be a good substitute to oral iron therapy. Outpatient treatment of anaemia in pregnancy and post partum period using iron sucrose is safe and feasible, with high patient compliance and cost savings from hospitalization fees (Tan and Siti, 2008). The reason being that iron sucrose consists of polynuclear complex analogous to ferritin with apoferritin component replaced by sucrose, that is well tolerated and least antigenic and being a large molecule less than 5% is excreted from kidneys. It is available for erythropoiesis within 5 minutes of infusion and has a 68-95% utilization rate after 2-4 weeks since it is stored in reticuloendothelial cells and not in parenchymal cells like liver, kidney, adrenal gland or other organs, hence organ toxicity (such as pancreatic, myocardial or hepatic hemosiderosis) is less likely even with iron sucrose overload (Bayoumeu *et al.*, 2002). Besides, the goal of iron therapy i.e. to supply sufficient iron to correct haemoglobin deficit as well as replenish iron stores is achieved without the need for further iron therapy throughout pregnancy and probably after. Unlike other parental iron preparation iron sucrose is safe with infrequent side effects.

The present study showed a haemoglobin rise from  $9.5 \pm 0.6$  to  $10.8 \pm 0.6$  in oral group and from  $9.3 \pm 0.7$  to  $11.0 \pm 0.8$  in the intravenous group. Intravenous group showed a statistically significant rise in haemoglobin compared to oral group. In a study done by Surraiya *et al.*, (2011), the rise in the haemoglobin was  $9.35 \pm 1.62$  to  $11.20 \pm 0.8$  gm/dL in the oral group and from  $9.2 \pm 1.69$  to  $12.6 \pm 1.06$  gm/dl in the intravenous group on day 30 (p value 0.0001). Al-Ragib *et al.*, (2005) had also reported a significant rise in haemoglobin levels in the intravenous group (p value 0.031).

## **Research Article**

In the present study, 58% in intravenous group attained target haemoglobin levels against 40% in oral group, the difference between the two groups was statistically significant with p value of 0.016. In a study by Wali *et al.*, (2002) Target Hb levels were achieved by 70% to 80% in intravenous group.

The present study showed an increased in haematocrit, and red cell indices [Mean corpuscular volume (MCV), Mean corpuscular haemoglobin (MCH) and Mean corpuscular haemoglobin concentration (MCHC)] in both the oral iron and intravenous group, although the difference was not statistically significant. The results were comparable with the study of Kumar *et al.*, (2005).

In the present study, serum ferritin had increased from  $11.0 \pm 1.8$  to  $16.5 \pm 3.7$  in oral group and  $11.8 \pm 2.0$  to  $26.2 \pm 6.3$  in intravenous group. Kumar *et al.*, (2005) had reported rise in serum ferritin from  $10.9 \pm 3.0$  to  $16.6 \pm 6$  in the oral group and  $11.6 \pm 3.4$  to  $22.1 \pm 10.5$  in the intravenous group. Bayousemeu *et al.*, (2002) also found a statistically significant rise in serum ferritin levels in the intravenous group compared to oral iron group.

Najma *et al.*, (2008) compared the efficacy of iron sucrose with ferrous sulphate for treatment of iron deficiency anaemia during pregnancy. Group A received ferrous sulphate 200mg three times a day for 60 days and Group B received iron sucrose according to formula. Group B (iron sucrose) showed significantly higher value of Hb, ferritin values were also higher in patients receiving intravenous iron sucrose. They suggested that iron sucrose can be considered as a useful alternative treatment for iron deficiency anaemia during pregnancy with no serious adverse reaction.

In the present study, both the oral and intravenous group showed an increase in serum iron and decrease in total iron binding capacity but the difference was not significant statistically. However Singh *et al.*, (1998) conducted a study to compare the efficacy of intravenous iron dextran with oral ferrous fumarate therapy in the treatment of iron deficiency anaemia in pregnancy. The study showed that treatment with intravenous iron dextran besides increase of haemoglobin and Serum ferritin resulted in a significant improvement in serum iron levels in the intravenous group compared to those given oral iron. In a study conducted by Kumar *et al.*, (2005); serum iron increased from  $56.2 \pm 6.7$  to  $72.3 \pm 7.4$  in oral group and from  $57.6 \pm 10.8$  to  $72.30 \pm 8.0$  in intravenous group, while as TIBC decreased from  $435.0 \pm 36.9$  to  $380 \pm 40.3$  in oral group and from  $450.3 \pm 59.8$  to  $350.9 \pm 48.9$  in intravenous group which is similar to our study.

In our study the change in haemoglobin and ferritin from baseline was significantly higher in the intravenous group than the oral group at each measurement. Blood transfusion was required for only one patient in the oral group against 3 in oral group.

In present study patients who had term delivery were 87% in oral and 92% in intravenous group while as 13% of the patients in oral group and 8% in intravenous group delivered before term. 58% patients in oral and 65% in intravenous group had normal vaginal delivery, 4% patients in oral group and 3 patients in intravenous group had instrumental delivery remaining cases were delivered by caesarean section. Mean birth weight (gm) in oral group was  $2816 \pm 544$  and  $2916 \pm 546$  in intravenous group. No statistically significant difference was seen in gestational age at delivery, type of delivery and mean birth weight between oral and intravenous group. Similar results were obtained by Bayoumeu *et al.*, (2002) and Sharma *et al.*, (2004).

## **Conclusion**

Present study clearly illustrates the efficacy of iron sucrose in achieving target haemoglobin levels in anaemic patients and if given in time intravenous iron therapy will help to reduce the risk of anaemia and subsequent maternal and fetal complications as well as risk of blood transfusion during pregnancy and at the time of delivery. Moreover the compliance of patients with parenteral iron is much better due to reduction of gastrointestinal side effects. So the current guidelines for the management of iron deficiency anaemia should incorporate intravenous iron sucrose as effective and safe treatment in pregnant women with IDA.



## **Research Article**

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