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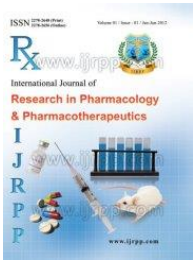

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Research article ***Open Access***

Intravenous iron sucrose versus oral ferrous sulphate therapy in moderate anaemia of antenatal women- a comparative study

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ABSTRACT

Introduction

The prevalence of iron deficiency anaemia among women during pregnancy is of concern and a cause of considerable morbidity and mortality. Anaemia results in an increased number of preterm births, IUGR, PPH, failure of lactation and increased risk of infections in the postpartum period. Oral iron therapy has less compliance due to inadequate absorption and side effects and in such conditions parenteral iron therapy like Intravenous sucrose is preferred.

Patients and methods

This study was prospective, comparative and interventional. The total duration of the study was six months. Two groups, each of 50 antenatal women were given ferrous sulphate and Intravenous sucrose. All antenatal women were reviewed after four weeks, and they were enquired about compliance, and adverse effects and the haematological investigations were repeated to know the post-treatment response. Unpaired t test and Chi square tests were used for statistical analysis and p value <0.01 was taken as highly significant (HS).

Results

Rise of Haemoglobin by 2.5g% was seen in IV sucrose group when compared to rise by 1.3g% in Oral group. Mean rise of PCV was 2.68± 1.13 with oral iron and mean rise of PCV was5.7± 2.77 with IV iron sucrose, both were HS but Mean rise in MCV values was not significant. Adverse effects were less in IV sucrose group and hence more compliance.

Conclusion

I.V Iron sucrose was found to be more effective in the treatment of moderate anaemia in antenatal women with less adverse effects and better tolerance.

Keywords: Haemoglobin, Packed cell volume (PCV), Mean Corpuscular Volume (MCV), Tolerance and Compliance.

INTRODUCTION

Iron deficiency anaemia is a common antenatal problem throughout the world with the burden of disease impacting on both the mother and the foetus during pregnancy. Anaemia affects many of the pregnant women in the world [1]. In India, up to 88% of pregnant women are affected by anaemia [2]. Among those, 50% of anaemia in pregnancy is due to iron deficiency [3]. The prevalence of iron deficiency anaemia among women during pregnancy is of concern and a cause of considerable morbidity and mortality.

Anaemia is estimated to contribute to 20% of all maternal deaths [4, 5] and 9% of perinatal mortality [6]. There is a 2-3 fold increase in perinatal mortality when Haemoglobin is less than 8gm/dl and 8-10 fold increase when maternal haemoglobin falls below 5gm/dl [7]. Anaemia results in an increased number of preterm births, IUGR, PPH, failure of lactation and increased risk of infections in the postpartum period [8]. Hence prevention and correction of anaemia during pregnancy will be very important for safe motherhood.

Iron deficiency anaemia exists for many years. Oral iron has been the first line of treatment for treating anaemia during pregnancy, but a considerable number of patients did not improve because of reasons like intolerance to oral iron, inadequate absorption, and side effects leading to non-compliance due to which treatment becomes insufficient and in such conditions parenteral Iron therapy is preferred.

According to the World Health Organisation (WHO), oral iron preparations have been proved to be inadequate to reduce the incidence of Iron deficiency anaemia. Many antenatal women have been observed to be iron deficient despite the routine use of iron prophylaxis adopted by health care centres in developing countries. The WHO technical group working on the prevention and treatment of anaemia has documented that parenteral iron therapy has produced a rapid and complete correction of iron deficiency anaemia than oral iron therapy [1].

Among all the parenteral iron preparations available, Iron sucrose appears to be efficient because of its safety record, and it overcomes the problems of absorption and compliance compared to iron dextran, iron gluconate and, also blood transfusion [9, 10].

Iron sucrose can correct anaemia, reduce the maternal morbidity and promote better neurological development of new born infants and improve the health status of women.

Iron deficiency anaemia in pregnancy needs to get corrected because of its related morbidity and mortality. The aim of this study was to compare the efficacy and adverse effect profile of oral iron and intravenous iron sucrose, in the treatment of moderate anaemia in antenatal women.

The study was prospective, comparative and interventional and was carried out in antenatal women with moderate anaemia, i.e. haemoglobin less than 8gm%. This study was carried out in patients attending antenatal checkups at the outpatient department of Obstetrics and Gynaecology, Government General Hospital, Vijayawada, Andhra Pradesh.

METHODOLOGY

The present study was taken up to compare and evaluate the efficacy and adverse effects profile of intravenous iron sucrose with oral iron used for the treatment of moderate anaemia in antenatal women attending Obstetrics outpatient department in Government General Hospital, Vijayawada.

Institutional ethics committee (IEC) approval was obtained from Siddhartha medical college, Vijayawada before initiating the study. From all antenatal women enrolled in this study, Informed consent was taken in the local language. The sample size is 100 antenatal women. The study design is prospective, comparative and interventional. The total duration of the study was six months.

Inclusion criteria

- Singleton pregnancy with the gestational age of 20-28weeks.
- Primi and Second gravidas attending antenatal OP.
- Haemoglobin concentration of more than 8 gm and less than10.5gm. (moderate anaemia)

Exclusion criteria

- Pregnancy- associated with medical problems like Diabetes, Heart disease, renal & hepatic disorders.
- Obstetrical complications like PIH, APH etc.

- Pregnancy with anaemia other than iron deficiency, like medical & surgical causes of bleeding.
- Antenatal women with multiple pregnancy.

Materials used for the study

- Tablet: Ferrous sulphate 200mg bd. Each tablet has 65mg of elemental iron (Govt. supply)
- Injection: Orofer-S 5ml ampoule containing 100mg 0f iron. (produced by EMCURE pharma)

A total of 122 antenatal women in the age group of 18-25yrs were enrolled and assessed for eligibility to participate in the study. Out of them, 22 women failed to meet the inclusion criteria were excluded.

Investigations like complete Haemogram (with all indices- Hb%, PCV, M.C.V, M.C.H.C, Reticulocytecount, Platelet count), Liver Function Tests, Serum Creatinine, Blood Urea, Bleeding Time, Clotting Time, and Random Blood Sugar and Ultra sonogram were done to rule out exclusion criteria. A thorough history was taken, and a clinical examination was done.

Antenatal women were randomly assigned into two groups A &B

- Group A: Received ferrous sulphate orally 200mg BD after food for four weeks.
- Group B: Received iron sucrose intravenously, the dose was calculated using the following formula,
- **2.4 x bodyweight in kgs x Hb deficit in gm%+ 500mg** [11, 12]**.**
- 500mg to replenish iron reserves.

Example

Target Hb was 12gm% so, for an antenatal woman with Hb 8gm% and weight 50kgs the calculation was done as follows,

2.4× 50(12-8)+ 500=980mg

Thus, the obtained dose is given in divided doses, with 48hrs apart, 200mg each time. Each 1 ml contains 20mg of elemental iron, and every 5ml of it is dissolved in 100ml of 0.9% of Normal Saline per day, maximum of 200mg infusion was given.

All these antenatal women were reviewed after four weeks, and they were enquired about compliance, and adverse effects and the haematological investigations were repeated to know the post-treatment response.

Statistical methods

The results were noted, tabulated, analysed and expressed as descriptive statistics. Students paired t-test has been used to find the significant rise in blood indices within the study groups before and after treatment. An Unpaired t-test was used to compare the efficacy between two groups. Percentages were compared using the Chi-square test. P-value, <0.001 was considered significant.

Statistical software

Microsoft Excel was used to generate tables and graphs. The results were analysed by using SPSS V-21 software.

OBSERVATION AND RESULTS

The results were compared as the rise in Blood indices, before and after taking oral treatment and also before and after receiving I.V Sucrose. Then finally, the mean increase in Blood indices, Hb, Haematocrit (PCV) and MCV after oral iron sulphate is compared with the mean rise after intravenous use of iron sucrose.

The adverse effect profile of oral iron sulphate was compared with those of Intravenous iron sucrose, and adverse effects were found to be less with IV sucrose. Demographic data were tabulated and analysed in tables1, 2, 3 and 4

Table-1: Distribution of age in both the groups

Age Group	Minimum	Maximum	Mean	D
A	20	26	22.48	1.31
B	20	24	22.12	1.04

Table-2: Distribution of weight in both Groups.

	Weight			
Group	**Minimum**	**Maximum**	**Mean**	**SD**
A	38	62	48.66	4.79
B	40	64	48.08	5.50

Table-3: Distribution of gestational age in both groups

	Gestational Age			
Group	**Minimum**	**Maximum**	**Mean**	**SD**
A	24	32	27.56	2.30
B	24	32	29.52	2.04

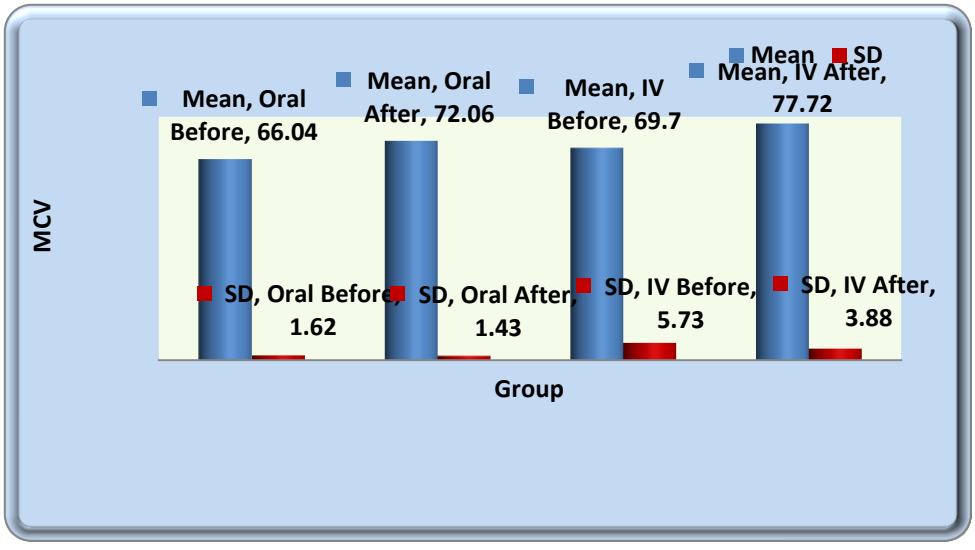
Table-4: Distribution of gravidity in both groups.

Parity	**Group**			
	Group-A		**Group-B**	
	Frequency	**Percentage**	**Frequency**	**%age**
PRIMI	26	52.00%	28	56.00%
G-2	21	42.00%	22	44.00%
G-3	3	6.00%	0	0%
Total	50	100.00%	50	100.00%
P-value	<0.01[Chi-square value=26.34]		<0.01[Chi-square value=39.12]	

Table-5: Distribution & comparison of MCV before and after treatment in both groups

Group	**At**	**Minimum**	**Maximum**	**Mean**	**SD**	**Paired t-value**	**P-value**	%age
A	Before	62	69	66.04	1.62	-21.68	<0.01	
	After	70	75	72.06	1.43		HS	9.1%
B	Before	56	78	69.7	5.73	-8.44	<0.01	
	After	70	86	77.72	3.88		HS	11.5%

This table shows, there is a 9.1% increase in MCV with oral iron and 11.5% increase in MCV with IV iron sucrose. Increase in MCV is highly significant (HS) with p-value <0.01



Graph-1: Comparison of mean & SD of MCV before & after treatment in both groups

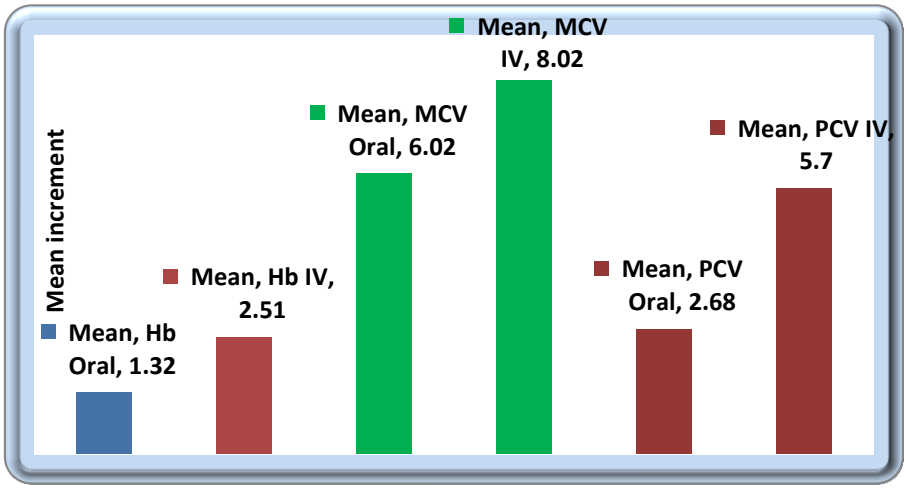
Table-6: Comparison of mean Haemoglobin before & after treatment in both groups

Group	At	Minimum	Maximum	Mean	SD	Paired t-value	P-value	%age
A	Before	7.6	9.6	8.51	0.46	-19.64	<0.01 HS	15%
	After	8.3	11.2	9.84	0.62			
B	Before	7.4	8.8	8.16	0.33	-40.01	<0.01 HS	30%
	After	10.2	12	10.66	0.39			

This table shows mean haemoglobin 8.51g% before treatment and 9.84g% after treatment in group A and therefore rise by 1.3g% in 4weeks. The mean haemoglobin 8.16g% before treatment and 10.66g% after treatment in group B and therefore rise by 2.5g% was seen in 4weeks. This rise is statistically highly significant (HS)

Table-7: Comparison of mean PCV (Haematocrit) before and after treatment.

Group	At	Minimum	Maximum	Mean	SD	Paired t-value	P-value	%age
Oral	Before	24	28	25.92	1.19	-16.73	<0.01 HS	10.3%
	After	25	31	28.6	1.40			
IV	Before	22	32	26.36	2.16	-14.54	<0.01 HS	21%
	After	30	36	32.06	1.65			

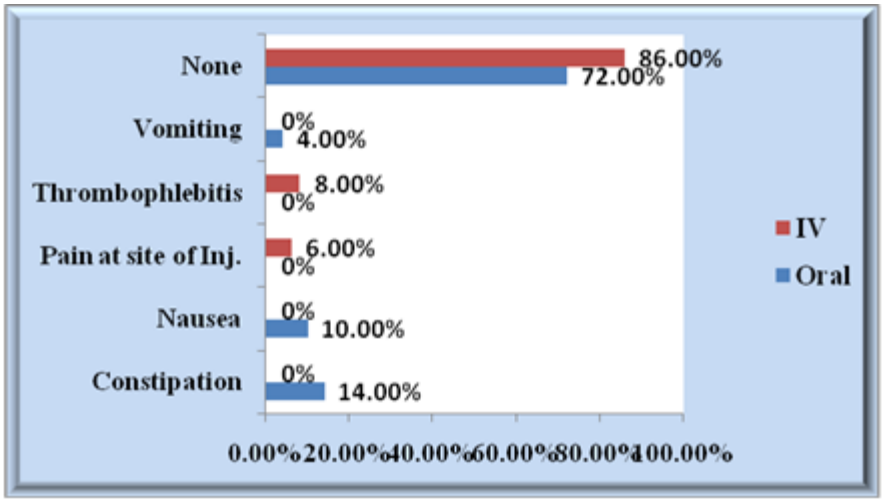


Graph-2: Comparision of mean increment of Hb, MCV and PCV before and after treatment.

This Graph 2 shows - Mean rise of Hb was 1.32± o.48 with oral iron and Mean increase of Hb was 2.51± 0.44 with IV iron sucrose this was highly significant (HS).

Mean increase in MCV was6.02±1.92 with oral iron and mean rise of MCVwas 8.02±6.72 with IV iron sucrose this was not significant (NS).

Mean rise of PCV was 2.68± 1.13 with oral iron and mean rise of PCV was5.7± 2.77 with IV iron sucrose. These findings showed improvement in Hb and PCV which were statistically highly significant (HS).



Graph-3 Distribution of adverse effects in both groups (Oral& IV)

Adverse effects as shown in Graph 3, were 28% in group-A (oral) whereas in group-B (IV) it was 14%. Though adverse effects were less with I.V Sucrose it was not statistically significant (P=0.09) [Applied Chi-square test: Chi-square value=2.95]

DISCUSSION

Throughout the world and in India, Iron deficiency anaemia is affecting 35-75% (average 56%) of pregnant women in developing countries and 18% of women from industrialised countries. Anaemia is estimated to contribute to 20% of all maternal deaths and 9% of perinatal mortality. Anaemia results in an increased number of preterm births, IUGR, PPH, failure of lactation and increased risk of infections in the postpartum period. Hence prevention and correction of anaemia during pregnancy are vital for safe motherhood.

The traditional treatments, i.e., oral iron therapy and blood transfusion, involve significant drawbacks. High doses of oral iron frequently cause side effects, and noncompliance is common. Administration of oral iron supplementations is not sufficient enough in order to treat anaemia effectively. Due to limited absorption, the gastrointestinal symptoms and the poor compliance for long term treatment of the patients.

As far as blood transfusions are concerned, because of the risk of infection (bacterial, viral, prions) and immunomodulation associated with allergenic blood products, especially in this young and otherwise healthy population, transfusions are used only in the most severe cases and particularly in life-threatening situations. Therefore, intravenous iron has been considered as an alternative in the management of iron deficiency anaemia.

This study was conducted in the Obstetrics & Gynaecology Department of Government General Hospital, Vijayawada, Andhra Pradesh.

A total of 100 antenatal women were recruited in this study, with 50 in each group. Majority of women were in the age group of 22-25 years. The mean age of the patients in other studies was approximately similar to the present study.

In all other studies, the maximum number of patients were primigravidas. In the present study 52% were primigravida in oral group (P-Value <0.01 & Chi-square value-26.34) and in Intravenous group 56% were primigravidas (P-Value<0.01 &Chi square these findings were significant. This was explained by the high prevalence of iron deficiency anaemia in adult non-pregnant women. When these anaemic women become pregnant, their anaemia will be aggravated by an increased need for iron during pregnancy, and it is important to screen iron deficiency anaemia in all non-pregnant child bearing age group women as recommended by the Centre for Disease Control and Prevention.

In this study, the mean gestational age at the time of inclusion in both the groups is comparable (in group A 27.56 ± 2.3 weeks and in group B 29.5 ± 2.) to the mean of gestational age in the study by Aggarwal Rohina et al. where it was 28.8wks and 28.2wks. [13] The mean baseline MCV was 66.04fl in oral (Group-A) & 69.7in Intravenous (Group -B). Post-treatment MCV after four weeks showed an

average rise of 6.2fl and 8.2fl in oral and IV group, respectively (p-value < 0.01), which is statistically significant.

In this study, the mean baseline haemoglobin was 8.05g/dl in the oral group and the intravenous group; it was 8.16g/dl, which was found to be statistically insignificant between the groups. Whereas, Post-treatment haemoglobin after four weeks showed a mean value of 9.84g/dl and 10.66gm/dl in oral and IV group, respectively (p-value <0.01), which is statistically significant.

In the present study, the average rise of haemoglobin is 1.3gm/dl in the oral group and 2.5g/dl in the IV group (p-Value <0.01).Therefore the overall increase in haemoglobin is more with IV iron. This data is similar to the study by Aggarwal Rohina et al., where the average rise of haemoglobin was 4.32g/dl in oral group, and an average rise of 5.03 g/dl was observed in intravenous group [13].

In the study of Momen AI et al, baseline haemoglobin was 7.6 g/dl and 7.5 g/dl in oral and IV groups, respectively. The average rise of haemoglobin was 3.54g/dl and 5.3g/dl in oral and IV group, respectively.[14]

With all these studies, it was evident that the rise in haemoglobin level is more with Intravenous iron Sucrose than with that of oral iron. This can be explained by the fact that absorption of iron is better when given intravenously.

The mean baseline haematocrit (PCV) in the oral group was 25.92%, and in the intravenous group, it was 26.36% after treatment mean PCV was 28.6% (P value<0.01) and 32.6 %(P Value<0.01) in oral and IV groups respectively. An average rise of 2.7% and 4% was observed in both groups. Paired t- value in the oral group was 16.73, and that of IV group was 14.54, which is statistically significant.

There were minimal side effects in the study groups; however, 28% in the oral group had minimal side effects like constipation, nausea and vomiting, but nobody had restrained from the study.

Among those women in the IV group, only 14% had minimal side effects like pain at the injection site, and mild thrombophlebitis P Value=0.09 and chi-square value=2.9, which indicate that these adverse effects were not significant. Similar observations were reported in other studies like Aggarwal Rohina et al, Momen AI et al, and Bayoumeu et al. without serious adverse effects [13, 14, 15].

This study is comparable to the other two studies. In a study done by Aggarwal Rohina.S et al. in 2010, showed baseline Hb 6.2g% and 5.95g%, Haematocrit 18.8 and 17.8%,MCV 71.28 and 70.1fl in IV and oral group respectively. [13] After 4wks, Hb% increased to 11.3 and 10.26g %, Haematocrit increased to 33.9, and 30.77% and MCV increased to 93 and 85.8fl in IV and oral group respectively.

In another study done by Momen AI et al. in 1996, has shown baseline Hb 7.58 & 7.66g% and MCV 68.6 &70.8fl in IV and oral group, respectively [14]. After 4wks Hb% increased to 12.8 & 11.1g% and MCV increased to 82.6 & 74.9fl in IV and oral group respectively. In both studies, no major side effects were seen. Bayoumeu et al (2002) in his study also suggested that the IV iron sucrose tolerance seemed to be excellent without adverse side effects [15].

Thus, it can be inferred from this study that, though both drugs have shown improvement in haemoglobin levels and PCV, Intravenous Iron sucrose showed superior efficacy and minimal adverse effects.

As most of the antenatal women attending government hospitals belong to low socioeconomic status, the drug iron sucrose if made available in government hospitals then there can be promising results in the treatment of moderate anaemia in antenatal women.

The limitations of this study

- Sample size in this study was small when compared to the prevalence of this most common disease.
- One ampoule of iron sucrose injection contains 100mg of iron costs around Rs.300. As most of the antenatal women attending government hospitals belong to the lower socio-economic group, the high price of iron sucrose may not be affordable by them.
- Specific investigations like TIBC and serum iron could not be done as they were not available in government and are very expensive in private labs.

CONCLUSION

The present study showed that treatment of anaemia with any of the drugs, either oral ferrous sulphate or intravenous iron sucrose would increase

the haemoglobin. This study proved that iron sucrose when given intravenously there was a rapid improvement in anaemia. IV iron sucrose was shown to be safe as it had fewer side effects.

In conclusion, I.V Iron sucrose was found to be more effective in the treatment of moderate anaemia in antenatal women. A superior tolerability profile to that of oral iron preparation (FS) and a better efficacy profile, strongly suggest that it can be considered as an alternative drug for the treatment of moderate anaemia in antenatal women.

However, further studies in large patient populations are required to confirm and strengthen the present study.

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