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Oral versus intravenous iron therapy for correction of iron deficiency anaemia in pregnancy

Abstract

Background: The high prevalence of anaemia in pregnancy has serious adverse consequences in both mother and baby. Management of anaemia in pregnancy should be given great importance in obstetric practice.The study was undertaken to compare the efficacy of oral iron (ferrous sulphate) and intravenous iron sucrose complex in the management of moderate anaemia in pregnancy.

Method: A randomized comparative hospital–based longitudinal analysis was conducted in the Department of Obstetrics and Gynaecology of a tertiary care hospital, involving 70 women with haemoglobin between 7- 9.9 g/dl and serum ferritin < 50 mcg/l, attending antenatal clinic. Intravenous iron sucrose complex was given in one group and tablet ferrous sulfate (100 mg elemental iron) to the oral group. Treatment efficacy was assessed by measurement of haemoglobin and reticulocytes on days 8, 15, 21 and 30 and ferritin on day 30.

Result: An increase in haemoglobin was observed in both groups, rising from 8.26 ±0.764g/dl to 11.08± 0.71g/dl in the intravenous group and from 8.14±0.767 g/dl to 10.98 ±0.61 g/dl on day 30 in the oral group. S.ferritin on day 30 was significantly higher in the intravenous group. The side effects in both groups were negligible though there were there were 3 dropouts due to adverse effects.

Conclusion : Both oral ferrous sulphate and intravenous iron sucrose complex are safe, convenient and effective in treatment of iron deficiency anaemia in pregnant women with negligible side effects, but intravenous iron sucrose complex is better in improving serum iron and in restoring maternal iron stores.

Keywords: haemoglobin, iron deficiency anaemia, iron sucrose, serum ferritin

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Introduction

The most common nutritional deficiency disorder in the world is iron deficiency anaemi. According to World Health Organization, anaemia was among women was 10% in developed countries and 42% in developing countries.[1] 50% of the worldwide maternal deaths because of anaemia happen in South Asian countries, Ezzati M et al.,[2] 80% occur in India.[3] Iron-rich diet or iron supplementation can improve iron deficiency. Difficulties in the management of iron deficiency anaemia are due to the tolerance and adverse effects of iron therapy in its various forms. Oral iron has been widely used in many hospitals and clinics, with blood transfusion only for severe or emergency cases. Decreased efficacy of iron orally may be due to lack of absorption, poor compliance, increased side effects (up to 56%) and stopping treatment (up to 20%). Blood transfusion has its own risks, which may be transfusion of wrong blood, blood borne infections and reaction.[4] Parenteral iron is a good option in the treatment of iron deficiency anaemia, with new intravenous iron preparations, in cases of poor tolerance or poor compliance to ingestion of iron, or gastrointestinal upset, massive loss of blood, pregnant women with iron deficiency anaemia or presenting late in pregnancy. Intravenous iron in the sucrose salt has been reported to be effective and safe in pregnancy.[5] This study was undertaken to compare the efficacy and side effects of oral iron (ferrous sulphate) and intravenous iron sucrose complex in the management of moderate iron deficiency anaemia in pregnancy.

Methods

This was a comparative hospital–based randomized, longitudinal study done in the Department of Gynaecology and Obstetrics of S.M.S. Medical College, Jaipur, a tertiary care hospital over a period of six months. The sample size was calculated at 80% study power and α error of 0.05 assuming SD of 1.3 g/dl in Haemoglobin as per the result of seed article.[6] For minimal detectable difference of 1 g/dl in Haemoglobin by unpaired 't' test between the groups 28 patients in each group are required as sample. This was further enhanced to 33 patients in each group assuming 15% dropouts or attrition, which was rounded up to 35 cases in each group. Coin tossing method was used to allocate the groups-for first woman in group A, after that they were allocated alternately in the two groups. All the data collected was recorded on a performa. Clearance was taken from the Review Board and Ethical Committee of the institute. Informed written consent was taken of all women.

Women with 24-28 weeks gestational age, with haemoglobin 7-9.9g/dl and serum ferritin <50µg/l were chosen for the study from the antenatal clinic of the hospital. Women with anaemia from causes other than iron deficiency, twin pregnancy, blood transfused earlier, h/o blood disorders, risk of preterm delivery, allegy to iron derivatives, active cardiac, pulmonary, renal, respiratory or hepatic disease, chronic debilitatory disease were excluded from the study. The intravenous calculated dose, was given in infusion form twice weekly. Single maximum dose, 200 mg elemental iron was infused over 20 minutes, in100 ml of normal saline. Routine oral iron supplementation was stopped and was restarted after 1 week of completion of intravenous therapy. All women were checked weekly. At each visit , evaluation was done for adverse events, immediate and delayed .Blood tests were performed at the time of initiation and completion (on day 30) of the study were peripheral smear, complete blood count, packed cell volume, mean corpuscular haemoglobin , mean corpuscular volume , mean corpuscular haemoglobin concentration , and iron profile. Haemoglobin and reticulocyte counts were done at days 8, 15, 21. Statistical analysis was done through computer software (MS Excel

and primer version 6). Proportion and percentages were used to expres the qualitative data and mean and standard deviations for quantitative data. Chi -square test was used to express the difference in proportion and the student t-test and paired test were used for difference in means of paired data. P value <0.05 was considered as significant

Results

This involved 65 women. Five women were excluded during the study, three did not complete the treatment due to adverse effects, one did not come for regular follow-up (oral group) and one left the study after three doses of intravenous iron due to inability to come frequently to the hospital. The two groups were similar in term of biologic and demographic details. Table 1 On day 30, an rise in haemoglobin was noted in both the groups, 2.8469±0.6491 in the intravenous iron group and 2.853±0.632 in the oral group, difference of rise between both groups was not significant statistically Table 2. Target haemoglobin was attained in three women in the intravenous group and four in the oral one after one month Table 3. the other blood parameters significantly rose after 30 days of therapy in the two groups but only total iron binding capacity and mean corpuscular haemoglobin showed statistically significant increase in intravenous iron group than oral iron.

Table 1 Demographic and Biological Characteristics

Parameter	Oral group (n=32)	Intravenous group (n=33)	P- value
Age (yrs)	26.5±3.959	26.42±4.316	0.866, not significant
Body Mass Index (kg/m 2)	20.81±1.779	21.20±2.045	0.414, not significant
Gravidity	2.44 ± 1.22,	2.45±1.30	0.997, not significant
Gestational age (wks)	26.38 ± 1.56	26 ± 1.73	0.36, not significant

Table 2 Change in Parameters after therapy

Parameters	Oral group	Intravenous group	p-value
Δ Hb	2.8469+0.6491	2.853+0.632	0.969, not significant
Δ RC	1.0375+0.3160	1.170+0.325	0.101, not significant
Δ PCV	4.7209+2.0363	5.434+2.416	0.204, not significant
Δ TRBC	0.1069+0.1077	0.237+0.127	<0.001, significant
Δ MCV	10.5634+4.6718	9.553+4.800	0.393, not significant
ΔMCH	7.2522+1.6345	9.981+2.032	<0.001, significant
ΔMCHC	4.3834+2.4117	3.566+2.651	0.199, not significant
ΔS.Ferritin	58.1156±8.5505	65.15±7.59	<0.001, significant
ΔS.TIBC	-65.2938±41.0805	-88.78±31.862	0.012, significant
ΔS.Iron	101.4281±11.0565	94.900±14.055	0.042, significant

Table 3 Haemoglobin Status After Therapy

Post –therapy haemoglobin (g/dl)	Oral group (n= 32)		Intravenous group (n=33)		p-value
<11.0	17	53.13%	15	45.45%	
11.0-11.9	11	46.87%	15	54.54%	0.711, not significant
≥12	4		3		

The change was significant in all iron indices in both groups but serum iron and ferritin, and total iron binding capacity showed statistically significant improvement with intravenous iron than with oral iron. Rise in mean serum ferritin level was 58.1156±8.5505 µg/l, in oral group and 65.15±7.59 µg/l in intravenous iron group, P value <0.001 Table 2. Although some women experienced side effects, most tolerated them well and continued with the treatment. In the oral group, 28.12% women experienced gastrointestinal side effects, one had diarrhea and one with nausea refused to continue with oral iron tablets and were excluded from the study, Others were treated symptomatically In the intravenous iron group, adverse reaction reported by women were pain at injection site in 12.12% and vertigo in 9.09% after completion of infusion. Pain abdomen and metallic taste were reported by fewer women than oral group. There were no major side effects and no allergic or anaphylactic reaction. Febrile reaction developed in one woman during intravenous infusion. Infusion was stopped, she was given inj dexamethasone and inj pheneramine maleate, kept in hospital for one day and she was shifted to oral iron excluded from the study. All other women tolerated the infusions well Table 4.

Table 4 Side-Effects of Iron Therapy

Side-Effects		Oral Iron Group		Intravenous Iron Group	
		No./ dropout	%	No.	%
Gastrointestinal	Nausea / Vomiting	1-Apr	12.5	-	-
	Constipation	3	9.37	-	-
	Diarrhoea	1-Feb	6.25	-	-
Pain Abdomen		5	15.62	3	9.09
Metallic Taste in Mouth		3	9.37	2	6.06
Pain at Injection Site		-	-	4	12.12
Vertigo		-	-	3	9.09
Arthralgia		-	-	2	6.06
Febrile Reaction		-	-	1-Jan	3.03
Headache		-	-	2	6.06

Discussion

The need of iron in pregnancy is one gm. It is taken care by mobilization of iron from iron stores. But, women who have low iron stores develop iron deficiency during pregnancy. Haemoglobin levels < 8 g% are associated with poor maternal outcome.[7] In our study, intravenous iron sucrose was compared with oral iron therapy. Quantity of dose was same as that reported by Bayoumeu which was calculated using woman's weight and Haemoglobin deficit

unlike oral iron, which has a fixed dose.[6] Our study showed that intravenous iron sucrose was safe and corrected the hematological parameters comparable with oral iron. Iron reserves were restored better by intravenous iron sucrose. This was also stated by Bayoumeu et al.[6] Ferritin rose because the intravenous iron sucrose released iron quickly to endogenous proteins which bind iron. There is no parenchymal deposition.[8] Different cut-offs are by varying machines and hence comparision with other studies is not possible. Also due to use of various available oral iron preparations. In the present study, post therapy haemoglobin was raised across time, which was similar in both groups. This differs from the findings of Al-Momen et al., [9] where by intravenous iron sucrose significantly higher haemoglobin level were noted. In a study by Gupta et al.[10] rate of haemoglobin rise was found to be earlier with intravenous iron sucrose than iron tablet. This could benefit if a pregnant women precomes with anaemia at a later gestation, though we did not find this difference in our study.

Bencaivo et al.,[11] evaluated the effectiveness and safety of intravenous and oral iron. There was only minimally higher rise increase in haemoglobin but iron stores levels were significantly higher by intravenous route than oral route,as was in our findings. Al RA et al.,[12] studied parenteral iron with oral iron polymaltose complex. The rise in haemoglobin from baseline was significantly higher by intravenous than the oral route at all point of time. Ferritin levels rose significantly by both but were more by the intravenous route. Intramuscular route has been evaluated in many Indiana studies and reported side-effects such as pain, staining at injection site and arthralgia.[13] Iron sucrose cannot be given by intramuscular route. Factors influencing the response to treatment of iron therapy were also evaluated. Gastrointestinal effects were about 28.125% after oral iron therapy. No serious drug reactions and no episodes of allegy was noted.

Conclusion

Present study concluded that both oral ferrous sulphate and iron sucrose by intravenous route are useful, safe and convenient in treatment of anaemia due to iron deficiency in pregnant women. Though increase in Haemoglobin with oral iron was comparable to intravenous route, intravenous iron was better in improving serum iron and in restoring maternal iron stores than oral ferrous sulphate.

Recommendations

Since the intravenous route is safe and effective with few side effects, it is suggested as a therapy in iron deficiency anaemia, where no-response occurs to oral iron. This can be given at primary health centers,since the side effects are minimal.

Limitations of the study

The research was done in a referral hospital, thus it is not reflective of the whole population. No follow-up was done till term to see levels of Haemoglobin and S. ferritin level at delivery. The women had to make multiple visits to the hospital within a short period of time. Only oral and intravenous routes were compared in the study, intramuscular route was not compared in the study.

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None.

Conflicts of interest

The author declares there is no conflict of interest.

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