ISSN 2515-8260 Volume 09 , Issue 04 , 2022

Comparative study of oral iron and intravenous iron sucrose for the treatment of iron deficiency anemia among pregnant women in India

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Abstract

Background: Anemia is a major public health problem worldwide, causing an unfavorable status in respect to upcoming pregnancy. About 20-50% world's population is anemic among them the most common risk factor is pregnancy.

Material and Methods: All pregnant women suffered from iron deficiency anemia with hemoglobulin level 6-10 gm/dl and gestational age 16-32 were included in this study.Total 300 antenatal patients were involved in this study. All women attending antenatal OPD were screened for anemia. All women attending antenatal clinic were screened for anemia between 16-32 weeks of gestation. All participants were subjected to thorough history followed by clinical examination blood investigations such as complete blood count, peripheral blood smear, serum ferritin values, liver and renal function tests, stool examinations for worm infestations and occult blood loss of all cases were carried out and antenatal investigations as per our institution protocol were undertaken. The cases were randomly divided into two groups of 150 each. **Oral Group:** was given oral iron tablets containing 100 mg of elemental iron and 500 microgram folic acid daily throughout pregnancy. **Intravenous Group:** was given a 100 mg of elemental iron as iron sucrose. The formula used for calculation of total required IV elemental iron in the form of iron sucrose, that is, Total iron dose required (mg) = 2.4 x weight in kg x (target Hb – actual Hb of patient) g/dl + 500.[17] The total calculated TDI was administered within three consecutive days, up to a maximum of 500 mg per day infusion in 500 ml of normal saline over a period of three to four hours. The infusion was given under supervision to avoid any untoward side effects. Any minor or major side effects were documented.

Result: Among 300 pregnant women 109 (36.33%) were age group of 25-30 years followed by 93 (31%) were age group of 20-25 years, 50 (16.67%) were age group of 30-35 years, 40 (13.33%) were age group of 18-20 years and 8 (2.67%) were age group of 35-40 years. On the basis of anemia among 300 patients 162 (54%) were mild, 89 (29.67%) were moderate and 49 (16.33%) were severe. Hemoglobulin was 7.95±0.64 g/dl at 2 weeks, 8.83±0.71 g/dl at 4 weeks, 9.72±0.79 g/dl at 6 weeks compared to IV iron which was 7.09±0.54 g/dl at 2 weeks, 8.04±0.59

g/dl at 4 weeks, 10.05±0.71 g/dl at 6 weeks. The hemoglobulin level was recorded significant variation in different times but according to mean hemoglobulin levels were observed increases in succeed time. Rise of mean Hb from baseline to 6 weeks in oral group is 2.4 g/dl where is in IV group it is 2.96 g/dl.

Conclusion: The study concluded; pregnant women who were on intravenous iron sucrose shown rapid increase in hemoglobin level as compare to the prolonged oral iron therapy. This indicates that administration of intravenous iron and oral iron is safe, efficacious and cost effective to treat sever and moderate iron deficiency anemia in short time. Additionally, it replaces iron reserves rapidly than oral iron.We recommend that iron sucrose therapy to treat more effectively iron deficiency anemia. There is paucity of data and study on this more studies required.

Key words: Irion, Iron Sucrose, Intravenous, Oral, Iron deficiency anemia, anemia

Introduction:

Anemia is a major public health problem worldwide, causing an unfavorable status in respect to upcoming pregnancy.About 20-50% world's population is anemic among them the most common risk factor is pregnancy.The prevalence of gestational anemia is about 25% with average of 56% in developing countries but 18% in developed countries.[1]According to recent WHO figures, India is included in the list of countries with high prevalence of anemia in pregnant women (>40%).[2]Iron deficiency anemia is the most common nutritional deficiency anemia worldwide with prevalence maximum among pregnant and postpartum women.[3] the prevalence of iron deficiency anemia in developing countries is approximately 52%.[4]

The center for disease control (CDC) defines anemia when hemoglobin and hematocrit values are less than 11 g/dl and 33% during first trimester and 10.5 g/dl and 32% in second trimester.[5] Anemia is implicated as the direct contributor of postpartum hemorrhage (PPH) which is the leading cause for maternal mortality in 20% of cases.[6] Prevalence was high in all states of the country with considerable variations in moderate to severe anemia.[7]Early marriage, teenage pregnancy, many pregnancies, closer spacing between births, an Indian cuisine heavy in phytates, poor iron and folic acid intake, and a high prevalence of worm diseases in the Indian population are other causes of the high frequency of anemia in our nation.[8]The amount of iron needed varies depending on the stage of pregnancy. Due to the cessation of menstruation, there is a saving of iron in the first trimester (0.56 mg/day), with the highest demand in the second half of pregnancy.[9]

Additionally, an inflammatory reaction could happen, especially after cesarean sections and surgically assisted deliveries, which would cause iron to be sequestered in macrophages and reduce intestinal absorption, preventing the supplied iron from being used for hemopoesis.[10]Since the endogenous iron stores have already been used up in most of these cases, oral iron is insufficient for erythropoesis. For treating such patients, parentral iron therapy is preferred because oral iron therapy has very low compliance and variable outcomes.[11]

There are many compounds available for parenteral therapy, including iron dextran (IM/IV), iron sorbitol (IM), iron sucrose (IV), ferric carboxymaltose, etc., but iron sucrose and ferric

carboxymaltose produce better results due to quick binding of iron to transferrin and quick travel to bone marrow, resulting in an early rise in Hb.[12]Both of these compounds are risk-free during the postpartum period and less likely to cause hypersensitivity reactions (no test dose required).[13] Skin or mucosal pallor, lack of vigor and shortness of breath, exhaustion, lack of attention, and impaired mental, physical, and cognitive performance are all examples of the clinical signs of anemia, and their severity might vary.[14]Premature birth and infection susceptibility are effects of moderate to severe anemia in pregnancy. the effects of prematurity and intrauterine growth restriction: higher prenatal morbidity and mortality.[15,16]

Material and Methods:

This prospective study was carried out in the department of obstetrics and gynecology at Gadag Institute of Medical sciences and District Hospital from January 2022 to March 2022 after taking ethical approval from institutional ethical committee was obtained before commencing the study and written informed consent were taken.

Inclusion criteria: All pregnant women suffered from iron deficiency anemia with hemoglobulin level 6-10 gm/dl and gestational age 16-32 were included in this study.

Exclusion criteria: Pregnant women had anemia due to other than iron deficiency, history of blood transfusion, history of hematological disease, multiple pregnancy and gestational age less than 16 weeks and more than 32 weeks. Patients with evidence of liver or kidney dysfunction or any form of chronic diseases were also excluded.

Total 300 antenatal patients were involved in this study.All women attending antenatal OPD were screened for anemia. All women attending antenatal clinic were screened for anemia between 16-32 weeks of gestation.

All participants were subjected to thorough history followed by clinical examination blood investigations such as complete blood count, peripheral blood smear, serum ferritin values, liver and renal function tests, stool examinations for worm infestations and occult blood loss of all cases were carried out and antenatal investigations as per our institution protocol were undertaken. The cases were randomly divided into two groups of 150 each.

Oral Group: was given oral iron tablets containing 100 mg of elemental iron and 500 microgram folic acid daily throughout pregnancy.

Intravenous Group: was given a 100 mg of elemental iron as iron sucrose. The formula used for calculation of total required IV elemental iron in the form of iron sucrose, that is, Total iron dose required (mg) = 2.4 x weight in kg x (target Hb – actual Hb of patient) g/dl +500.[17]The total calculated TDI was administered within three consecutive days, up to a maximum of 500 mg per day infusion in 500 ml of normal saline over a period of three to four hours. The infusion was given under supervision to avoid any untoward side effects. Any minor or major side effects were documented.

At first visit: Detailed history, physical examination, obstetrics examination, CBC, Peripheral blood film and Urine examination was done.

During follow up visit: Patients were enquired about adverse reaction. CBC was repeated after 2, 4, 6 weeks of beginning of iron therapy.

Statistical analysis: Tables were generated with the help of Microsoft office software. Results were tabulated and statistically analyzed according to chi-square test and Z test.

Results:

Total 300 pregnant women were included in this study. They were divided into two groups. 150 were kept on oral group and 150 were in intravenous group.Among 300 pregnant women 109 (36.33%) were age group of 25-30 years followed by 93 (31%) were age group of 20-25 years, 50 (16.67%) were age group of 30-35 years, 40 (13.33%) were age group of 18-20 years and 8 (2.67%) were age group of 35-40 years (fig- 1).On the basis of anemia among 300 patients 162 (54%) were mild, 89 (29.67%) were moderate and 49 (16.33%) were severe (fig 2).

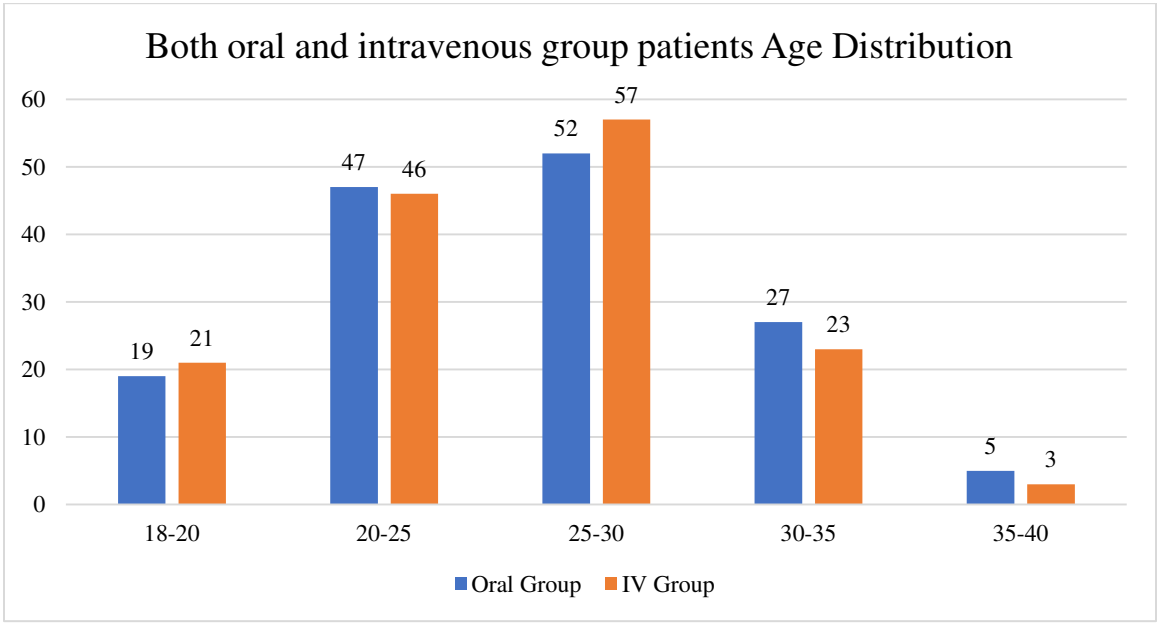

Fig 1: Both oral and intravenous group patients Age Distribution

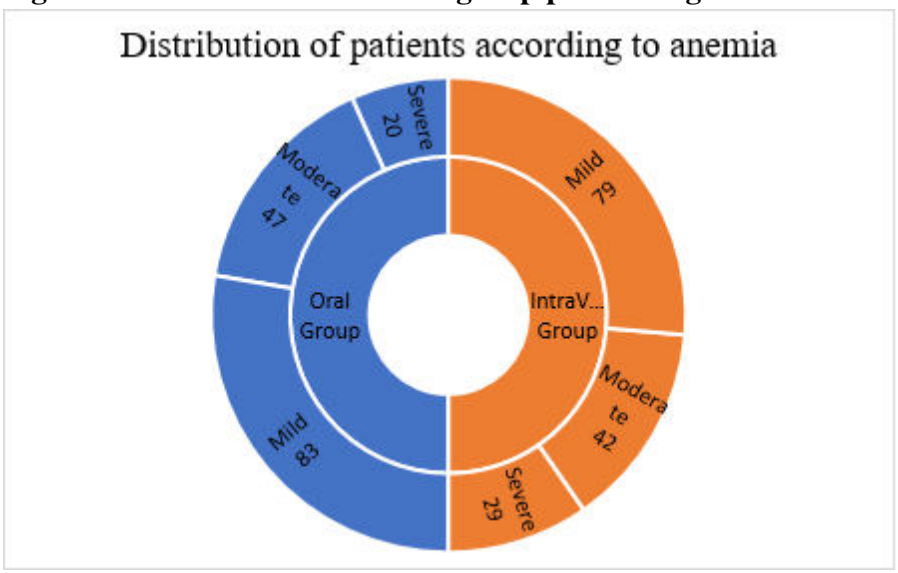

Fig 2: Distribution of patients according to anemia

Table 1: Distribution of Hb in different time in oral group and intravenous group.

	Oral Group			Intravenous Group		
Hb (g/dl)	**Mean (g/dl)**	**SD**	**P value**	**Mean (g/dl)**	**SD**	**P value**
Mean Hb at Firstvisit	7.32	0.62	<0.0001	7.09	0.54	<0.0001
Mean Hb at 2nd week	7.95	0.64		8.04	0.59	
Mean Hb at 4th week	8.83	0.71		9.26	0.69	
Mean Hb at 6th week	9.72	0.79		10.05	0.71	

The demographic and clinical representation were similar in both oral and intravenous group. The hemoglobin level was 7.32±0.62 g/dl and 7.09±0.54 g/dl in oral and Intravenous group respectively. The hemoglobulin level was observed increase in each from first visit to six weeks but in comparison to Oral group intravenous group hemoglobulin were increased more. Hemoglobulin was 7.95±0.64 g/dl at 2 weeks, 8.83±0.71 g/dl at 4 weeks, 9.72±0.79 g/dl at 6 weeks compared to IV iron which was 7.09±0.54 g/dl at 2 weeks, 8.04±0.59 g/dl at 4 weeks, 10.05±0.71 g/dl at 6 weeks (Table 2). The hemoglobulin level was recorded significant variation in different times but according to mean hemoglobulin levels were observed increases in succeed time. Rise of mean Hb from baseline to 6 weeks in oral group is 2.4 g/dl where is in IV group it is 2.96 g/dl.

Table 2: Comparison of Hemoglobulin in Intravenousgroup and Oral group in different time period.

Hb (g/dl)	**Group**	**Mean (g/dl)**	**SD**	**P value**
Mean Hb at First visit Hb	Oral iron	7.32	0.62	0.036
	IV iron	7.09	0.54	
Mean Hb at 2nd week Hb	Oral iron	7.95	0.64	0.491
	IV iron	8.04	0.59	
Mean Hb at 4th week Hb	Oral iron	8.83	0.71	0.005
	IV iron	9.26	0.69	
Mean Hb at 6th week Hb	Oral iron	9.72	0.79	0.005
	IV iron	10.05	0.71	

Table 3: Patients who reached target hemoglobulin.

Follow up	**Oral group (n=150) N (%)**	**Intravenous group (n=150) N (%)**	**P value**
Six weeks	142 (94.66)	137 (91.33)	0.05

Among 300 patients 279 (93%) achieved the target hemoglobulin in six weeks, in oral group 142 (94.66%) and in intravenous group 137 (91.33%) achieved target hemoglobulin (Table 3).

Table 4: Adverse reactions wise distribution of cases in oral group and Intravenous group.

Symptoms	Intravenous Group (n=150)	Percentage	Oral Group (n=150)	Percentage	P value
Nausea	0	00	04	2.66	<0.5
vomiting	0	00	01	0.66	<0.5
Constipation	2	1.33	08	5.33	<0.5
Fever/chills	00	00	00	00	-
Rashes	0	00	0	00	-
Pain in abdomen	00	00	1	0.66	<0.5
Dizziness	4	2.66	0	00	<0.5
Thrombophlebitis	2	1.33	0	00	<0.5
Total	**8**	**5.33**	**14**	**9.33**	

In this study we observed that adverse effect occurred 14 (9.33%) in oral group, whereas the nausea 4 (2.66%), vomiting 1 (0.66%), constipation 8 (5.33%) and pain in abdomen 1 (0.66%) but 8 (5.33%) in intravenous group, whereas constipation 2 (1.33%), dizziness 4 (2.66%) and thrombophlebitis 2(1.33%). (Table 4)

Discussion:

This study was done to compare and to know intravenous iron sucrose therapy in iron deficiency anemia is safe and fruitful in the form of raising Hemoglobulin and iron stores in comparison to conventional oral iron supplement. Poverty, poor literacy rate, increase parity, early marriage and less use of contraceptive causes more common maternal iron deficiency and also associated with intrauterine growth radiation and maternal malnutrition in rural India. About two third of pregnant women in developing countries affected with anemia.[18]

During pregnancy total iron requirement is approximately 1 gram, 500 mg is required for development of foetus and placenta and 500 mg for red cell increment.[19] This iron is typically obtained from iron stores. Women with low iron stores, on the other hand, become iron deficient during pregnancy. According to research, moderate to severe hemoglobulin levels in pregnancy are associated with increased maternal morbidity.[20,21]

Increased demands exacerbate IDA during pregnancy. Iron is in high demand to meet the demands of red blood cell mass expansion in the mother, fetal and placental blood, and blood loss during delivery.[22,23] This is exacerbated by iron absorption problems caused by pregnancy-induced nausea, vomiting, motility problems with indigestion, and a phytate-rich Indian diet. Early marriage, teenage pregnancy, multiple pregnancies, less birth spacing, low iron and folic acid intake, and a high incidence of hookworm infestation in the Indian population are also factors contributing to the high incidence of IDA in India.[24]

Al Momenet et al.[25] compared the treatment of 59 women with 300 mg of oral iron sulfate with 52 women who received intravenous iron sucrose. In a shorter amount of time6.9 ±1.8 versus

14.9 ±3.1 weeks in the control groupintravenous iron sucrose complex dramatically increased hemoglobin levels, reaching 128.5 ±6.6 against 111.4 ±12.4 g/l in the oral iron group (p 0.001). Iron sucrose complex had no significant side effects, however 4 (6%) of the ferrous sulphate patients could not handle it, and 30% experienced gastro intestinal issues. These findings match those of our investigation.

In contrast to oral iron, which was 0.5550±0.456 at 2 weeks, 1.39±0.4402 at 4 weeks, and 1.9±0.3020 at 6 weeks, Deeba S. et al.[26] study found that the difference in Hb from baseline in the IV group was 1.720.484 at 2 weeks, 2.18±0.865 at 4 weeks, and 2.89±0.5989 at 6 weeks. The clinically significant P value of 0.0001 indicated that the intravenous group's Hb levels had grown more than the control group's. These findings match those of our investigation.

This study's findings were consistent with those of Bayoumeu in 2002.[27] and Gabriela et al in 2009.[28] However, in a study comparing the efficacy of intravenous iron to oral iron in the treatment of anemia in pregnancy, AL RA (2005) discovered that hemoglobin from baseline was significantly higher in the intravenous group compared to the oral group at each measurement.

Though the evidence for iron sucrose's efficacy in improving hemoglobin is compelling, its effect on maternal and fetal outcomes is unknown. This is primarily due to a scarcity of well-designed, larger studies with sufficient power to detect differences in clinical outcomes. As a result, evidence from a well-designed large randomized clinical trial is required.[29]

Conclusion:

In comparison to protracted oral iron therapy, the study found that pregnant women receiving intravenous iron sucrose experienced a quick increase in hemoglobin levels. This shows that treating severe and moderate iron deficiency anemia quickly with intravenous iron and oral iron is safe, effective, and economical.It also replenishes iron stores more quickly than oral iron does. Contrary to appearances, this kind of treatment has little side effects and may be suggested for the treatment of iron deficiency anemia.Women with mild anemia would benefit more from intravenous iron therapy under supervision given that oral iron did not significantly enhance anemia correction in these pregnant women. To better successfully treat iron deficiency anemia, we advise iron sucrose treatment. There is a lack of information and research on this, so additional research is needed.

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