A Prospective Study on Efficacy of Oral Iron in Comparison with Intravenous Iron Sucrose in the Treatment of Iron Deficiency Anemia in Pregnant Women in a Rural Scenario

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Research Article

Abstract: **Objectives:** To determine the current prevalence and severity of iron deficiency anemia in a rural scenario and to document the response to oral iron supplementation in comparison to intravenous iron sucrose for better efficacy, compliance and safety in treatment of iron deficiency anemia in pregnancy. **Methods:** This comparative study was conducted at rural medical hospital in Karnataka, India during the period November 2010 to October 2012. 80 patients who fulfilled the inclusion criteria were randomized into either of the two groups, 40 to the oral iron group and 40 to the IV iron group and the improvement of hemoglobin was recorded meticulously. Comparison between the two groups was done based on the initial Hb, the total dose of iron required, the side effects and the final Hb. Statistical analysis was done using Chi-square test. **Results:** The following observations were made from this study age of patients ranged from 19-35years. Samples are age matched with P= 1.000. Majority of the anemic women in this study belonged to the age group of 20-25years.Majority of the women belonged to SE class II. SES distribution is statistically similar in two groups with p=1.000. In this study, anemia was equally common in Primi-gravida and multigravidas. Parity distribution is statistically similar in both groups with P=0.369. Majority of anemic patients in this study belonged to gestational age of 14-29weeks. Mean Gestational age is statistically similar in two groups with P = 0.408. Mean body weight is statistically significantly less Oral Rx group P = 0.017*. Levels of initial hemoglobin is statistically similar in two groups studied with P=0.624. MCV <70 is more associated with IV Rx group of patients with P=0.096+. Majority of the women in this study had a microcytic hypochromic smear picture. Distribution of PS is statistically similar in both groups with P=0.845. Mean total drug required(TDR) is significantly more in IV Rx group (881.50) when compared to Oral Rx Group (856.98) with P=0.149. Levels of Final Hb is statistically significantly less in Oral Rx group of patients than in the IV group with p=0.001**. **Conclusion:** This study was attempted to analyze the safety and efficacy of oral iron in comparison to IV iron on the hematological parameters in pregnant women with iron deficiency anemia. This study confirms that IV iron caused a rapid and effective improvement in the hematological parameters when compared to oral iron. In our country, with a higher incidence of iron deficiency anemia in pregnancy, especially in a rural scenario, this type of treatment may be helpful in management of these patients in a cost-effective manner. Following a rigorous research and evaluation iron sucrose has established its full place and potential and may be the solution.

Keywords: Intravenous Iron Sucrose. Oral Iron. Iron Deficiency, Anemia, Pregnant Woman.

Introduction

Iron deficiency anemia (IDA) remains the commonest medical disorder in pregnancy in the developing world [1-5], with the burden of disease impacting on both the mother and the newborn (and subsequent child and later adult). India is leading in iron-deficiency anemia in the world. It is very common in rural population due to poverty and an inadequate diet. It can be temporary or longterm. It can range from mild to severe. Anemia-free India is practically possible when the consequences of anemia and its preventive and curative measures are popularized among the common public especially among the rural population. In India, the maternal mortality is around 350 -450/100,000 live births, a figure similar to that found in Europe 200 years ago [6,7]. Anemia is estimated to contribute to 20 percent of all maternal deaths and nine times higher risk of perinatal mortality [8]. The odds for low birth weight are tripled, while those for preterm delivery more than doubled in association with IDA [9]. Anemia and iron deficiency in pregnancy are associated with large placental weight and a high ratio of placental weight to birth weight (placental ratio) [10], both of which are predictors of adult hypertension.[11] A vast majority of women in rural India embark upon pregnancy with frank iron deficiency anemia. The majority of anaemic women in the rural pregnant population had a moderate degree of anemia (43.5%), while the majority of urban women had

mild degree of anemia (35.7%). Anemia is a neglected tragedy that continues to exert a heavy toll of suffering and death on women, and also the not-so-obvious but potentially just as devastating on the newborn child's motor and intellectual development, and future risk of cardiovascular disease. Anemia also exposes women to an increased risk of blood transfusion during the peripartum period because the parturient can no longer cope with the physiologic blood losses of delivery, l*et al*one those associated with hemorrhagic delivery. The risk is equally increased by conditions that incur chronic bleeding during gestation, such as placenta praevia.[2,3] In the newborn, IDA is associated with poor performance in the Bayley Mental Development Index[12]. Poor mental and motor performance improves with iron therapy in iron-deficient infants at 12-18 months to age 13. While nutritional factors may be contributory, it seems more than likely that IDA in infancy and early childhood is largely secondary to maternal iron deficiency during pregnancy. There is also evidence that infants born to women taking iron have more than double the iron reserves at 2 months of age and beyond when compared with the offspring of un-supplemented mothers. Thus to address the problem of iron deficiency in infancy and early childhood is to treat the iron deficiency status of the mother. At face value the solution is potentially both simple and cheap.

Materials and Methods

All booked cases coming to the antenatal outpatient department in rural medical college, willing to participate in the study were included.

Pregnant women of gestation age 14-34 weeks with iron deficiency anemia (Hb of less than 11mg/dl and greater than 7mg/dl was included in the study).

Inclusion Criteria

- All booked cases coming to Rural Medical Hospital in Karnataka, willing to participate in the study and give consent.
- Normal singleton pregnancies
- Gestation age 14-34 weeks with iron deficiency anemia
- Hb of less than 11mg/dl and greater than 7mg/dl
- No complicating factors
- Proven iron deficiency anemia

Exclusion Criteria

- Anemia not linked to iron deficiency
- Hemoglobin <7g/dl
- Medical disorders complicating pregnancy
- Obstetric complications of pregnancy
- Patients with asthma, cirrhosis, viral hepatitis, multiple pregnancy, suspected acute infection
- H/o parenteral iron treatment before inclusion
- Intolerance to iron derivatives.
- Patients who did not give their consent.

Study Procedure

All selected women and their relatives were explained regarding the procedure and their consent was taken in a written form. All women selected were clinically evaluated by a detailed history and a proper general, systemic and obstetric examination. Special attention was taken to rule out the exclusion criteria Patients Hemoglobin estimation was done followed by a peripheral smear examination, RBC indices and a stool examination.

Hb estimation was done using Sahli's method of hemoglobinometry.

The amount of iron needed by an individual patient was calculated by the following formula:

- ✓ Total iron deficit (mg) = Amount of iron deficient + Amount to replenish
- ✓ stores
- ✓ Amount of iron deficit (mg) = Pre-pregnancy BW (Kg) X Hb deficit X 2.4
- ✓ Hb deficit = target Hb – initial Hb
- ✓ Amount of iron to replenish = BW (Kg) X 10

All the patients were treated with a de-worming agent, Tab. Mebendazole 100mg BD for 3 days.

The patients were then randomly allotted into two groups:

Group A: Are the patients who were given ferrous sulphate 100 mg tablets three times a day. Each tablet containing 100 mg of elemental iron.

Group B: Are the patients who were given iron sucrose (2 Ampoules, 100mg) as a bolus injection intravenously over 10mins. Patient was observed for any allergic reactions. If no reaction occurred, the same dose was repeated on alternate days till the total dose was over. Oral iron was withheld during this treatment.

After the entire dose is administered, the patients were seen every 2 weeks and assessed for side effects, compliance and laboratory response. This was assessed by repeating Hb level.

Results and Analysis

Table 1: Age distribution of patients studied

Age in years	IV Rx group		Oral Rx group	
	No	%	No	%
19-20	13	32.5	11	27.5
21-25	18	45.0	22	55.0
26-30	8	20.0	4	10.0
>30	1	2.5	3	7.5
Total	40	100.0	40	100.0
Mean ± SD	22.70±3.26		22.70±3.65	

The age of patients ranged from 19-35years. Majority of the anemic women in this study belonged to the age group of 20-25years. Samples are age matched with P = 1.000

Table 2: Distribution of socio-economic status in two groups of patients studied

SES	IV Rx group		Oral Rx group	
	No	%	No	%
Class I	1	2.5	0	0.0
Class II	25	62.5	26	65.0
Class III	14	35.0	14	35.0
Class IV	0	0.0	0	0.0
Class V	0	0.0	0	0.0
Total	40	100.0	40	100.0

In this study, majority of the women belonged to SE class II. SES distribution is statistically similar in two groups with p=1.000

Table 3: Distribution of Obstetric Score in two groups of patients studied

Obst. Score	IV Rx group		Oral Rx group	
	No	%	No	%
Primi	20	50.0	16	40.0
Multi	20	50.0	24	60.0
Total	40	100.0	40	100.0

In this study, anemia was equally common in primigravida and multigravidas. Parity distribution is statistically similar in both groups with P=0.369

Table 4: Distribution of gestational age (wks) in two groups of patients studied

Gestational weeks	IV Rx group		Oral Rx group	
	No	%	No	%
<29	27	67.5	28	70.0
29-32	9	22.5	11	27.5
>32	4	10.0	1	2.5
Total	40	100.0	40	100.0
Mean ± SD	25.97±5.00		25.05±4.94	

Majority of anemic patients in this study belonged to gestational age of 14-29weeks. Mean Gestational age is statistically similar in two groups with P = 0.408

Table 5: Distribution of Body weight in two groups of patients studied

Bodyweight (kg)	IV Rx group		Oral Rx group	
	No	%	No	%
<50	20	50.0	33	82.5
51-60	18	45.0	7	17.5
61-70	2	5.0	0	0.0
Total	40	100.0	40	100.0
Mean ± SD	51.15±5.70		48.70±2.82	

Table 6: Distribution of initial hemoglobin in two groups of patients studied

Initial hemoglobin	IV Rx group		Oral Rx group	
	No	%	No	%
<7	1	2.5	0	0.0
7-8	20	50.0	20	50.0
8-9	19	47.5	18	45.0
>9	0	0.0	2	5.0
Total	40	100.0	40	100.0

Levels of initial hemoglobin is statistically similar in two groups studied with P=0.624

Table 7: Distribution of mean corpuscular volume in two groups of patients studied

MCV	IV Rx group		Oral Rx group	
	No	%	No	%
<70	18	45.0	8	20.0
>70	22	55.0	32	80.0
Total	40	100.0	40	100.0

MCV <70 is more associated with IV Rx group of patients with P=0.096+

Table 8: Distribution of peripheral smear in two groups of patients studied

Peripheral smear	IV Rx group		Oral Rx group	
	No	%	No	%
Microcytic Hypochromic	28	70.0	28	70.0
Dimorphic	11	27.5	9	22.5
Normocytic Hypochromic	0	0.0	1	2.5
Normocytic normochromic	1	2.5	2	5.0
Total	40	100.0	40	100.0

Majority of the women in this study had a microcytic hypochromic smear picture. Distribution of PS is statistically similar in both groups with P=0.845

Table 9: Total drug required (TDR) in the two groups of patients studied

TDR	IV Rx group		Oral Rx group	
	No	%	No	%
<800	10	25.0	7	17.5
800-900	14	35.0	22	55.0
>900	16	40.0	11	27.5
Total	40	100.0	40	100.0
Mean ± SD	881.50±85.61		856.98±62.56	

The maximum total drug required was 1103mg and the minimum total drug required was721mg. Mean TDR is significantly more in IV Rx group (881.50) when compared to Oral Rx Group (856.98) with P=0.149

Table 10: Distribution of final hemoglobin in two groups of patients studied

Final hemoglobin	IV Rx group		Oral Rx group	
	No	%	No	%
<7	-	-	-	-
7-8	-	-	-	-
8-9	-	-	-	-
9-10	3	7.5	16	40.0
>10	37	92.5	24	60.0
Total	40	100.0	40	100.0

Levels of Final Hb is statistically significantly less in Oral Rx group of patients with p=0.001**

Table 11: Distribution of side effects in two groups of patients studied

Side Effects	IV Rx group		Oral Rx group	
	No	%	No	%
Burning	2	5.0	0	0.0
Diarrhea	0	0.0	1	2.5
Giddiness	1	2.5	0	0.0
GII	0	0.0	6	15.0
Sweating	2	5.0	0	0.0
NR	35	87.5	33	82.5
Total	40	100.0	40	100.0

Table 12: Comparison of hemoglobin in two groups of patients studied

Hemoglobin	IV Rx group	Oral Rx group	P value
Initial hemoglobin	7.85±0.59	7.92±0.55	0.616
Final hemoglobin	10.99±0.72	10.13±0.64	<0.001**
Hb deficit	3.10±0.58	3.06±0.54	0.722

Table 13: Comparison of Hb Rise in two groups of patients studied

Hb(gm%) rise	IV Rx group		Oral Rx group	
	No	%	No	%
≤2.0	2	5.0	20	50.0
2.1-3.0	22	55.0	15	37.5
3.1-4.0	10	25.0	5	12.5
>4.0	6	15.0	0	0.0
Total	40	100.0	40	100.0
Mean ± SD	3.16±0.79		2.21±0.68	
Inference	Mean rise in Hb rise is significantly more in IV Rx group compared to Oral Rx group with P<0.001**			

Discussion

The prevalence of iron deficiency anemia in pregnancy in different regions of the world ranges from 5-45%. Increased iron requirement in pregnancy and lactation carries with it, an increased susceptibility to iron deficiency anemia. Iron deficiency anemia in pregnancy results in increased fetal and maternal risks. So iron deficiency anemia remains a major problem in India. Among patients included in this study, anemia was more common in the early second trimester. The similar results were seen in a study conducted by Kapil U, Saxena N, *et al* [13]. Most patients in this study belonged to the socio-economic class II. This result is similar to a study done in a rural area of Haryana for the prevalence of Multiple Micronutrient Deficiencies amongst Pregnant Women by Priyali Pathak, Umesh Kapil, *et al.*[14] A total of 283 pregnant women (mean age: 22.9 years) were enrolled for the study. Data revealed that 31.8% pregnant women were illiterate and majority (81.9%) belonged to the lower middle and middle socio-economic status.[15] All patients in this study who had been administered intravenous iron sucrose had increased hematological parameters at final follow up compared to those who received oral iron, indicating that iron sucrose not only corrects the deficit in the hemoglobin levels but also restores the iron stores as seen by significant improvement in the Hb levels. These results are comparable with the results of earlier studies done by Al Momen *et al* which showed that iron sucrose group achieved a significantly higher Hb level (128.5 + 6.6 g/l vs. 11.4 + 12.4 g/l in the control group, P < 0.001) in a shorter period (6.9 + 1.8 weeks vs. 14.9 + 3.1 weeks in the control group, P < 0.001) and showed no major side effects. While the oral group could not tolerate ferrous sulfate, complained of distributing gastrointestinal symptoms and had poor compliance. The similar results were also seen in a study done by Ragip *et al.*16 in 90 women with hemoglobin levels between 8 and 10.5 g/dl and ferritin values less than 13 g/dl received either oral iron polymaltose complex (300 mg elemental iron per day) or intravenous iron sucrose in the treatment of anemia in pregnancy. The change in Hb from baseline was significantly higher in the IV group than the oral group at each measurement the changes with respect to subsequent hemoglobin were significantly higher on the 14th and 28th days. Ferritin values were higher in patients receiving intravenous iron throughout pregnancy. No serious adverse during reactions were observed. A random, prospective, open study with individual benefit was performed involving 50 patients with hemoglobin levels between 8 and 10 g/dL and a ferritin value of <50 µg/L conducted by Françoise Bayoumeu, MD,a Carole Subiran-Buisset, MD,a Nour-Eddine Baka, MD,a *et al* [17]. An increase in hemoglobin was observed, rising from 9.6 ± 0.79 g/dL to 11.11 ± 1.3 g/dL on day 30 in the IV group and from 9.7 ± 0.5 g/dL to 11 ± 1.25 g/dL on day 30 in the oral group (not significant). On day 30 ($P < .0001$) and at delivery ($P = .01$) ferritin was higher in the IV group. A mean higher birth weight of 250 g was noted in the IV group (not significant). Their study concluded that Iron sucrose appears to be a treatment without serious side effects indicated in correction of pregnancy anemia or iron stores depletion similar to the results of this study. (Am J Obstet Gynecol 2002; 186: 518-22) In the present study, among the patients included in the intravenous iron group, only a few developed mild side effects and none had any serious anaphylactoid reactions to the drug. This result is comparable to the earlier study done by Van Wyck *et al*[18] who studied 23 anemic patients with Hb <7g/dl and had sensitivity to IV iron. In their study, each patient received 10 doses of iron sucrose without a test dose by IV infusion or IV bolus. Results showed no serious adverse drug reactions after a total of 223 doses.

Conclusion

This study was attempted to analyze the safety and efficacy of oral iron in comparison to intravenous iron on the hematological parameters in pregnant women with iron deficiency anemia. This study confirms that intravenous iron caused a rapid and effective improvement in the hematological parameters when compared to oral iron. In our country, with a higher incidence of iron deficiency anemia in pregnancy, especially in a rural scenario, this type of treatment may be helpful in management of these patients in a cost-effective manner. Following a rigorous research and evaluation iron sucrose has established its full place and potential and may be the solution.

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