Original Research Article

Assessment of efficacy of Parenteral Iron Therapy for Treatment of Moderate to Severe Anemia in Pregnancy

Mohd. Rais Alam[1], Deepika Singh[2*]

[1,2]Assistant Professor, Department of General Medicine, TSM Medical College Lucknow, Uttar Pradesh, India

Received: 19-10-2020 / Revised: 28-11-2020 / Accepted: 24-12-2020

Abstract

Background: Anemia is a condition where the red blood cell number or their oxygen-carrying capacity is insufficient to meet physiologic needs, and is conventionally taken as a hemoglobin (Hb) value that is less than two standard deviation (SD) below the median value for healthy matched population by age, sex, altitude, smoking, and pregnancy status. Intravenous iron is very effective in the treatment of iron deficiency anemia and should be considered when oral iron is ineffective. **Aim of the study:** To assess efficacy of Parenteral Iron Therapy for Treatment of Moderate to Severe Anemia in Pregnancy. **Materials and methods:** The present study was conducted in the Department of General Medicine of the Medical institution. For the study, a total of 100 pregnant women diagnosed with iron deficiency anemia were selected. All the pregnant women were given antihelminthic therapy with mebendazole 100 mg twice daily for 3 days. Folicacid were given to all women during the therapy. Baseline investigations including blood (LFT, RFT), Urine (routine, microscopy and culture) and stool examination (ova and cyst) were done. **Results:** In the present study, a total of 100 pregnant females with iron deficiency anemia were selected. The mean age of the participants was 32.69 years. We observed that significant change was seen in different hematological parameters over the time period of treatment. It was observed that mean Hemoglobin increased from 7.26 g at baseline to 11.26 after 8 weeks. Similar trend was seen for serum iron, TIBC, serum ferritin, reticulocyte count and MCV. **Conclusion**: Within the limitations of the present study, it can be concluded that parenteral iron therapy provides significantly efficacious treatment for moderate to severe anemic pregnant patients. It should be considered as successful treatment option for IDA in pregnant women.

Keywords: Anemia, iron deficiency anemia, pregnant women, parenteral therapy.

Introduction

Anemia is a condition where the red blood cell number or their oxygen-carrying capacity is insufficient to meet physiologic needs, and is conventionally taken as a hemoglobin (Hb) value that is less than two standard deviation (SD) below the median value for healthy matched population by age, sex, altitude, smoking, and pregnancy status.[1] Defining anemia in pregnancy is not straight-forward given the physiologic plasma expansion, the ethnic variations of Hb values and the frequent use of iron supplementation in pregnancy. Center of Disease Control (CDC) defines anemia as pregnancy hemoglobin less than 11 g/dl (Hematocrit{Hct} < 33%) in the first and third trimester and less than 10.5 g/dl (Hct < 32%) in the second trimester while World Health Organisation (WHO) defines anemia in pregnancy as Hb values less than 11gm/dl.[2, 3] Intravenous iron is very effective in the treatment of iron deficiency anemia [4] and should be considered when oral iron is ineffective.[5] The efficacy of oral iron is diminished when uptake through the gut is impaired or when iron losses are large and/or continuous (eg, with menorrhagia, gastrointestinal bleeding, or postsurgery). Diminished patient compliance due to side effects also limits the efficacy of oral iron. In these situations, intravenous iron therapy is preferred because the gut is bypassed, allowing faster repletion. Ferritin expression increases shortly after administration and reaches higher levels than with oral iron, [6] which can diminish the recurrence of iron deficiency anemia in the long term. Hence, the present study was conductedto assess efficacy of Parenteral Iron Therapy for Treatment of Moderate to Severe Anemia in Pregnancy.

**Correspondence*
Dr. Deepika Singh
Assistant Professor, Department of General Medicine, TSM Medical College, Lucknow, Uttar Pradesh, India.
E-mail: drsinghdeepika11@gmail.com

Materials and methods

The present study was conducted in the Department of General Medicine of the Medical institution. The ethical clearance for the study was approved from the ethical committee of the hospital. For the study, a total of 100 pregnant women diagnosed with iron deficiency anemia were selected. We excluded the patients who had multiple preganancies, high risk for preterm labor, history of recent blood transfusion, and other causes of anemia other than

IDA. An informed written consent was obtained from the participants of the study after explaining them the protocol of the study. All the pregnant women were given antihelminthic therapy with mebendazole 100 mg twice daily for 3 days. Folicacid were given to all women during the therapy. Baseline investigations including blood (LFT, RFT), Urine (routine, microscopy and culture) and stool examination (ova and cyst) were done. The iron sucrose dose was calculated by using the formula as follows,

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

Here 2.4 is standard co-efficient. Normal Hb is taken as 14 gms. To the value calculated by above formula 1000 mg is added for replenishment of stores. The required elemental iron dose varied depending on index Hb and prepregnancy weight of patients. The dose requirement was 1600 -2200 mg. The duration to complete total therapy was 2.5 to 4.5 weeks. The iron sucrose was given as outpatient basis, in a dose of 200 mg intravenously, three times a week, in 200 ml of NS over a period of 15-20 minutes. Patients were observed during transfusion and one hour post transfusion for side effects. FHR was assessed before and after transfusion. Blood samples were collected to measure Hb, serum ferritin and other red cell indices prior to transfusion and again 3, 6 and 8 weeks. The primary outcome measures were change in Hb concentration and serum ferritin levels after 3, 6 and 8 weeks. Secondary outcome measures were improvement in serum iron level, reticulocyte count, TIBC, MCV, any adverse effects and perinatal outcome(period of gestation at the time of delivery, mode of delivery, fetal birth weight, PPH and need of blood transfusion). The statistical analysis of the data was done using SPSS version 11.0 for windows. Chi-square and Student's t-test were used for checking the significance of the data. A p-value of 0.05 and lesser was defined to be statistically significant.

Results

In the present study, a total of 100 pregnant females with iron deficiency anemia were selected. The mean age of the participants was 32.69 years. **Table 1** shows the mean values of hematological parameters at baseline and at 3 weeks, 6 weeks and 8 weeks after iron sucrose therapy. We observed that significant change was seen in different hematological parameters over the time period of treatment. It was observed that mean Hemoglobin increased from 7.26 g at baseline to 11.26 after 8 weeks. Similar trend was seen for serum iron, TIBC, serum ferritin, reticulocyte count and MCV. The results on comparison were found to be statistically significant ($p<0.05$). **[Fig 1]**

Table 1: Mean values of hematological parameters at baseline and at various time intervals after iron sucrose therapy

Mean values	Baseline value	3 weeks	6 weeks	8 weeks	p-value
Hb (g)	7.26	8.39	9.29	11.26	0.002
S. iron (µg/dl)	28.29	40.12	59.36	81.29	0.003
TIBC (µg/dl)	370.2	351.29	325.9	309.29	0.04
S. Ferritin (µg/dl)	13.62	17.83	28.05	69.31	0.02
Reticulocyte count (%)	1.42	3.93	4.95	5.69	0.03
MCV (fl)	64.32	75.36	81.26	87.29	0.0001

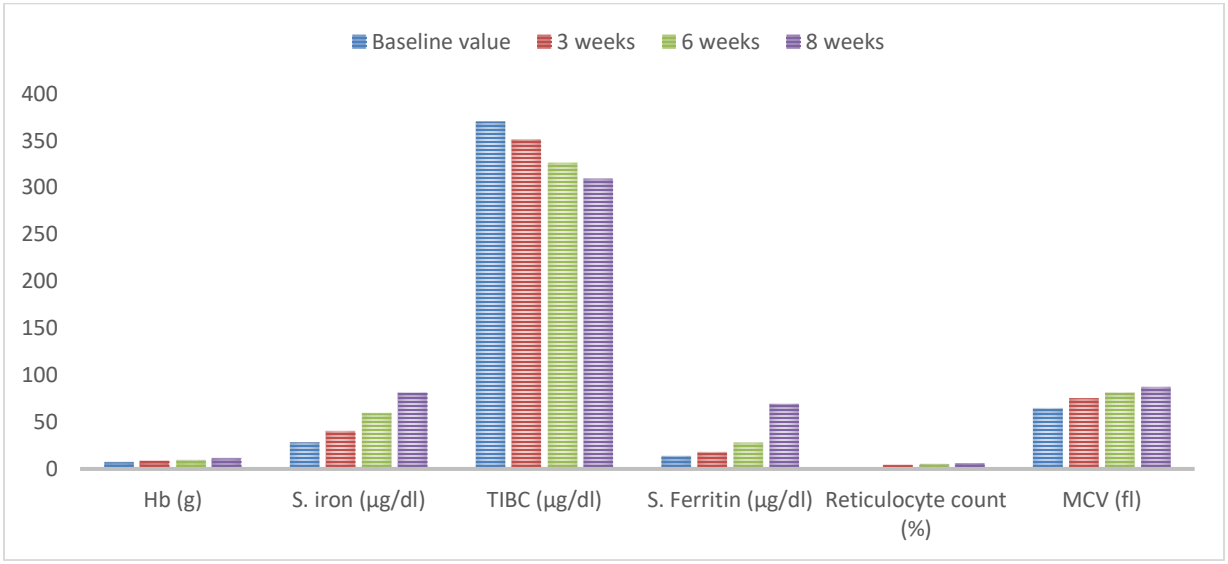

Fig 1: Change in Hematological parameters with iron sucrose therapy

Discussion

In the present study, we studied 100 patients with IDA for effect of parenteral iron therapy on the moderate to severe IDA. It was observed that significant increase in hematological parameters can be seen over treatment period with IV iron sucrose therapy. We observed statistically significant results over the period of 8 weeks. The results were compared with previous studies from the literature and found to be statistically significant. Neeru S et al [7] compared the efficacy and tolerance of intravenous iron sucrose (IVIS) therapy with oral iron (OI) therapy in pregnant women with IDA. All patients were monitored for laboratory response and adverse effects. Although hemoglobin increased in both the groups, increase in the reticulocyte count and percentage increase in hemoglobin was significantly higher in the IVIS group than in the OI group (23.62% vs. 14.11%). Serum ferritin was significantly higher in the IVIS group than in the OI group. They concluded that IVIS is safe and effective in the treatment of IDA during pregnancy. Iron stores increased better with IVIS compared with OI. Bhavi SB et al [8] compared the efficacy, safety and tolerability of intravenous iron sucrose with that of oral ferrous fumarate in iron deficiency anemia during 14 to 34 weeks of pregnancy. 112 patients attending the antenatal clinic at Shri B.M.Patil Medical college Hospital, Bijapur from October 2011 to August 2012,with hemoglobin levels between 70-110 g/L and serum ferritin of < 15 ng/ml were included. In the intravenous group, 200 mg of iron sucrose was administered in 100 ml 0.9% sodium chloride per day. Participants in the oral group were given 200 mg of ferrous fumarate per day. The change in haemoglobin in women receiving intravenous iron was higher than with oral ferrous fumarate 22 ± 11.5 g/L vs 12 ± 9 g/L. Similarly the change of serum ferritin was significantly higher in women receiving intravenous iron compared to oral iron. 55% participants in the intravenous group had an improvement in haemoglobin more than 20 g/L compared to only 11% of the oral therapy group.48% of patients in I.V group showed increase in ferritin level between 51 to 100 ng/ml in comparison to only 3.5% in oral group. They concluded that intravenous iron sucrose is more effective than 200 mg a day ferrous fumarate in increasing maternal iron stores.

Khalafallah AA et al [9] compared the efficacy and safety of intravenous (IV) iron preparation, ferric carboxymaltose (FCM), against IV iron polymaltose (IPM), and standard oral iron (ferrous sulphate) for the treatment of IDA in pregnancy. A 3-arm randomised controlled trial was conducted comparing a single IV infusion of 1000mg of FCM over 15 minutes against a single IV infusion of 1000mg of IPM over 2 hours against 325mg daily oral ferrous sulphate until delivery, for the treatment of IDA in pregnancy. The primary outcome was the change in ferritin and Hb levels at 4 weeks after intervention. Secondary outcomes included ferritin and Hb improvements at predelivery, safety, tolerability, quality of life (QoL), cost utility, and fetal outcomes. The mean Hb level differences between the baseline intervention time point and 4 weeks thereafter were significantly higher in the FCM versus the oral group by 4.35g/L and in the IPM vs the oral group by 4.08g/L, but not different between the FCM and IPM groups. The mean ferritin level differences were significantly higher at 4 weeks in the FCM vs oral iron group by 166µg/L and in the IPM vs oral iron group by 145µg/L, but not between the 2 IV groups. Administration of IV FCM during pregnancy was safe and better tolerated than IV IPM or oral iron. Compliance to oral iron was the lowest amongst treatment groups with one-third of the patients missing doses of daily iron tablets. Significant improvement in overall QoL scores was observed in both IV iron supplement groups by achieving normal ferritin following effective and prompt repletion of iron stores, compared to the oral iron group. The overall cost utility of IV FCM and IV IPM appear to be similar to oral iron. There were no differences in the fetal outcomes between the 3 trial arms. This study demonstrated that a single IV iron infusion is an effective and safe option for treatment of IDA during pregnancy. FCM was more convenient than other treatments. Rapid parenteral iron repletion can improve iron stores, Hb levels and QoL in pregnant women, with ongoing benefits until delivery. Radhika AG et al [10] compared anaemic pregnant and post-partum women treated with intravenous iron sucrose versus oral iron. The primary outcomes were mean maternal haemoglobin, serum ferritin and haematocrit at the end of 1st, 2nd, 4th and 6th weeks and comparison of adverse effects. Eighteen studies including 1633 antenatal women were randomly assigned to intravenous iron sucrose or oral iron group in ten trials. Another eight studies compared iron sucrose infusion with oral iron in 713 post-partum women who were randomly assigned to intravenous iron sucrose group or oral iron group. Cumulative analysis of all the time points indicates that the estimated mean values of Hb in the intravenous iron sucrose and oral iron groups were 10.11 g/dl and 9.33 g/dl, respectively, in antenatal group, while it was 10.57 g/dl and 9.74 g/dl in post-partum. The estimated mean ferritin level from first week to six weeks was 63.1 µg/l and 28.6 µg/l, respectively, in intravenous and oral iron groups. Cumulative estimate of haematocrit in the intravenous sucrose and oral iron over 6 weeks showed that the mean values in the respective groups were 30.5% and 29.5% in antenatal and 33.8% and 31.6%, respectively, in post-partum groups.

Froessler B et al [11] evaluated the efficacy and safety of intravenous ferric carboxymaltose administration to pregnant women with varying severities of iron deficiency anemia and iron deficiency without anemia. They analyzed data from 863 pregnant women with iron deficiency according to anemia status and severity. All women were treated with intravenous ferric carboxymaltose in pregnancy. Treatment efficacy was assessed by repeat hemoglobin measurements at 3 and 6 week post-infusion and ferritin levels, where available. Safety was assessed by analysis of adverse events, fetal heart rate monitoring, and newborn health outcome data. Ferric carboxymaltose significantly increased hemoglobin in women with mild, moderate, and severe iron deficiency anemia and women with iron deficiency alone at 3 and 6 week post-infusion. No hemoconcentration occurred in iron-deficient women without anemia. No serious adverse events were recorded, with minor temporary side effects occurring in 96 (11%) women. No adverse fetal or neonatal outcomes

were observed. They concluded that Ferric carboxymaltose infusion corrects iron deficiency or various degrees of iron deficiency anemia efficaciously and safely pregnant women, and does not cause hemoconcentration.

Conclusion

Within the limitations of the present study, it can be concluded that parenteral iron therapy provides significantly efficacious treatment for moderate to severe anemic pregnant patients. It should be considered as successful treatment option for IDA in pregnant women.

References

1. Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? Blood. 2006;107(5) :1747–1750.
2. CDC. CDC criteria for anemia in children and childbearing-aged women. MMWR Morbidity and mortality weekly report. 1989;138(22):400–404.
3. WHO (2001) Iron deficiency anemia: assessment, prevention and control. WHO/NHD/01.3, Geneva. World Health Organization, Switzerland
4. Koutroubakis IE, Oustamanolakis P, Karakoidas C, Mantzaris GJ, Kouroumalis EA. Safety and efficacy of total-dose infusion of low molecular weight iron dextran for iron deficiency anemia in patients with inflammatory bowel disease. Dig Dis Sci. 2010;55(8):2327–2331.
5. Onken JE, Bregman DB, Harrington RA et al. A multicenter, randomized, active-controlled study to investigate the efficacy and safety of intravenous ferric carboxymaltose in patients with iron deficiency anemia. Transfusion. 2014;54(2):306–315.
6. Lindgren S, Wikman O, Befrits R et al. Intravenous iron sucrose is superior to oral iron sulphate for correcting anaemia and restoring iron stores in IBD patients: a randomized, controlled, evaluator-blind, multicentre study. Scand J Gastroenterol. 2009;44(7):838–845.
7. Neeru S, Nair NS, Rai L. Iron sucrose versus oral iron therapy in pregnancy anemia. Indian J Community Med. 2012;37(4):214-218.
8. Bhavi SB, Jaju PB. Intravenous iron sucrose v/s oral ferrous fumarate for treatment of anemia in pregnancy. A randomized controlled trial. BMC Pregnancy Childbirth. 2017 May 8;17(1):137.
9. Khalafallah AA, Hyppa A, Chuang A, Hanna F, Wilson E, Kwok C, Yan C, Gray Z, Mathew R, Falloon P, Dennis A, Pavlov T, Allen JC. A Prospective Randomised Controlled Trial of a Single Intravenous Infusion of Ferric Carboxymaltose vs Single Intravenous Iron Polymaltose or Daily Oral Ferrous Sulphate in the Treatment of Iron Deficiency Anaemia in Pregnancy. Semin Hematol. 2018 Oct;55(4):223-234.
10. Radhika AG, Sharma AK, Perumal V, Sinha A, Sriganesh V, Kulshreshtha V, Kriplani A. Parenteral Versus Oral Iron for Treatment of Iron Deficiency Anaemia During Pregnancy and post-partum: A Systematic Review. J Obstet Gynaecol India. 2019 Feb;69(1):13-24.
11. Froessler B, Gajic T, Dekker G, Hodyl NA. Treatment of iron deficiency and iron deficiency anemia with intravenous ferric carboxymaltose in pregnancy. Arch Gynecol Obstet. 2018;298(1):75-82.

Conflict of Interest: Nil
Source of support:Nil