

Original Research Article

A PROSPECTIVE INTERVENTIONAL STUDY-ORAL VERSUS PARENTERAL IRON THERAPY IN IRON DEFICIENT EXPECTANT MOTHER

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Received : 07/12/2024
Received in revised form : 19/01/2025
Accepted : 02/02/2025

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DOI: 10.70034/ijmedph.2025.1.76

Source of Support: Nil,
Conflict of Interest: Nonedeclared

Int J Med Pub Health
2025; 15 (1): 400-404

ABSTRACT

Background: Anaemia in pregnancy is a global problem and Iron Deficiency Anaemia (IDA) being the most common form and it is mostly of nutritional origin. In a country like India, anaemia is frequently severe and contributes to maternal mortality and morbidity. It deserves more attention than what it is currently receiving. **Aims and Objectives:** To compare the efficacy of Oral Iron (Ferrous sulphate, Carbonyl Iron) versus Parenteral Iron (Iron Sorbitol-intramuscular, Iron Sucrose - intravenous).

Materials and Methods: This is a prospective randomised clinical and interventional study done in the Satya sai medical college and year from oct 2022-oct 2024 with sample size of 100 pregnant women attending the antenatal OP with gestational age of 16 – 34 weeks with Single viable fetus with no obvious ultrasonologic congenital anomalies, haemoglobin between 7 – 10 gm% were recruited in this study with informed consent. A total of hundred women were allotted into two major groups of 50 subjects each. A detailed history including the demography, complaints, period of gestation, diet history, previous obstetric history and drug history. Complete general physical examination was carried out along with other system examination. Apart from routine antenatal profile, stools for ova, cyst and occult blood, serum ferritin (CLIA) were done and diagnosis of Iron deficiency anaemia confirmed. Haematological parameters were analysed by Beckman & Coulter, USA (automated). Initial blood examination was done between 16 and 34 weeks. Final tests were done after 4 weeks of Iron supplements in both groups.

Results: Into this study, 100 pregnant women of gestational age 16-34 weeks with moderate Iron deficiency anaemia were recruited. They were divided into two broad groups receiving oral Iron and parenteral Iron. The oral group was again subdivided into those to receive Ferrous sulphate and Carbonyl Iron. The parenteral group was further subdivided into Iron sorbitol and Iron sucrose groups. The response to therapy was noted by mean rise in Haemoglobin at the end of 4 weeks. Iron deficiency anaemia was found to be more prevalent among age group 21-25yrs. Multigravidas were found to be more anaemic compared to primigravidas. With regard of the treatment results of Iron deficiency anaemia, among the oral group (Ferrous/Carbonyl Iron), Carbonyl Iron showed a better mean Hb rise compared to FeSO₄. Among the parenteral group, intravenous Iron sucrose showed better and quick response in terms of mean Hb rise compared to intramuscular Iron sorbitol. Overall comparison of all four types of medications together, in terms of mean Hb rise, indicated that intravenous Iron sucrose is found to be superior over others. Apart from mean Hb rise, Iron sucrose administration was also found to be associated with minimal side effects.

Keywords: Iron deficiency anemia, Oral Iron, Parenteral Iron.

INTRODUCTION

Anemia is said to be present when the measured haemoglobin (Hb) falls below a defined level or range. However, there are differences in Hb concentrations between pregnant and non-pregnant women due to well-recognised physiological changes in the Hb concentration during the course of a normal pregnancy. Regardless of the etiology, the WHO defines anemia as the presence of a Hb level less than 11 g/dl during pregnancy and less than 10 g/dl in the puerperium.^[1]

Anemia in pregnancy is a global problem and Iron Deficiency Anaemia (IDA) being the most common form and it is mostly of nutritional origin. Anaemia is major public health concern in economically disadvantaged segments of population especially in developing countries.

In a country like India, anaemia is frequently severe and contributes to maternal mortality and morbidity. It deserves more attention than what it is currently receiving. Recently lot of programmes have been focused on safe motherhood; "Drive the anaemia out" is one among them. Apart from economic backwardness, gender discrimination is more prevalent in India and other Asian countries; the girl child right from birth is neglected with regard to nutrition and education thereby leading to anemia problem during pregnancy.

Aims and Objectives

The main aim of the study is to compare the efficacy of Oral Iron (Ferrous sulphate, Carbonyl Iron) versus Parenteral Iron (Iron Sorbitol- intramuscular, Iron Sucrose - intravenous).

MATERIALS AND METHODS

Study design: Prospective randomised clinical and interventional study

Duration of study: 2yrs (oct 2022-oct 2024)

Study population: The IDA antenatal women attending the antenatal OP in the Department of Obstetrics and Gynecology, Satyasai medical college with gestational age 16 – 34 weeks with haemoglobin between 7 – 10 gm%

Inclusion Criteria

1. Iron deficiency anemia with Hb values between 7 – 10 gm%
2. Gestational age 16 – 34 weeks.
3. Single viable fetus with no obvious ultrasonologic congenital anomalies

Exclusion Criteria

1. Anemia due to causes other than Iron deficiency.
2. History of blood transfusion and erythropoietin treatment in this pregnancy
3. Other medical disorders complicating pregnancy
4. Multiple pregnancy
5. Specific allergy to Iron derivatives.

6. Recent administration of any form of oral or parenteral Iron therapy for treatment of anemia. A detailed history including the demography, complaints, period of gestation (depending upon the LMP / early scan), diet history was also taken to know if her diet had adequate source of Iron. Emphasis was made on previous obstetric history and drug history. Complete general physical examination was carried out along with examination of the cardiovascular system and respiratory system. Abdominal examination was carried out. Apart from routine antenatal profile, stools for ova, cyst and occult blood, serum ferritin (CLIA) were done and diagnosis of Iron deficiency anemia confirmed. Haematological parameters were analysed by Beckman & Coulter, USA (automated). Initial blood examination was done between 16 and 34 weeks. Final tests were done after 4 weeks of Iron supplements in both groups.

Following specific haematological investigations were done at the first visit other than routine investigations:

1. Haemoglobin (Hb)
2. Peripheral smear

The recruited pregnant women (100) were divided into two major groups and further into subgroups to make a comparative study with oral and parenteral iron therapy.

Group A: 50 pregnant women were divided into two subgroups (A1 & A2) and given oral iron supplementation.

A1: Group (25 women) is given Ferrous sulphate (100g of elemental iron/day)

A2: Group (25 women) is given carbonyl Iron (100mg of elemental iron/day)

Group B: 50 pregnant women were divided into two subgroups (B1 & B2) and given parenteral iron therapy after calculation of required total dose of Iron.

B1: Group (25 women) is given intramuscular therapy (Iron sorbitol) B2: Group (25 women) is given intravenous therapy (Iron sucrose) Haemoglobin (Hb) was restimated after 4 weeks of therapy.

RESULTS

Table 1 showed that in the age group 18-20yrs, 2, 8, 12 pregnant women presented with Hb 7-7.9, 8 -8.9 and 9 -10 gm % respectively. In the age group 21-25 yrs, 17, 20, 19 pregnant women came to OPD with Hb 7-7.9, 8 -8.9, 9-10gm% respectively. In the age group 26-30yrs, 4, 5, 8 pregnant women had initial Hb as 7-7.9, 8-8.9, 9-10 gm% respectively above 30 yrs of age, 4 women had a Hb of 8-8.9 gm% and 1 woman had Hb of 9-10 gm%.

Figure 1 showed that out of total 100 cases, number were primiparas were 37 and multiparas were 63. Among primipara, 7, 14, 16 women were found to

have a haemoglobin range of 7- 7.9, 8-8.9, 9-10 gm% respectively. Among multiparas, 16, 23, 24 had a initial haemoglobin range of 7-7.-, 8-8.9, 9-10 respectively.

There was significant association ($p < 0.001$) between the mean pretreatment and post-treatment rise of Hb with ferrous sulphate was 8.89 ± 0.82 and 9.14 ± 0.82 respectively. The mean rise of Hb with was 0.25 ± 0.09 . There was no significant association ($p = 0.22$) between the mean rise of Haemoglobin with ferrous sulphate in primiparas (6/25) and multiparas (19/25) were 0.28 ± 0.04 and 0.25 ± 0.10 respectively.

There was significant association ($p < 0.001$) between the mean pretreatment and post-treatment rise of Hb with carbonyl iron was 8.70 ± 0.72 and 9.50 ± 0.65 respectively. The mean rise of Hb with carbonyl iron was 0.80 ± 0.16 . There was no significant association ($p = 0.81$) between the mean rise of Haemoglobin with carbonyl iron in primiparas (6/25) and multiparas (19/25) were 0.78 ± 0.20 and 0.80 ± 0.11 respectively.

There was significant association ($p < 0.001$) between the mean pretreatment and post-treatment rise of Hb with iron sorbitol was 8.19 ± 0.77 and 9.95 ± 0.76 respectively. The mean rise of Hb with iron sorbitol was 1.76 ± 0.23 . There was no significant association ($p = 0.41$) between the mean rise of Haemoglobin with iron sorbitol in primiparas (6/25) and multiparas (19/25) were 0.78 ± 0.20 and 0.80 ± 0.11 respectively.

There was significant association ($p < 0.001$) between the mean pretreatment and post-treatment rise of Hb with iron sucrose was 8.18 ± 0.91 and 10.63 ± 0.81 respectively. The mean rise of Hb with iron sucrose was 2.45 ± 0.23 . There was no significant association ($p = 0.28$) between the mean rise of Haemoglobin with iron sucrose in primiparas (6/25) and multiparas (19/25) were 2.53 ± 0.23 and 2.42 ± 0.22 respectively.

There was significant association ($p < 0.001$) between the mean difference in Hb rise between Iron sucrose

and Ferrous sulphate. The mean difference in Hb rise between Iron sucrose and Ferrous sulphate is 2.19. The mean Hb rise for Iron sucrose and Ferrous sulphate being 2.45 ± 0.23 and 0.25 ± 0.09 respectively.

There was significant association ($p < 0.001$) between the mean difference in Hb rise between Iron sucrose and Carbonyl iron. The mean difference in Hb rise between Iron sucrose and Carbonyl iron was 1.67. The mean Hb rise for Iron sucrose and Carbonyl iron was 2.45 ± 0.23 and 0.78 ± 0.16 respectively.

There was significant association ($p < 0.001$) between the mean difference in Hb rise between Iron sucrose and iron sorbitol. The mean difference in Hb rise between Iron sucrose and iron sorbitol was 0.69. The mean Hb rise for Iron sucrose and iron sorbitol was 2.45 ± 0.23 and 1.76 ± 0.22 respectively.

There was significant association ($p < 0.001$) between The mean Hb rise in Ferrous sulphate, Carbonyl iron, Iron sorbitol, Iron sucrose. The mean Hb rise in Ferrous sulphate, Carbonyl iron, Iron sorbitol, Iron sucrose are 0.25 ± 0.09 , 0.78 ± 0.16 , 1.76 ± 0.22 , 2.45 ± 0.23 respectively.

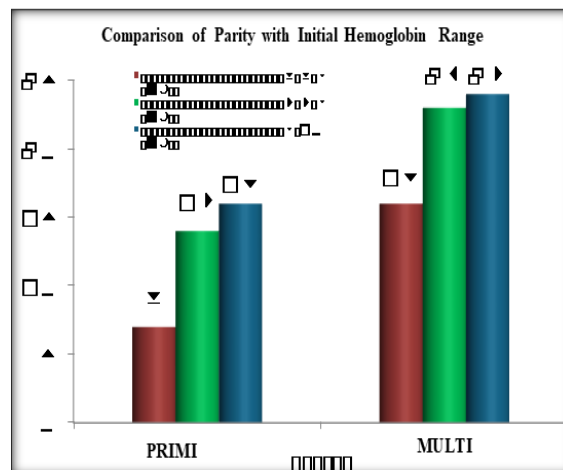


Figure 1: Nutritional anemia vs Parity

Table 1: Comparison of Haemoglobin values by distribution of age

AGE GROUP*HAEMOGLOBIN VALUES CROSSTABULATION					
Age group (yrs)	No. of patients (%)	Haemoglobin range (gm%)			Total
		7-7.9	8-8.9	9-10	
18-20		2 (9%)	8 (36%)	12 (54%)	22
21-25		17 (30%)	20 (35%)	19 (33%)	56
26-30		4 (23%)	5 (29%)	8 (47%)	17
>30		0 (0%)	4 (80%)	1 (20%)	5
Total		23	37	40	100

Table 2: Comparison of All Four Drugs in Rise of Hb

DESCRIPTIVES								
HbRISE								
	NUMBER	MEAN Hb	STD. DEVIATION	STD. ERROR	95% CONFIDENCE INTERVAL FOR MEAN		MINIMUM	MAXIMUM
					LOWER BOUND	UPPER BOUND		
FERROUS SULPHATE	25	0.25	0.09	0.02	0.22	0.29	0.1	0.4
CARBONYL IRON	25	0.78	0.16	0.03	0.73	0.86	0.5	1.1

IRON SORBITOL	25	1.76	0.23	0.05	1.66	1.85	1.4	2.2
IRON SUCROSE	25	2.45	0.23	0.05	2.36	2.55	2	2.8
TOTAL	100	1.31	0.87	0.09	1.14	1.49	0.1	2.8

DISCUSSION

Iron deficiency is a leading cause of anaemia, affecting over 500 million people worldwide. According to the National Family health survey III (2005-2006), the prevalence of anaemia in India is 57.9%.^[2]Federation of Obstetric and Gynaecological Societies of India/ World Health Organization (FOGSI-WHO) study (1997) on maternal mortality revealed that 64.4% of women who died had a haemoglobin of 8 gm%.^[3]

According to Malviya et al 2003⁴,Singh et al 1998⁵ suggest a connection between age and the occurrence of anaemia since other studies have reported that young women (<18 or <20 years) showed a higher tendency to be anaemic.^(23,24)In our study, the most affected (56 out of 100 women), by IDA in pregnancy were in the age group of 21-25 yrs. Majority (40 out of 100 women) presented with a haemoglobin range of 9 – 10 gm% followed by range of 8 - 8.9 gm% (37 out of 100 women). The reasons for incurring negative balance and iron deficiency in pregnancy is due to the substantial iron demands during this period. In this group, women give less consideration to their own diets which deteriorate in quality (poor bioavailability of dietary in most developing countries) and quantity year after year probably due to increased responsibilities in family which ultimately lead to reduction in pre-pregnant iron stores.

Christopher U Andert et al 2006 found that IDA to be more prevalent in primiparous women though not significantly.^[6]As reported by Dreyfuss et al., (2000) parity seems to have no effect on the prevalence of anaemia.^[7] Lalitha et al 2011, reported that prevalence of anaemia increases with the parity of women.⁸ Similarly in our study, we found that prevalence of anaemia was more in multiparas. In multiparas women, the Iron stores depletion from pregnancy-delivery-lactation cycle results in even more Iron losses. Replenishment of Iron stores before she enters into the next pregnancy is important. For the same reason, post natal clinics should counsel the postpartum women as these aspects are very important, in fact as important as antenatal clinics.

Till date no study has been done to report the haemoglobin rise with various Iron preparations in primiparas and multiparas. In our study, taking the parity into consideration, the mean rise of Haemoglobin in primiparas v/s multiparas with various Iron preparations were found to be as follows: Ferrous sulphate - 0.28 ± 0.04 v/s 0.25 ± 0.1 gm%; Carbonyl iron 0.78 ± 0.2 v/s 0.80 ± 0.11 gm%; Iron sorbitol - 1.84 ± 0.22 & 1.70 ± 0.23 gm%; Iron sorbitol - 2.53 ± 0.23 & 2.42 ± 0.22 gm% (P value > 0.001). This showed

there was no significant difference in rise in haemoglobin between primiparas and multiparas.

In the study done by Suharno et al 1993⁹ – the Hb rise with FeSO₄ was found to be in the range of 0.26- 0.55. In our present study, the Hb rise with Ferrous sulphate is found in the range of 0.16 – 0.34 gm% which was almost similar to Suharno et al, 1993.

There were no studies conducted with regard to the Hb rise with Carbonyl Iron in pregnant women. In our study, the mean Haemoglobin rise was 0.78 ± 0.16 gm% with Carbonyl Iron.

Choudhury A., 2007¹⁰ and Sharma A. et al 2008,^[11] found that there was significant rise of Hb with Irons or bitolin their studies. In our study, it is observed that there is a significant rise of Hb with Iron sorbitol was 1.76 ± 0.2 gm%; a finding consistent with above studies.

Khurshid SR et al 2003,^[12] showed a Hb rise of 3.5 gm% with Iron sucrose therapy. As per Farhat Naz et al 2009,^[12] the Hb rise with Iron sucrose therapy was 2.6 gm%. In the present study, the mean rise of Hb with Iron sucrose is 2.45 ± 0.23 gm% which is at par with the above studies.

In comparative studies of Hb rise with FeSO₄ v/s Iron sucrose, Al-Momen et al 1996,^[13] and Kochchar et al 2012,^[14] reported Hb rise in Iron sucrose group is better than Ferrous sulphate group whereas Bayoumeu et al 1999,^[15] showed no difference in Hb rise in both the studies. The above three studies took other variables, e.g, serum ferritin, MCV which also showed a better rise in Iron Sucrose group but in all three studies, dosage of FeSO₄ and Iron sucrose were different. In the present study, Hb rise in Iron sucrose group was better than that of Ferrous sulphate – findings were consistent with first two studies. This illustrates that intravenous Iron sucrose is superior to oral iron (FeSO₄) in improving the mean Hb concentration.

No studies have been done with carbonyl iron in IDA in pregnancy till date. The studies were done in non pregnant females with IDA. In our study, the mean rise of Hb in Carbonyl Iron was 0.78 ± 0.16 gm% whereas in Iron sucrose group was 2.45 ± 0.23 gm% showing that Iron sucrose (i.v) had better rise in Hb than Carbonyl Iron (oral).

In our study, compliance with oral treatment was surprisingly good similar to a study conducted by Bayoumeu F et al,^[15] in contrast to the findings described in some other studies. Gastrointestinal troubles, with a frequency of up to 30% as described by Al-Momen et al,^[16] have been reported in patients groups treated with oral Iron (Ferrous sulphate). In our study, among the two oral iron groups, Carbonyl Iron showed a better rise in haemoglobin more than Ferrous sulphate similar to study by Gordeuk et al 1986.^[17]

Only one study is available by Wali A. et al 2002,^[18] reported a better rise of Hb in Iron sucrose group when compared to Iron sorbitol. Results of present study also agrees with the above study. This showed that Iron sucrose (i.v) therapy is better than Iron sorbitol (i.m) therapy in treating Iron Deficiency anaemia (IDA) in pregnancy.

Comparison of oral, intramuscular and intravenous Iron therapies, as done in present study, has not been done so far in the past. In our study, while correlating the Hb rise, with various types of iron preparations given, showed Hb rise (mean±SD) with Ferrous sulphate, Carbonyl Iron, Iron sorbitol and Iron sucrose were 0.25±0.09, 0.78±0.16, 1.76±0.23, 2.45±0.23 gm% respectively, thus, clearly demonstrating the superiority of Iron sucrose over the others (P value <0.001, significant).

Our study illustrates clearly that intravenous iron sucrose complex is effective and has a rapid and profound response in improving anaemia as compared to Ferrous sulphate, Carbonyl Iron, Iron sorbitol (intramuscular) therapies.

CONCLUSION

As there is an increased demand for Iron during pregnancy, women when not on supplements may slip into the depleted state. Since there is an increased morbidity among the mothers and fetus and adverse long term sequelae due to Iron deficiency during pregnancy, Iron supplementation is advised. There is a definite improvement in the Haemoglobin percentage with Iron supplementation. Iron sucrose helps in the improvement of serum Ferritin thus replenishing the Iron stores. The improved hematological outcome with Iron sucrose is evidence based. Although Iron sucrose therapy may appear invasive, expensive and time consuming, it is highly and rapidly effective without major side effects. This makes it convenient and cost effective in pregnant Iron deficient women who are unable to obtain adequate amount of Iron rapidly by the oral route. If used in time, it obviates the need for blood transfusions during peripartum period. Hence, Iron sucrose therapy can be considered as the first-line option for the safe and rapid reversal of Iron deficiency anemia in pregnancy.

Conflict of Interest: None

Funding Support: Nil

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