Indian J Hematol Blood Transfus (Apr-June 2015) 31(2):251–254
DOI 10.1007/s12288-014-0443-8

ORIGINAL ARTICLE

Role of Intravenous Iron Sucrose in Correction of Anemia in Antenatal Women with Advanced Pregnancy

Avantika Gupta · Asmita Muthal Rathore · Usha Manaktala · Ashutosh Gupta · Sangeeta Gupta

Received: 6 November 2013 / Accepted: 28 July 2014 / Published online: 5 September 2014

Abstract The aim of this study is to observe rise in haematological parameters after treatment with iron sucrose in antenatal patients with moderate anemia with period of gestation 32 to 35 weeks. The study included 45 antenatal patients with period of gestation from 32 to 35 weeks having iron deficiency anemia with haemoglobin levels 7–9 g% and serum ferritin levels less than 12 ng/mL. Intravenous iron sucrose was given in the dose of 200 mg on alternate days, according to the calculated dose. The mean haemoglobin and red blood cell indices were compared on days 7, 14, 21, 28 and at the time of delivery from the baseline value. There was a statistically significant rise in haemoglobin value from baseline on days 14, 21, 28 as well as at the time of delivery (p value <0.0001). The mean rise in haemoglobin values was 0.56 g% on day 14, 1.44 g% on day 21 and 2.0 g% on day 28. At the time of delivery, mean haemoglobin was 11.24 g%. After 28 days of treatment, there was a statistically significant rise in the levels of serum ferritin from 10.33 ± 3.8 ng/mL to 36.89 ± 5.7 ng/mL. Thus, earlier response achieved by iron sucrose can be utilised in the patients presenting at an advanced period of gestation with iron deficiency anemia.

A. Gupta (✉)
Department of Obstetrics & Gynaecology, Maulana Azad Medical College, House no. 93-94, Pocket 2, Sector 22, Rohini, New Delhi 110086, India
e-mail: dravantikagupta@gmail.com

A. M. Rathore · U. Manaktala · S. Gupta
Department of Obstetrics & Gynaecology, Maulana Azad Medical College, New Delhi, India

A. Gupta
Department of Medicine, Sarojini Naidu Medical College, Agra, India

Keywords Pregnancy near term · Blood transfusion · Side effects

Introduction

Iron deficiency anemia is the most common prevalent nutritional deficiency affecting around 50 % of the pregnant women worldwide and tends to be three–four times higher in the non industrialised than in the industrialised countries [1]. During pregnancy, there is a great demand for iron to meet the requirement of red blood cell (RBC) expansion in the mother, fetal and placental blood and the blood loss at delivery. Moreover in the developing countries, most women begin their pregnancy with little or no iron reserve, which is further compounded by repeated and closely spaced pregnancies.

When the patient is approaching term, the target is to achieve desired haemoglobin level in a limited time period. The oral and the older parenteral iron preparations take at least 3 weeks for haemoglobin to rise [2]. Parenteral iron therapy ensures that patient gets complete dose of iron as required, replenish iron stores and overcomes the problem of compliance. Pain on injection, staining of the skin, unpredictable delivery and absorption make the intramuscular route undesirable. The use of older iron preparations, like iron dextran is associated with allergic reactions and fatal anaphylaxis and hence were not used as first line iron therapy.

Iron sucrose complex is a relatively newer drug which shows an early hematological response as shown in the recent studies [3–5]. The biggest advantage of iron sucrose is that, unlike the iron dextrans, it is not necessary to administer a test dose during first time administration [6]. The early rise in hemoglobin levels is crucially important

during final period of pregnancy, as there is reduction in the risk of blood transfusion during peripartum period.

Previous study done in the same institution shows earliest rise in hemoglobin on day 14 of starting therapy with iron sucrose [4]. So, the present study was conducted with an aim to observe rise in haemoglobin with iron sucrose in antenatal patients with anemia with period of gestation more than 32 weeks.

Material and Method

This prospective study was carried out from January 2010 to January 2012 in Department of Obstetrics and Gynaecology, Maulana Azad Medical College and associated hospitals, a tertiary care teaching hospital. The study included antenatal patients, with period of gestation from 32 to 35 weeks having iron deficiency anemia with haemoglobin levels between 7 to 9 g% and serum ferritin levels less than 12 ng/mL. Exclusion criteria included women who delivered before completion of study i.e., 28 days, multiple pregnancy, anemia due to other causes, hypersensitivity to iron, chronic liver disease, kidney disease or heart disease. Hemoglobin, hematocrit and RBC indices were measured at the time of inclusion by automated counters. For the estimation of serum ferritin, 2 mL of blood was centrifuged at 2,000 rpm for 10 min in a refrigerated centrifuge. The separated serum was then transferred to microcentrifuge tubes, and the aliquots were stored at −80 °C for later measurement of serum ferritin by using enzyme linked immunosorbent assays with pathozyme ferritin kits.

The study protocol was approved by the Institutional Ethics Committee. Hemoglobinopathies were ruled out on Naked Eye Single Tube Rapid Osmotic Fragility Test (NESTROFT). HPLC was done in patients who had positive NESTROF test. To detect the difference of 5 mg% of serum ferritin change from baseline to end of the study at 4 weeks, with α risk of 5 %, power = 80.0 % the sample size is calculated as 35. Each woman was given a course of antihelminthic treatment with 100 mg mebendazole twice daily for 3 days due to high prevalence of worm infestation reported in the same institution [7].

Women received total dose of iron sucrose calculated as:

Body weight in kg × (target Hb−actual Hb in g/dL) × 2.4 + 500 mg [4, 8].

Target haemoglobin was taken as 11 g% and 500 mg is for the restoration of iron stores. Intravenous (I/V) iron sucrose was given in the dose of 200 mg on alternate days with a maximum of 600 mg/week as recommended by French Drug Agency. Written informed consent was obtained from each subject. When iron sucrose was given for the first time, the first 10–15 mL was given over 15 min (50 mL/h). If no adverse reaction was observed, the rate of administration was slowly increased to 100 mL/h. Hemoglobin, hematocrit and RBC indices were repeated on days 14, 21, 28 and at the time of delivery. Coulter hematology analyzer was used for the estimation of hemoglobin and RBC indices. Serum ferritin was measured again on day 28. The mode of delivery, gestation at delivery, and the birth weight of the newborn were noted in all cases. Data was entered in the predesigned proforma. Entire data was expressed by the descriptive statistics i.e., mean and standard deviation. For quantitative data, difference between means at subsequent weeks was measured by Student's paired t test. If p value was less than 0.05, the difference was considered to be statistically significant.

Results

After excluding women who delivered within 28 days of treatment, data was available for 45 women. The mean age of the patients was 26.45 ± 2.8 years and the mean period of gestation was 33.2 ± 1.2 weeks.

Table 2 Rise in mean haemoglobin values from baseline

Weeks	Hemoglobin (mean ± SD, g/dL)	Rise from baseline (g/dL)	p value
Day 0	7.81 ± 0.43	–	–
Day 7	7.83 ± 0.5	0.02	0.84
Day 14	8.37 ± 0.42	0.56	<0.0001
Day 21	9.25 ± 1.66	1.44	<0.0001
Day 28	9.81 ± 0.46	2.0	<0.0001
Delivery	11.24 ± 0.78	3.7	<0.0001

Table 1 Improvement in haemoglobin and RBC indices

Hematological parameters	Baseline (mean ± SD)	Day 7 (mean ± SD)	Day 14 (mean ± SD)	Day 21 (mean ± SD)	Day 28 (mean ± SD)	Delivery (mean ± SD)
Hemoglobin	7.81 ± 0.43	7.83 ± 0.5	8.37 ± 0.42	9.25 ± 1.66	9.81 ± 0.46	11.24 ± 0.78
MCV (fL)	71.98 ± 1.42	72.00 ± 1.44	73.46 ± 1.10	78.20 ± 2.41	81.00 ± 2.98	85.36 ± 3.24
MCH (pg)	23.80 ± 0.36	23.82 ± 0.42	24.00 ± 0.52	24.8 ± 0.80	25.6 ± 1.06	28.02 ± 2.41
MCHC (g/dL)	29.74 ± 0.34	29.7 ± 0.37	29.8 ± 0.50	30.24 ± 0.40	30.88 ± 0.62	32.8 ± 1.20

The mean haemoglobin level and RBC indices at the time of inclusion and their rise over 28 days till delivery have been shown in Table 1. The mean haemoglobin values was compared on days 7, 14, 21, 28 and at the time of delivery from the baseline value using Student's paired *t* test, as shown in Table 2. The earliest rise in haemoglobin was seen on day 14. There was a significant rise in the hemoglobin value from baseline on days 14, 21, 28 as well as at the time of delivery, *p* value being <0.0001. The serum ferritin rose from 10.33 ± 3.8 to 36.89 ± 5.7 ng/mL on day 28, the difference being statistically very significant, $p < 0.0001$.

The mean period of gestation at the time of delivery was 39.23 ± 1.2 weeks and the mean birth weight was 2,540 ± 180 g. There was no major side effect observed in the study and only one patient complained of shivering half an hour after the administration of the first dose which resolved on its own and didn't recur in the subsequent dosings. None of the patients in the study required blood transfusion.

Discussion

The main aim of the correction of anemia is to achieve an acceptable level of haemoglobin at the time of delivery to avoid various complications and to reduce the risk associated with blood transfusions. Parenteral iron should be considered from the second trimester onwards and during the postpartum period for women with confirmed iron deficiency who fail to respond to or are intolerant of oral iron [9]. Several authors have now reported on their experience with use of parenteral iron therapy for iron deficiency anaemia in pregnancy, with faster increases in hemoglobin and better replenishment of iron stores in comparison with oral therapy, particularly demonstrated for iron sucrose [3, 5, 8, 10].

The women approaching term require a rapid correction of anemia due to limited time period. It is generally accepted that I/V iron therapy with older preparations, like iron dextran induce a similar or slightly more rapid erythropoietic response than oral iron replacement. However, this statement may not be generalised for I/V iron sucrose treatment.

In the present study, mean rise in haemoglobin levels from the baseline on days 14, 21 and 28 was 0.56, 1.44 and 2.0 g%. The rise in haemoglobin value from the baseline was statistically very significant on days 14, 21 and 28, *p* value being <0.0001. In a previous study done in the same institution on antenatal women, mean rise in haemoglobin from the baseline on days 14 and 28 was 0.58 and 1.99 g% [4]. The RBC indices also showed a parallel rise to haemoglobin values as shown in Table 1. Ragip et al. [3] observed a significant rise of 0.6 g/dL on day 14 and a rise of 1.2 g/dL on day 28 in the I/V group. Kriplani et al. [10] noticed a haemoglobin rise of 0.26 g/dL on day 14 and 2.27 g/dL on day 28 ($p < 0.05$) and a rise in MCV of 8.76 fL on day 14 and of 12.1 fL on day 28. The earlier response in the iron sucrose group can be explained by the fact that iron sucrose consists of polynuclear iron complex analogous to ferritin, with apoferritin component replaced by sucrose which is well tolerated and least antigenic. It is available for erythropoiesis within 5 min of infusion and has a 68–97 % utilisation rate after 2–4 weeks since it is stored in reticuloendothelial cells and not in the parenchymal cells of the body [11].

The mean haemoglobin level at the time of delivery was 11.24 ± 0.78 g%, rise from the baseline value being 3.7 g%, which is quite significant (*p* value <0.0001). None of these patients required blood in the peripartum period.

The serum ferritin level is the most useful and easily available parameter for assessing iron deficiency. Levels below 15 μg/L are diagnostic of established iron deficiency [9]. A significantly greater increase in serum ferritin with parenteral administration of iron than with oral administration is important for correction of anemia, especially in patients with malnutrition and repeated pregnancies at short intervals. The adequate iron stores are also important during lactation and for future pregnancies. Ragip et al. [3] showed that the rise in serum ferritin at day 28 was 5 ± 2.2–11 ± 11 μg/L in the oral group as compared to the I/V group where serum ferritin rose from 4.1 ± 2.5 to 28 ± 26 μg/L at fourth week, *p* value <0.001. Bayoumeu et al. [8] also noticed an extremely significant difference in the ferritin levels on day 30 between the two groups with iron reserves restored only in the I/V group (*p* value <0.0001) and a significant difference was also observed at the time of delivery between the two groups, p value $= 0.01$.

The biggest advantage of iron sucrose is that unlike iron dextran, it doesn't require a test dose before administration. The reported incidence of reaction to iron sucrose is 0.002 % [12]. There was no reaction or any other major side effect observed in the study. Only one patient complaint of self limiting shivering after first dose which didn't recur in the subsequent dosages. However, the number of women in the study was not enough to establish safety of the iron sucrose.

In a metaanalysis including 75 trials and 72 studies, it was found that I/V iron preparations was associated with an increase in haemoglobin concentration as well as a reduced risk of requirement of RBC transfusion (risk ratio 0.74, 95 % confidence interval 0.62–0.88) [13]. A relatively earlier rise with iron sucrose administration can be used in patients with advanced period of gestation or approaching term gestation so that these patients have an optimum

haemoglobin levels at the time of delivery and hence blood transfusion can be avoided. Regarding I/V iron sucrose, the current guidelines released by government of India recommend to wait for the results from ongoing clinical trials [14].

Conclusion

The earliest response achieved by iron sucrose is seen on day 14 of starting the therapy and the mean rise in hemoglobin was 1.44 g/dL after 3 weeks and 2.0 g/dL after 4 weeks of treatment. Thus, it can be utilised in the patients who present at a later period of gestation with iron deficiency anemia, when oral iron therapy may not be helpful. This can avoid the need of blood transfusion in the peripartum period.

References

1. Bhatt R (1997) Maternal mortality in India—FOGSI WHO study. J Obstet Gynecol 47:207–214
2. Adamson JW (2005) Iron deficiency and other hypoproliferative anemia. In: Harrison's principles of internal medicine, 17th edn. McGraw Hill, New York, pp 586–591
3. Ragip A, Unlubilgin E, Kanderim O, Yalvac S, Cakir L, Haberal A (2005) Intravenous versus oral iron treatment of anemia in pregnancy: a randomized trial. Obstet Gynaecol 106:1335–1340
4. Gupta A, Rathore AM, Manaktala U (2013) A randomised controlled trial to compare intravenous iron sucrose and oral iron in treatment of iron deficiency anemia in pregnancy. Indian J Hematol Blood Transfus. doi:10.1007/812288-012-0224-1. Published online: Jan 2013
5. Kochhar PK, Kaundal A, Ghosh P (2013) Intravenous iron sucrose versus oral iron in treatment of iron deficiency anemia in treatment of iron deficiency anemia in pregnancy: a randomised controlled trial. J Obstet Gynecol Res 39(2):504–510
6. Yee J, Anatole B (2002) Iron Sucrose: The Oldest Iron Therapy becomes new. Am J Kidney Dis 40(6):1111–1121
7. Sharma JB, Arora BS, Kumar S, Goel S, Dhamija A (2001) Helminth and protozoan intestinal infestations: an important cause for anemia in pregnant women in Delhi. J Obstet Gynaecol India 51:58–61
8. Bayoumeu F, Subiran-Buisset C, Baka NE, Legagneur H, Monnier-Barbarino P, Laxenaire MC (2005) Iron therapy in iron deficiency anemia in pregnancy: intravenous route versus oral route. Eur J Obstet Gynecol 123:S15–S19
9. Pavord S, Myers B, Robinson S, Allard S, Strong J, Oppenheimer C, British Committee for Standards in Haematology (2012) UK guidelines on the management of iron deficiency in pregnancy. Erratum Br J Haematol 158(4):559
10. Kriplani A, Mahey R, Dash BB, Kulshreshta V, Agarwal N, Bhatla N (2013) Intravenous iron sucrose therapy for moderate to severe anemia in pregnancy. Indian J Med Res 138:78–82
11. Johnson CA (1999) Intravenous iron products. ANNA J 26:522–524
12. Silverstein SB, Rodgers GM (2004) Parenteral iron therapy options. Am J Hematol 76:74–78
13. Litton E, Xiao J, Ho KM (2013) Safety and efficacy of intravenous iron therapy in reducing requirement for allogenic blood transfusion: systemic review and metaanalysis of randomized controlled trials. BMJ 347. doi:10.1136/bmj.f4822. Published 15 Aug 2013)
14. Kalaivani K (2013) Use of intravenous iron sucrose for treatment of anemia in pregnancy. Indian J Med Res 138(1):16–17