

EFFICACY, TOLERABILITY AND SAFETY OF INTRAVENOUS IRON SUCROSE IN POSTPARTUM ANAEMIA

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ABSTRACT

Background: Anemia is one of major contributing factor in maternal mortality and morbidity in third world countries and according to the WHO, contributes to 40% maternal deaths. Postpartum anemia is observed in up to 27% of women. It is a common problem throughout the world. Treatment of postpartum iron deficiency anemia includes oral and parenteral iron supplementation as well as blood transfusion in severe cases. **Methods:** This was a prospective longitudinal study carried out in Department of Obstetrics & Gynaecology of PRH, Loni. Total 80 women suffering from postpartum anemia of age above 18 years with haemoglobin (HB) level below 11gm/dl and above 6gm/dl were included for the study. After history taking, clinical examination and baseline Hb level, all of them were administered intravenous iron sucrose 200 mg per dose per day till the total calculated dose was administered. The post therapy evaluation was done with the estimation of Hb on day 1, day 7, day 14 and day 21. **Results:** 31.25% women belonged to the age group each of 19-21 years and 22-24 years. Maximum number of patients received 3 doses of IV Iron sucrose (i.e. total 600mg) followed by 2 doses (i.e. total 400mg), 4 doses (i.e. total 800mg) and 5 doses (i.e. total 1000mg) respectively. Hb level rises extremely significantly ($p < 0.001$) after IV Iron Sucrose administration on day 1, 7, 14 & 21 as compared to corresponding values before delivery as analyzed by Friedman Test (Nonparametric Repeated Measures ANOVA). 16 patients (20%) experienced thrombophlebitis to IV Iron Sucrose administration. About 12 (15%) patients experienced rigor followed by sweating in 10 patients (12.5%) and fever in 8 patients (10%). About 62 patients (77.5%) from total 80 reported well tolerability to IV Iron Sucrose while remaining 18 patients (22.5%) reported poor tolerability to IV Iron Sucrose. **Conclusion:** Intravenous iron sucrose increases the haemoglobin more rapidly in first week as compared to second and third week in women with postpartum iron deficiency anemia. Hypersensitivity reaction, chest pain, dyspnoea reported with iron dextran and iron sorbitol citric acid were not observed with iron sucrose. Intravenous iron sucrose can be used safely to fill a rift between blood transfusion and oral iron in treatment of postpartum iron deficiency anemia.

Keywords: Postpartum anemia; Iron Sucrose; Efficacy; Safety and tolerability of Iron Sucrose.

INTRODUCTION

Anemia is one of major contributing factor in maternal mortality and morbidity in third world countries and according to the WHO, contributes to 40% maternal deaths. Postpartum anemia is observed in up to 27% of women [1]. It is a common problem throughout the world [2]. It is a major cause of maternal morbidity such as lethargy, headaches, tiredness, dizziness, lactation failure, and postpartum depression and mortality in resource poor countries [3, 4]. Depending on the grade of postpartum anemia, symptoms like reduced exercise performance, tiredness, headache, increased cardiovascular strain, higher risk for infections, and lactation problems occur [5]. Iron deficiency is the principle cause of anemia [6]. Iron deficiency anemia is very much prevalent in the tropics particularly amongst women of child bearing age, especially in under privileged sector. Nutrition of a woman in the family is always at bay because of various social and cultural prac-

tices and on top of it she always remains in the dark about her own health. To highlight this, there is a saying in the countryside that '*Gold is the metal she remembers and iron is the metal she forgets!*'

High prevalence of iron deficiency is attributable to faulty dietetic habit, faulty absorption mechanism because of high prevalence of intestinal infestation and increased iron loss as consequence of repeated pregnancies at short intervals, excessive blood loss during menstruation, hookworm infestation and chronic malaria [7]. Irrespective of mode of delivery, blood loss is a contributing factor. Majority of anemic women are received directly in labour without having any chance of correcting anemia antenatally. Postpartum anemia is associated with longer hospital stays, depression, anxiety, and delayed infant development [8].

At the present time, there is no consensus on the management of postpartum anemia, and clinical practice varies from one clinic to another. The standard approach to treatment in the majority of institutions is oral supplementation, with blood transfusion reserved for more severe or symptomatic cases [9]. There are number of hazards of blood transfusion including transfusion of wrong blood, anaphylaxis and infections, any of which would be devastating for the young mother [10]. Oral iron is unreliable in treatment of severe anemia due to



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its limited absorption and gastrointestinal side effects that affect compliance [3]. Parenteral iron therapy by intramuscular injection of iron dextran is a painful alternative with a variable degree of efficacy. Because of its site of administration and side effects, compliance is low. In practice the use of iron dextran is not generally recommended due to the unpredictable risk of life-threatening or serious acute reactions in 0.6 to 2.3% of patients and the availability of safer agents [11-13]. Parental iron administration with ferrous sucrose is now available and can be used for treatment of iron deficiency anemia in postpartum period [14].

This study was proposed to carry out a prospective randomized study of intravenous iron sucrose in the treatment of postpartum anemia.

MATERIALS AND METHODS

Study design: An observational study.

Ethics approval: The study was approved by the institutional ethics committee and informed consent was obtained from the participants.

Study location: Department of Obstetrics and Gynecology (OBGY) of Rural Medical College, Loni.

Study period: Study was carried out over the period of 2 years from 15th Sep 2016 to 14th June 2018.

Inclusion criteria: Total 80 Women suffering from postpartum anaemia aged 18 years or more with Hemoglobin of less than 10 g/dl but more than 6g/dl at 24 to 48 hours after delivery who have treated with IV iron sucrose and those showing side effects to oral iron therapy were included in the study after written informed consent.

Exclusion criteria: Women who have received recent blood transfusion, Known cases of complications of pregnancy like eclampsia, heart disease etc where intensive monitoring is required or any other medical/ surgical complications and those with known allergy to parenteral Iron Sucrose were excluded from the study.

Methodology:

After careful history taking, clinical examination and minimal investigations other causes of anemia were ruled out. The initial iron status of the woman was assessed by the clinical and laboratory examinations (complete blood picture). The Haemoglobin (Hb) status of pregnant women who are clinically diagnosed with anemia was estimated by Sahli's acid- haematin method. 2 ml of EDTA chelated blood from severely anaemic patients was sent for peripheral smear examination to the Central Lab, Rural medical hospital, Loni. Microcytic, hypochromic appearance of RBCs confirm IDA. The Hb status of the patients confirmed with IDA was documented.

Women having Hb levels less than 10 gm/dl at 24-48 hours post-delivery were included in the study. They were administered intravenous iron sucrose 200 mg per dose per day till the total calculated dose was administered.

Iron sucrose was administered as an infusion in 250ml of 0.9% sodium chloride over a period of more than 30 minutes. Patients were monitored for 30 minutes for

signs of intolerance such as anaphylactic reactions, skin rash, dyspnoea, facial flushing, metallic taste, urticaria, hypotension, headache, chest pain, tachycardia, breathlessness etc. The treatment was stopped after the administration of total calculated dose and received no further iron supplementation. The post therapy evaluation was done with the estimation of Hb on day 1, day 7, day 14 and day 21.

Statistical analysis - Data analysis was done by using appropriate statistical methods.

RESULTS

The maximum number of women 28(35%) belonged to the age group of 25-27 years. 31.25% women belonged to the age group each of 19-21 years and 22-24 years. Only 2 women (2.5%) were from age of 28 years. There were no women above 28 years of age (Table I).

Table 1. Age distribution in study population

Age (yrs)	No. of women	%
19-21	25	31.25
22-24	25	31.25
25-27	28	35
28	2	2.5
Total	80	100

Among 80 women, 44 (55%) women were delivered by FTND (full term normal vaginal delivery) while remaining 36 (45%) women were delivered by LSCS (lower segment Caesarean section).(Table 2)

Table 2. Mode of Delivery of Patients

Mode of Delivery	Number of Patients (n=80)	%
FTND	44	55
LSCS	36	45

Maximum number of women reported blood loss in the range of 751-1000ml (55%) followed by 450-750ml (27.5%) and then 1001-1750ml (17.5%). (Table 3)

Table 3. Amount of Blood Loss during and after delivery

Blood Loss during delivery (ml)	Number of Patients	%
450-750	22	27.5
751-1000	44	55
1001-1750	14	17.5

Maximum number of patients received 3 doses of IV Iron sucrose (i.e. total 600mg) followed by 2 doses (i.e. total 400mg), 4 doses (i.e. total 800mg) and 5 doses (i.e. total 1000mg) respectively (Table 4)

Table 4. Total number of doses of IV Iron Sucrose administered

Total Doses administered (One dose=200mg)	Number of Patients (n=80)	%
2	25	31.25
3	37	46.25
4	14	17.5
5	4	5

Hb level rises extremely significantly ($p<0.001$) after IV Iron Sucrose administration on day 1, 7, 14 & 21 as compared to corresponding values before delivery as analyzed by Friedman Test (Nonparametric Repeated Measures ANOVA). Also Hb level rises extremely significantly ($p<0.001$) after IV Iron Sucrose administration on day 7, 14 & 21 as compared to corresponding values on Day 1 as analyzed by Friedman Test (Nonparametric Repeated Measures ANOVA). However there is no statistically significant difference in Mean Hb values observed between Day 7 and Day 14 as well as between Day 7 and Day 21. Also, Mean Hb values between Day 14 & Day 21 did not differ significantly from each other.

16 patients (20%) experienced thrombophlebitis to IV Iron Sucrose administration. About 12 (15%) patients experienced rigor followed by sweating in 10 patients (12.5%) and fever in 8 patients (10%). 4 patients (5%) suffered from nausea, 3 (3.75%) from vomiting and 2 (2.5%) from flushing after IV Iron Sucrose administration. (Table 5)

Table 5. Adverse effects reported to IV Iron Sucrose administration

Adverse Effects	Number	%
Fever	8	10
Rigors	12	15
chest pain	0	0
Dyspnoea	0	0
Flushing	2	2.5
Sweating	10	12.5
Nausea	4	5
Vomiting	3	3.75
Thrombo-phlebitis	16	20
Total	55	100

About 62 patients (77.5%) from total 80 reported well tolerability to IV Iron Sucrose while remaining 18 patients (22.5%) reported poor tolerability to IV Iron Sucrose. (Table 6)

Table 6. Tolerability to IV Iron Sucrose administration

Tolerability	N (%)
Well	62 (77.5%)
Poor	18 (22.5%)

DISCUSSION

Iron deficiency anemia in pregnancy is a global public issue, affecting an estimated 41.8% of the pregnant women (McLean et al 2008) [15]. It is associated with increased risk for low birth weight, preterm delivery, maternal and perinatal morbidity and mortality globally, especially in low resource settings [16, 17]

Current UNICEF/WHO recommendations for the prevention and treatment of anemia in pregnancy state that, where prevalence of anemia is $<40\%$; mothers should receive 60 mg of iron plus 400µg of folic acid every day for 6 months in pregnancy and where prevalence is $>40\%$; mothers should receive this dose, continuing to 3 months post partum.

In the present study we investigated efficacy of IV Iron sucrose administration after comparing Hb values at different times and also found out the safety and tolerability to IV Iron sucrose.

While studying the distribution of anemia in various age groups in present study, the median age was 23 years. All study subjects were between 19-28 years (Table I). In some studies investigators had not found any significant difference in the age on anemic and nonanemics women (Amy et al 2000, Geelhoed et al 2006) [18, 19] but one study had found significant difference of age in the studied population (Peterson et al) [20] where the mean age of anemic population was 25.8 ± 5.6 (p value 0.017). Women with less than 20 years of age were 6.25% in the present study. Thus percentage of teenage pregnancy is low indicating that teenage pregnancy is showing a decreasing trend in our rural area. When we compared our teenage pregnant population with the other study, the figures were much less compared to the other rural study population (Geelhoed et al) [19] in which 22.9% women were of age less than 20 with the mean Hb levels less than 8gm%.

While comparing the mode of delivery in the present study, 44 (55%) patients included in the study had undergone full term normal vaginal delivery while 36 (45%) underwent caesarean delivery. During the literature search we could find no evidences to correlate maternal anemia and the mode of delivery.

In our study, maximum number of women reported blood loss in the range of 751-1000ml (55%) followed by 450-750ml (27.5%) and then 1001-1750ml (17.5%) but none required blood transfusion as all three women were clinically and hemodynamically stable. All these women were managed with IV Iron sucrose administration.

Iron sucrose is a high molecular weight complex of iron hydroxide with sucrose that on i.v. injection is taken up by RE cells, where iron dissociates and is utilized. It is safer than the older formulations and a dose of 100 mg (max 200 mg) can be injected i.v. taking 5 min, once daily to once weekly till the total calculated dose (including that to replenish stores) is administered.

In our study, we have given IV Iron sucrose 200mg once daily to all patients till the total calculated dose was administered. The iron sucrose complex was administered first and was diluted in 250 mL 0.9 % sodium chloride, followed by 5 mL saline to flush iron particles from the tubing. The formula for calculating total

iron requirement is

Iron requirement (mg) = $4.4 \times \text{body weight (kg)} \times \text{Hb deficit (g/dl)}$

Maximum number of patients received 3 doses of IV Iron sucrose (i.e. total 600mg) followed by 2 doses (i.e. total 400mg), 4 doses (i.e. total 800mg) and 5 doses (i.e. total 1000mg) respectively.

Hb level rises extremely significantly ($p < 0.001$) after IV Iron Sucrose administration on day 1, 7, 14 & 21 as compared to corresponding values before delivery as analyzed by Friedman Test. This indicated that maximum increase in Hb level occurred in first week while in second and third week, rise in Hb level is not that too fast as iron may be utilized to replenish the lost body stores.

Study performed by Krafft et al [21] had also found efficacy of IV iron sucrose in patients of postpartum anemia. Hb level rises from baseline 7.5gm/dl to mean 10.5gm/dl in 20 women after 15 days of IV iron sucrose administration.

Safety analysis of IV iron sucrose administration revealed that it was safer molecule as compared to earlier iron dextran and other compounds. No patient experienced chest pain and dyspnoea while only 2 patients suffered from flushing which was common with Iron dextran and Iron Sorbitol citric acid. These results were highly encouraging for Gynaecologists and general practitioners as they can safely give iron sucrose in treatment of iron deficiency anemia. Only significant adverse effects reported were thrombophlebitis, rigors, fever and sweating which can be avoided by giving it slowly IV in diluted normal saline.

Tolerability analysis to IV iron sucrose administration revealed that about 62 patients (77.5%) from total 80 reported well tolerability while remaining 18 patients (22.5%) reported poor tolerability to IV Iron Sucrose.

CONCLUSION

Intravenous iron sucrose increases the haemoglobin more rapidly in first week as compared to second and third week in women with postpartum iron deficiency anemia. So, IV iron sucrose is well efficacious in the treatment of postpartum anemia. Hypersensitivity reaction, chest pain, dyspnoea were not observed with iron sucrose so Iron sucrose should be considered safe treatment in postpartum anemia. About 77.5% women reported good tolerability to IV Iron sucrose so it should also be considered well tolerated option.

Intravenous iron sucrose should be considered efficacious, safe and well tolerable option to fill a rift between blood transfusion and oral iron in treatment of postpartum iron deficiency anaemia.

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