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Assessing the efficacy of parenteral iron therapy in treating pregnancy anemia of mild to moderate severity: A clinical study

Dr Poonam Atul Patil
MBBS, DGO, DNB, Assistant Professor, Department of Obstetrics and Gynaecology, Dr Vasantrao Pawar medical college, Hospital And Research Center, Nashik, Maharashtra
Email: poonam27j@gmail.com

Dr. Padmaja Satyen Joshi
MS, DNB, FCPS, Associate Professor, Department of Obstetrics and Gynaecology, Dr. Vasantrao Pawar Medical College, Hospital And Research Center Nashik, Maharashtra
Corresponding author email: drpadmajajoshi78@gmail.com

***Abstract*---**Background: Anemia is a clinical condition characterized by the decreased number of red blood cells or their capacity to carry oxygen needed for physiological functions. Hemoglobin (Hb) value less than 2 standard deviations, less than the median value for healthy subjects matched for pregnancy status, smoking, altitude, gender, and age. Anemia is commonly seen in pregnancy where intravenous iron has proven to be highly effective as a treatment even in cases where oral iron seems ineffective. Aim: The present study was conducted to assess the efficacy of parenteral iron therapy in treating pregnancy anemia of mild to moderate severity Materials and methods: The present study included 120 pregnant females having confirmed diagnoses of iron deficiency anemia. All the included subjects were given 100mg Mebendazole in a dose twice daily as an anti-helminthic therapy for 3 days duration. Also, during the therapy, folic acid was given to all the subjects. Stool examination for cyst and ova, urine culture, microscopy, and routine urine examination, Renal function test (RFT) was done for all the subjects. Results: The results of the present study showed that significant changes were seen in various hematologic parameters from baseline to follow-up. The study results also showed that mean hemoglobin values increased significantly from 8.28 gm to 11.28 gm from baseline to 8 weeks. Similar results were seen for MCV, reticulocyte counts, serum ferritin and TIBC.Conclusion: The present study concludes that parenteral iron therapy is an efficacious treatment modality for moderate to

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severe pregnancy anemia with significant improvement of various parameters over time, and hence, should be considered for managing iron deficiency anemia of pregnancy.

***Keywords*---**anemia, hemoglobin values, iron deficiency anemia, parenteral therapy, pregnant women.

Introduction

Anemia is a clinical condition characterized by the decreased number of red blood cells or their capacity to carry oxygen needed for physiological functions. Hemoglobin (Hb) value less than 2 standard deviations less than the median value for healthy subjects matched for pregnancy status, smoking, altitude, gender and age. The iron-deficiency anemia of pregnancy is not easily defined as various changes are seen in the female body during pregnancy including frequent iron supplementation use, hemoglobin (Hb) values variations with ethnicity, and the physiological expansion of the plasma.[1]

Anemia of pregnancy is also defined by CDC (Center for disease control) as hemoglobin value of less than 11gm/dl or the Hct (hematocrit) values of <33% during the first trimester and third trimester of pregnancy, and hemoglobin value of <10.5gm/dl or hematocrit of <32% in the second trimester of pregnancy. On the other hand, WHO (World Health Organization) defines the anemia of pregnancy as a condition characterized by hemoglobin values of less than 11gm/dl during any trimester of pregnancy. For treating all the iron-deficiency anemia including the anemia of pregnancy, intravenous iron is proven to be very effective, and hence, should be taken into consideration in cases where oral iron therapy is proven ineffective.[2]

Another limitation associated with treating the iron-deficiency anemia with oral iron compared to the parenteral iron is that its efficacy is reduced during its impaired uptake through the gut or when the loss of iron is continuous or large in cases such as post-surgical subjects, gastrointestinal bleeding cases and in subjects with menorrhagia. Also, another vital factor is compromised patient compliance owing to its side effects, which also reduce the efficacy of the oral iron therapy. In such situations, intravenous iron therapy is preferred over oral therapy as the gut is bypassed with parenteral therapy leading to the faster repletion of iron.[3]

In a short span after the iron administration, expression of ferritin is increased and higher levels are attained compared to the use of oral iron which also prevents the recurrence of iron-deficiency anemia during the long term.[4] Hence, the present clinical study was conducted to assess the efficacy of parenteral iron therapy in treating pregnancy anemia of mild to moderate severity.

Materials and Methods

The present clinical study was conducted to assess the efficacy of parenteral iron therapy in treating pregnancy anemia of mild to moderate severity. The study was

carried out at Department of Obstetrics and Gynaecology, in a tertiary care center after obtaining clearance from the concerned Ethical committee. The study population was comprised of the females visiting the Department of Obstetrics and Gynecology of the Institution during their pregnancy. After explaining the detailed study design, informed consent was taken from all the study subjects.

The study included a total of 120 pregnant female subjects having confirmed diagnosis of iron deficiency anemia. The exclusion criteria for the study were subjects having anemia of cause other than iron deficiency anemia, subjects with recent blood transfusion history, high-risk pre=term labor females, and females with multiple pregnancies. After the final inclusion of the study subjects, anti-helminthic therapy was given using tab Mebendazole 100 mg twice daily for 3 days along with the folic acid. At baseline, stool examination for cyst and ova, culture, microscopy, and routine urine examination, Renal function test (RFT), was done for all the subjects. The dose of sucrose iron was evaluated with the following formula:

Required elemental iron in mg = 2.4 x (normal Hb – patents actual Hb) x Prepregnancy weight in kg + 1000.

In this formula, the standard coefficient was 2.4 and 14gm/dl was taken as normal hemoglobin. For the replenishment, 1000mg was added to the values obtained from the above formula. The dose of required elemental iron was varying based on the weight of the subjects before pregnancy and index Hb, where the dose required was 1600-220mg. The total therapy duration was 2.5 weeks to 4.5 weeks. The iron sucrose was administered in 200mg intravenous dose in 200 ml of normal saline in 15-20 minutes three times a week.

During ingestion, the subjects were observed till 1 hour after intravenous drug administration to assess any side effects. Fetal heart rate was also assessed before and following administration. The blood sample from all the subjects was collected under aseptic and sterile conditions for evaluation of red cell indices, serum ferritin, and hemoglobin (Hb) before the drug administration, and at 3, 6, and 8 weeks after drug administration.

The primary outcomes in the present study were Hb concentration change and change in the levels of serum ferritin after 3 weeks, 6 weeks, and 8 weeks, Other secondary parameters were any adverse effects, MCV (mean corpuscular volume), TIBC (total iron-binding capacity), reticulocyte count, and serum iron level improvements. The collected data were subjected to the statistical evaluation using SPSS software version 21 (Chicago, IL, USA) and one-way ANOVA and t-test for results formulation. The data were expressed in percentage and number, and mean and standard deviation. The level of significance was kept at $p<0.05$.

Results

The present clinical study was conducted to assess the efficacy of parenteral iron therapy in treating pregnancy anemia of mild to moderate severity. The study included a total of 120 pregnant female subjects having confirmed diagnosis of iron deficiency anemia. The demographic characteristics of the study subjects are

listed in Table 1. The mean age of the study subjects was 28.26±1.24 years and the age range was 19-31 years. The mean weight of the study subjects was 57.3±4.6kg and the mean BMI was 20.5±1.6kg/m2. The anemia type was moderate in 95.83% (n=115) subjects and was mild in 4.16% (n=5) of study subjects (Table 1).

On assessing the hematological parameters from baseline to 8 weeks in the study subjects, it was seen that MCV at baseline was 64.34 which increased to 3 weeks, 6 weeks, and 8 weeks significantly to 75.38, 81.28, and 87.27 with p=0.0001, reticulocyte counts also increased significantly from baseline 1.44% to 3.95%, 4.97%, and 5.67% to 3, 6, and 8 weeks respectively with p=0.03, serum ferritin at baseline was 13.64 µg/dl which significantly increased to 17.85, 28.07, and 69.33 µg/dl with p=0.02, TIBC at baseline was 370.4 µg/dl at baseline which decreased significantly to 351.27, 325.7, and 309.27 to 3 weeks, 6 weeks, and 8 weeks respectively. This was statistically significant with p=0.04. Hemoglobin also increased significantly from baseline, 8.28gm to 9.37 gm at 3 weeks, 10.27 gm at 6 weeks, and 11.28 gm at 8 weeks respectively with p=0.002 as depicted in Table 2.

Discussion

The present clinical study was conducted to assess the efficacy of parenteral iron therapy in treating pregnancy anemia of mild to moderate severity. The study included a total of 120 pregnant female subjects having confirmed diagnosis of iron deficiency anemia. The mean age of the study subjects was 28.26±1.24 years and the age range was 19-31 years. The mean weight of the study subjects was 57.3±4.6kg and the mean BMI was 20.5±1.6kg/m2. The anemia type was moderate in 95.83% (n=115) subjects and was mild in 4.16% (n=5) study subjects. These demographics were comparable to the studies of Bhavi SB et al[5] in 2017 and Froessler B et al[6] in 2018 where authors assessed subjects with comparable demographics in their studies as in the present study.

For the assessment of the hematological parameters from baseline to 8 weeks in the study subjects, it was seen that MCV at baseline was 64.34 which increased to 3 weeks, 6 weeks, and 8 weeks significantly to 75.38, 81.28, and 87.27 with p=0.0001, reticulocyte counts also increased significantly from baseline 1.44% to 3.95%, 4.97%, and 5.67% to 3, 6, and 8 weeks respectively with p=0.03, serum ferritin at baseline was 13.64 µg/dl which significantly increased to 17.85, 28.07, and 69.33 µg/dl with p=0.02. These results were consistent with the studies of Radhika AG et al[7] in 2019 and Onken JE et al[8] in 2014 where authors reported similar hematologic parameter change as in the present study.

TIBC at baseline was 370.4 µg/dl which decreased significantly to 351.27, 325.7, and 309.27 to 3 weeks, 6 weeks, and 8 weeks respectively. This was statistically significant with p=0.04. Serum iron at baseline was 28.27 µg/dl which significantly increased to 40.14, 59.38, and 81.27 µg/dl to 3, 6, and 8 weeks which was statistically significant with p=0.003. Hemoglobin also increased significantly from baseline, 8.28gm to 9.37 gm at 3 weeks, 10.27 gm at 6 weeks, and 11.28 gm at 8 weeks respectively with p=0.002. These results were in agreement with the findings of Koutroubakis IE et al[9] in 2010 and Neeru S et al[10]

in 2012 where comparable changes for TIBC, and hemoglobin were reported by the authors in their study subjects as in the present study.

Conclusion

Within its limitations, the present study concludes that parenteral iron therapy is an efficacious treatment modality for mild to moderate pregnancy anemia with significant improvement of various parameters over time, and hence, should be considered for managing iron deficiency anemia of pregnancy. The present study had a few limitations including small sample size, shorter monitoring period, and geographical area biases. Hence, more longitudinal studies with a larger sample size and longer monitoring period will help reach a definitive conclusion.

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Tables

Characteristics	Percentage (%)	Number (n)
Mean age (years)	28.26±1.24	
Age range (years)	19-31	
Mean weight (kg)	57.3±4.6	
BMI (kg/m2)	20.5±1.6	
Anemia Type		
Moderate	95.83	115
Severe	4.16	5

Table 1: Demographic and disease characteristics of the study subjects

Hematologic parameters	Baseline	3 weeks	6 weeks	8 weeks	p-value
MCV (fl)	64.34	75.38	81.28	87.27	0.0001
Reticulocyte counts (%)	1.44	3.95	4.97	5.67	0.03
Serum Ferritin (µg/dl)	13.64	17.85	28.07	69.33	0.02
TIBC (µg/dl)	370.4	351.27	325.7	309.27	0.04
Hemoglobin (gm)	8.28	9.37	10.27	11.28	0.002

Table 2: Assessment of the changes in the parameters from baseline to follow-up