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Original Research Article

Oral versus intravenous iron therapy among pregnant women with iron deficiency anaemia: a comparative study

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ABSTRACT

Background: Anaemia during pregnancy is considered to be a serious health concern. Whilst oral supplementation is most prevalent, it is also possible to provide iron parentally to replace the deficit.
Methods: An observational study was conducted in the department of obstetrics and gynaecology of a tertiary care hospital, in Maharashtra. Total 110 women with iron deficiency anaemia were randomly divided into two groups using computer generated random numbers. Group A received oral iron therapy and group B received intravenous sucrose therapy. The haemoglobin and serum ferritin were assessed before and after treatment.
Results: In the oral iron therapy group the age ranged between 19.3 to 27.1 years and in intravenous iron therapy group from 19.2 and 26.5 years. Baseline (0 day) haemoglobin in oral iron therapy group was 8.21±1.12 gm/dl and 8.36±1.14 gm/dl in intravenous iron group. The mean difference of 3.38 gm/dl was seen in the intravenous therapy group at 8th weeks against the mean difference of 1.63 gm/dl in oral iron therapy group. The mean difference of serum ferritin 18.92 µg/l was found in the oral iron therapy at the 8th week while the mean difference of 63.79 µg/l was seen in the intravenous therapy group.
Conclusions: The intravenous sucrose therapy is found to be safe and effective alternative treatment for iron deficiency anaemia in pregnancy though the cost of treatment is significantly higher than the oral therapy.

Keywords: Anaemia, Haemoglobin, Iron deficiency anaemia, Serum ferritin

INTRODUCTION

Anaemia is a major health issue and its prevalence has reached 30% of the world's population.[1,2] According to World Health Organization report, about 32.4 million pregnant women suffer from anaemia worldwide, of which 0.8 million women are severely anaemic.[3] Almost 58 percent of pregnant women in India are anaemic and it is estimated that anaemia is the underlying cause for 20-40 percent of maternal deaths in India.[4] The most common cause of anaemia worldwide is iron deficiency, resulting from prolonged negative iron balance, caused by inadequate dietary iron intake or absorption, increased needs for iron during pregnancy.[5] Iron deficiency anaemia is considered when the haemoglobin of less than 11 gm% in the first and third trimester of pregnancy and less than 10.5 gm% in the secondtrimester of pregnancy.[6,7] According to WHO anaemia during pregnancy is graded as severe when haemoglobin concentration is less than 7.0 gm/dl, moderate when haemoglobin falls between 7.0-9.9 gm/dl, and mild from 10.0-11 gm/dl.[8] Iron deficiency anaemia evolves through three distinct stages- depletion of iron storage occurs in the first phase (stage I), where the total body ironis decreased but red cell indices and haemoglobin (Hb) synthesis remain unchanged. Both these indices change when the supply of iron to bone marrow is reduced (stage II or iron deficient erythropoiesis). In stage III, eventually, iron deficiency anaemia develops due to insufficient supply of iron to sustain anormal haemoglobin concentration.[9]

Conventionally, the first choice in the treatment of iron deficiency anaemia for the majority of patients is the oral iron replacement therapy which is easily available at all peripheral health centers and subcenters.[10] The major problem with oral iron therapy in its classic ferrous form is poor tolerability and up to 40% adverse reaction rate.[11,12] The most common complaints are nausea, abdominal pain, diarrhoea and constipation.

Parenteral iron is indicated when oral iron is not tolerated or absorbed or patient compliance is in doubt or if the woman is approaching term and there is insufficient time for oral supplementation to be effective.[13] Of all the parenteral iron preparations available, intravenous administration has emerged as an effective alternative to oral iron therapy in pregnant women like iron sucrose (IS), ferric carboxymaltose, ferric gluconate (FG), and iron isomaltoside.[14] Apart from its quick absorption, intravenous mode is also known to impart a lesser incidence of hypersensitive reactions. Additionally, intravenous iron sucrose (IVIS) has been reported to be safe and effective during pregnancy, the injection can be given without test dose.[15]

This study was conducted to assess the effect of oral versus intravenous iron sucrose therapy in relation to change in serum haemoglobin level and ferritin levels.

METHODS

An observational study was conducted in the department of obstetrics and gynaecology of a tertiary care hospital, in Maharashtra, for a period of two years from October 2020 to October 2022. Institutional ethical committee approval was obtained prior to the study. This is a busy public hospital in the rural community with a minimum number of 24 to 30 deliveries per day. All registered pregnant women with iron deficiency anaemia who were available at the time of data collection as per the inclusion and exclusion criteria were included in the study. Informed consent was taken from all the participants from both the groups.

Inclusion criteria

Normal singleton pregnancies. Gestation age 16-34 weeks with iron deficiency anaemia. Haemoglobin 7-10 mg/dl. No complicating factors. Proven iron deficiency anaemia. Serum ferritin <13 µg/l.

Exclusion criteria

Medical disorders complicating pregnancy. Obstetric complications of pregnancy. History of parenteral iron treatment. Intolerance to iron derivatives.

Procedure

A sample size of 120 pregnant women, between the gestational age of 16 and 34 weeks with haemoglobin 7-10 gm/dl were assessed for the study, out of which 10 were excluded as not fulfilling the inclusion criteria. Total 110 pregnant women with iron deficiency anaemia were randomly divided into two groups (group A and group B) using computer generated random numbers. Group A participants received oral iron therapy and group B received intravenous sucrose therapy. The haemoglobin and serum ferritin of the participants in both the groups were assessed at the baseline (day- 0), at 3 weeks (day 21-22) and 8 weeks (day 57-58).

Visit I- (baseline- 0 day)- On entry into the study, eligibility was checked according to the inclusion and exclusion criteria and informed consent was taken from each participant. Information regarding patient's name, address, age, and history of amenorrhea was obtained and results of general and obstetric examination were noted, maternal weight was noted. Investigations included estimation of haemoglobin value, serum ferritin level and peripheral smear examination to note the type of anaemia.

Group A consisted of pregnant women, who were given oral iron therapy. A total of 300 mg ferrous fumarate with 100 mg of elemental iron tablets were prescribed for each day. Tablet folic acid was also given to the oral iron group. They were advised regarding diet and asked to take the iron tablet between meals and avoid coffee or tea before and after taking the tablets. They were also explained for repeating investigations during follow-up visits, after 3 weeks and 8 weeks respectively. Group B consisted of pregnant women who were given iron sucrose at the rate of 200 mg every other day.

The dose for total iron sucrose was calculated from the formula as below:

Body weight in Kg × (target haemoglobin – actual haemoglobin) gm/dl × 2.4 + 500 mg (iron stores).[16]

The weight represents the weight of women before pregnancy in kilograms. Since the pre pregnant body weight was not known, weight on first visit was taken. The target haemoglobin was set at >10 gm/dl. In each infusion, the maximum total dose of 200 mg iron sucrose was administered intravenously in 100 ml of normal saline, slowly over 30 minutes. Monitoring was done throughout the infusion to observe for any side effects. The women were discharged without oral iron supplements. The iron intravenous sucrose group was also administered folic acid. The participants were advised to report any adverse side effects immediately. They were explained about repeating investigations during follow-up visits, after a period of 3 weeks and 8 weeks respectively.

Visit II (after 3 weeks) on 21st-22nd day- Haemoglobin and serum ferritin estimation was done in both the groups. The side effects reported by the women were noted and they were advised to continue the tablets, in the oral iron group. The intravenous iron sucrose group was advised to continue tablet folic acid.

Visit III (after 8 weeks) on 57th- 58th day- Haemoglobin and serum ferritin estimation was done in both groups to note the improvement in values. The women were monitored for any adverse side effect.

On every visit, general and obstetric examination was done and assessed for any adverse side effects.

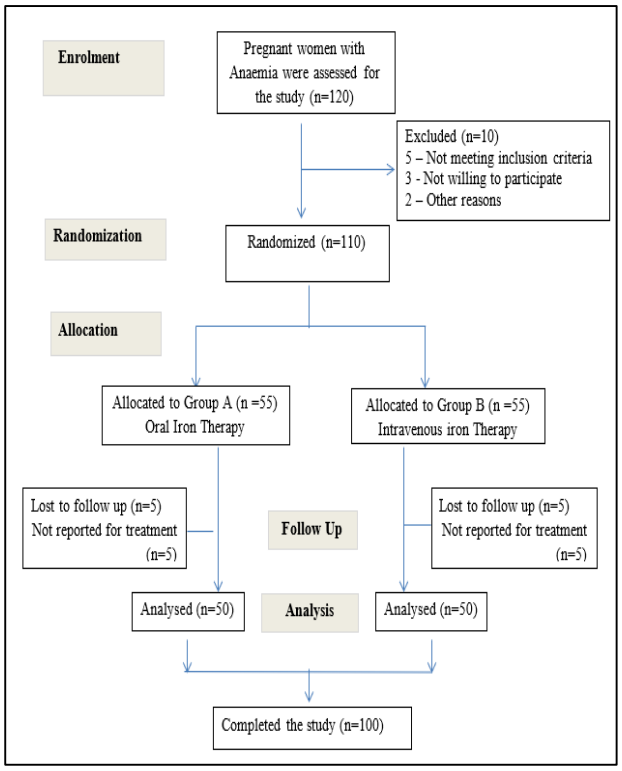

Figure 1: Consort flow diagram.

RESULTS

Out of 100 pregnant women with anaemia 50% were between 21 to 25 years, 20% between 26 to 30 years and 30% were less than 20 years with the age ranging between 19.3 to 27.1 years in oral iron therapy group. The intravenous iron therapy group consisted of 44% in the age group between 21 to 25 years, 20% between 26-30 years and 36% were less than 20 years with age ranging between 19.2 and 26.5 years.

The weight of pregnant women with anaemia in oral iron therapy group ranged between 47.0-51.7 kg and between 45.2-54.8 kg in intravenous iron therapy group. Both the groups were found comparable as the difference was not statistically significant (t=1.85, p value <0.07) (Table 1).

Anaemia was found common in primi as well as multigravida women. The parity distribution was similar in both the groups with CHI=0.98 (<3.841). The peripheral smear of 76% of women who participated in the study was found with microcytic anaemia in both the groups. The mean gestational age in weeks in oral iron therapy group was 25.96±2.82 while 26.64±2.06 weeks in intravenous iron therapy group with p value at 0.34 which indicates that both the groups had similar characteristics.

In the oral iron therapy group the baseline (0 day) haemoglobin was 8.21±1.12 gm/dl and in the intravenous iron group it was 8.36±1.14 gm/ dl. The haemoglobin (Hb) of oral as well as intravenous group was assessed after 3 weeks (21-22 day) and 8 weeks (57-58 day) of the treatment (Table 2). At 3 weeks the haemoglobin raised to (mean±SD) 9.17±0.34 gm/dl and at 8 weeks 9.84±0.42 gm/dl in oral iron group.

Table 1: Age and body weight of pregnant women with anaemia.

Variables	Oral iron group		Intravenous group		T value	P value
	Mean	SD	Mean	SD		
Age in years	23.2	3.9	22.8	3.7	-0.50	0.89
Range in years	19.3-27.1		19.2-26.5			
Maternal weight	49.4	2.32	50.08	4.8	1.85	0.07
Range in kg	47.0-51.7		45.2-54.8			

Table 2: Haemoglobin and serum ferritin level at the baseline and post treatment intervals among oral and intravenous iron therapy groups.

Variables	Mean haemoglobin gm/dl		Serum ferritin in µg/l	
	Oral Mean±SD	Parental Mean±SD	Oral Mean±SD	Parental Mean±SD
Visit 1- (baseline)	8.21±1.12	8.36±1.14	7.38±0.17	6.75±0.42
Visit 2- (after 3 weeks)	9.17±0.34	10.28±0.68	16.92±2.01	29.96±8.21
Visit 3- (after 8 weeks)	9.84±0.42	11.74±0.88	26.30±21.61	70.54±50.25

In the intravenous group the mean baseline haemoglobin was 8.36±1.14 gm/dl while at 3 weeks it raised to 10.28±0.68 gm/dl and 8 weeks to 11.74±0.88 gm/dl which shows a significant increase in haemoglobin post treatment (Figure 2). Similarly mean serum ferritin was found increased at the 3 weeks and at 8th week in both the groups.

The mean serum ferritin value in intravenous group rose to 70.54±50.25 (mean±SD) at 8th week as compared to oral iron therapy group 26.30±21.61 (mean±SD).

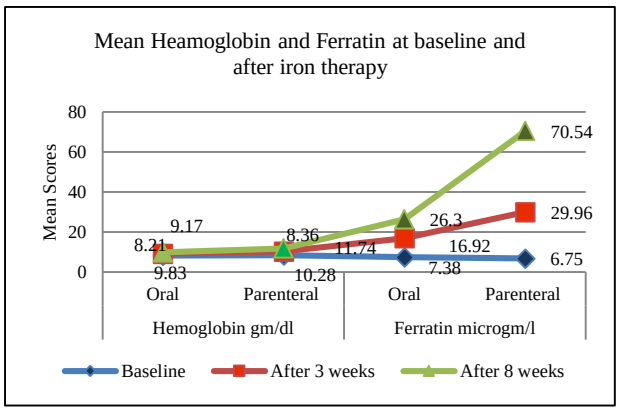

Figure 2: Mean haemoglobin and serum ferritin level at baseline, 3 weeks and 8 weeks.

The difference in mean haemoglobin in oral iron therapy was found slightly increased at 3 weeks and significantly improved by difference of 1.63 gm/dl at 8 weeks from the baseline as p value is found <0.0001. The mean difference in haemoglobin was found to be increased in intravenous iron therapy at 3 weeks and 8th weeks (Table 3). The difference in mean of 3.38 from the baseline to 8th weeks was found in the intravenous iron therapy group which shows a significant difference in mean within the group p value <0.0001.

The mean difference of 3.38 gm/dl was seen in the intravenous therapy group at 8th weeks against the mean difference of 1.63 gm/dl in oral iron therapy group which indicates that intravenous iron therapy is found more effective in increasing the haemoglobin among the pregnant women with iron deficiency anaemia.

The difference in mean serum ferritin in oral iron therapy was found increased at 3rd weeks and significantly improved at 8th weeks from the baseline as p value is found <0.0001. The mean difference in serum ferritin µg/l was found to be increased in intravenous iron therapy at 3rd weeks and 8th weeks as p value <0.0001 (Table 4).

The mean difference of serum ferritin 18.92 µg/l was found in the oral iron therapy at the 8th week while the mean difference of 63.79 µg/l was seen in the intravenous therapy group. It indicates that intravenous iron therapy is found more effective in increasing the serum ferritin among the pregnant women with iron deficiency anaemia.

Table 3: Comparison of difference in mean haemoglobin gm/dl from baseline to post treatment intervals among oral and intravenous iron therapy groups.

Different visit points	Difference in mean haemoglobin g/dl after treatment			
	Oral iron therapy		Intravenous therapy	
	Mean difference	SE	Mean difference	SE
Baseline to 3 weeks	0.96	0.17	1.92	1.88
3 weeks to 8 weeks	0.67	0.76	1.46	0.15
Baseline to 8 weeks	1.63	0.17	3.38	0.20
T value	9.63		16.59	
P value	<0.0001		<0.0001	

Table 4: Comparison of difference in mean serum ferritin in µg/l from baseline to post treatment intervals among oral and intravenous iron therapy groups.

Different visit points	Difference in mean serum ferritin in µg/l after treatment			
	Oral iron therapy		Intravenous therapy	
	Mean difference	SE	Mean difference	SE
Baseline to 3 weeks	9.54	0.29	23.21	1.16
3 weeks to 8 weeks	9.38	3.07	40.58	7.20
Baseline to 8 weeks	18.92	3.06	63.79	7.11
T value	6.19		8.98	
P value	<0.0001		<0.0001	

DISCUSSION

In the present study the mean age in years for oral iron therapy group was 23.18±7.8 (mean±SD) with 68% primigravida and 32% for multigravida while in intravenous iron therapy group the mean age was 22.8±7.3 with 28% for primigravida and 62% for multigravida. According to Neeru et al study the mean age in years for oral iron group was 27±2.99 and in intravenous iron group the mean age was found as 27±4.09 years.[17] The study by Sunita et al revealed the mean age in years for oral iron

group as 24.4±2.71 with 62.2% primigravida and 37.8% multigravida while in intravenous iron group the mean age in years was found as 24.2±2.82 with 55.5% primigravida and 45.5% for multigravida.[18] According to Rudra et al the mean age in years for oral iron group was 25.12±3.73 with 22% primigravida and 78% multigravida and in intravenous iron group the mean age in years was 25.08±3.32 with 20% for primigravida and 80% for multigravida.[19] Eralil et al study shows mean age in years for oral iron group as 26.58±4.24 and in intravenous iron group as 26.09±4.47 with a p value of 0.59.[20]

In the present study the peripheral smear of 76% women was found with microcytic anaemia and 24% others in both the groups. Similar results were seen in the study by Qurram et al in which peripheral smear of oral iron therapy group was 70% with microcytic anaemia and 30% with others and in intravenous iron therapy group 72% for microcytic and 28% for others with a chi square value of 0.096 which was statistically insignificant.[21]

In the present study the mean gestational age in weeks in oral iron therapy group was 25.96±2.82 and 26.64±2.06 weeks in intravenous iron therapy group while the mean gestational age in Tigga et al study oral iron group was 27.76±2.31 and 27.61±2.43 in intravenous iron therapy group.[22]

In the present study the mean body weight in kg among the anaemic pregnant women for oral iron group as 55.42±2.32 and for intravenous iron therapy group as 50.08±6.18 which was statistically insignificant while the mean body weight in a study by Regip et al for oral iron group was 56 and for intravenous iron group was 58.2.[23] The study by Eralil et al found mean body weight in kg for oral iron group as 54.15±9.85 and for intravenous iron group was 53.72±8.86.[20] Tigga et al study the mean body weight in kg for oral iron group was 51.15±0.85 and for i.v. iron group was 52.93±1.06 kg.[22]

The mean MCV in femtolitres among oral iron group was 73.8±13.74 and in intravenous iron group was 71.76±17.16 with a p value of 0.21 which was statistically insignificant. Similar results were found in the study by Neeru et al and Rudra at al while the study by EI Wahed et al. and Prajapati et al showed a significant difference in the mean MCV values.[17,19,24,25]

In the present study the haemoglobin (Hb) of oral as well as intravenous group was found to be raised from baseline. In the oral group it was increased at baseline (Mean±SD) 8.21±1.12 to 9.17±0.34 gm/dl at 3 weeks and 9.84±0.42 gm/dl at 8 weeks. In the intravenous group the mean baseline haemoglobin was 8.36±1.14 gm/dl while at 3 weeks it raised to 10.28±0.68 gm/dl and 8 weeks to 11.74±0.88 gm/dl which shows a significant increase in haemoglobin post treatment as p value was <0.0001 for both the groups. But the mean difference of 3.38±0.34 gm/dl was significantly higher in the intravenous therapy group at 8th weeks against the mean difference of 1.63±0.26 gm/dl in oral iron therapy group. According to El Wahed et al study the serum haemoglobin increase in mg/dl for oral iron group was 1 and for intravenous iron group was 2 with a p value of 0.002 which was statistically significant.[24] The study by Sunita et al informed serum haemoglobin increase in in oral iron group was 0.3±0.02 and for intravenous iron group was 1.2±0.05 with a p value of 0.001 which was statistically significant.[18] According to Eralil et al study the serum haemoglobin increase in oral iron group was 1.09 and for intravenous iron group was 1.49 with a p value of 0.105 which was statistically insignificant.[20] According to Tigga et al the haemoglobin increase was found in oral iron group was 2.9 and for intravenous iron group 4.03 with a p value of 0.01 which was statistically significant.[22]

In the present study the difference in mean serum ferritin in oral iron therapy as well as intravenous group was found increased at 3rd weeks and at 8th weeks from the baseline as p value was found <0.0001. The mean difference of serum ferritin from baseline to 8th week was found as 18.92 µg/l in oral group while the mean difference of 63.79 µg/l with statistically significant p value. Similar results were also found by Neeru et al with serum ferritin increase in in oral iron group as 12.59 and for intravenous group iron group as 131.33 with a p value of 0.000 which was statistically significant.[17] According to Sunita et al study the serum ferritin increase in oral iron group was 19.96±2.38 and for iv iron group was 30.66±4.93 with a p value of <0.001 which was statistically significant.[18]

CONCLUSION

The study concluded that intravenous iron sucrose therapy improved serum haemoglobin and serum ferritin faster than oral iron. The intravenous sucrose is found to be safe and more effective alternative treatment for iron deficiency anaemia in pregnancy though the cost of treatment is significantly higher than the oral therapy. As the intravenous sucrose therapy includes hospital cost apart from the cost of the injection it requires efficient counselling of anaemic women to visit the hospital as per the schedule for complete treatment.

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