THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

The Journal of Obstetrics and Gynecology of India (May–June 2012) 62(3):281–285
DOI 10.1007/s13224-012-0216-y

ORIGINAL ARTICLE

Assessment of Intravenous Iron Sucrose in the Management of Anemia in Gynecological and Obstetrical Practice

Dewan Bhupesh · Philipose Nisha · Balasubramanian Aarthi

Received: 27 October 2009 / Accepted: 29 May 2012 / Published online: 1 August 2012

Abstract
Objective The present study was undertaken to assess the impact of intravenous iron sucrose (Feronia IV) in the treatment of iron deficiency anemia observed in gynecological and obstetrical practice.
Methods Seventy-seven practicing gynecologists and obstetricians throughout India collaborated in the recruitment of 145 women over a period of 1 year, of which 143 were analyzable cases.
Results The overall mean rise in hemoglobin level was observed to be 2.43 gm % at the end of 4 weeks. The dose of iron sucrose administered ranged from 100 to 1,050 mg. In women who received 200 mg of the drug, and the mean Hb rise was found to be 2.21 ± 1.06 gm %. The highest observable rise in hemoglobin level was 5.5 gm % with 800 mg of iron sucrose. No serious adverse reactions were reported during the observation period.
Conclusion Intravenous Iron sucrose is a safe and effective treatment for the rapid reversal of iron deficiency anemia, in obstetric and gynecological settings.

Keywords Anemia · Iron sucrose · Hemoglobin · Pregnancy

Dewan B. (✉), Chief Medical Advisor ·
Philipose N., Clinical Research Associate ·
Balasubramanian A., Clinical Research Associate
Zuventus Healthcare Ltd, 5119 'D' Wing, Oberoi Garden Estate, Chandivilli, Mumbai 400 072, India
e-mail: Bhupesh.Dewan@zuventus.com; medico@zuventus.com

Introduction

Iron deficiency continues to be the leading single-nutrient deficiency in the world, affecting the lives of more than two billion people despite considerable efforts to decrease its prevalence [1]. When women of all ages are considered, iron deficiency remains the most frequently encountered health problem worldwide. The origins and the medical consequences of iron deficiency differ in women who are premenopausal or pregnant, who have the highest risk of iron deficiency, and in those who are postmenopausal [2]. Estimates from the World Health Organization report that from 35 to 75 % of pregnant women in developing countries and 18 % of women from industrialized countries are anemic [3]. Studies done in India have shown that among the women attending antenatal clinics, the prevalence of anemia in pregnancy is over 80 %. As reported in 2008, data from surveys carried out by various Indian organizations like the Indian Council of Medical Research also show that there has not been any decline in the prevalence of anemia in pregnancy [4].

Current knowledge indicates that iron deficiency anemia in women is a risk factor for preterm delivery and subsequent low birth weight, and possibly for inferior neonatal health. Iron supplementations are recommended in addition to prenatal vitamins in the treatment and prevention of iron deficiency anemia in pregnant women [5]. Even for women who enter pregnancy with reasonable iron stores, iron supplements improve iron status during pregnancy and for

considerable length of time during postpartum period, thus providing some protection against iron deficiency in the subsequent pregnancy [5].

In cases of severe iron deficiency anemia, oral iron therapy, although found to be a very effective way of supplementing iron, has its limitations—it does not stimulate erythropoiesis quickly and reliably enough, is required to be continued for a longer duration of time, and has many side-effects [6]. Parenteral iron, on the other hand, has been shown to be the only effective therapy to supply enough iron for erythropoiesis in cases of severe anemia [6], thereby reducing the need for blood transfusion [7]. Intravenous iron dextran, iron gluconate, and iron sucrose have been considered for the correction of iron deficiency anemia during pregnancy. Up to 30 % of patients who are given iron dextran suffer from adverse effects like arthritis, fever, urticaria and anaphylaxis. On the other hand, iron sucrose seems to be safe with low incidences of fever and other milder, self-limiting side-effects [8]. Cases of extensive liver necrosis have been reported with iron gluconate [9]. Because of these drawbacks—coupled with the availability of a safer intravenous iron-bearing agent like iron sucrose—iron dextran and iron gluconate, owing to their life-threatening side effects, are used hesitantly and judiciously with caution, whereas the confidence on using iron sucrose in the clinical practice is growing at much faster rate. This may be because clinical data on intravenous iron therapy during pregnancy primarily deal with intravenous iron sucrose [8, 10].

The present post-marketing surveillance study has been undertaken to assess the impact of intravenous iron sucrose in the treatment of pregnancy-induced anemia, and other types of anemia observed in gynecological and obstetrical practice by observing the improvement in hemoglobin (Hb) levels.

Materials and Methods

This post-marketing surveillance study was an open, multicentric, observational survey carried out among 77 practicing gynecologists and obstetricians from across 18 different states of India. The study was carried out from April 2008 to April 2009. The required medications to initiate the therapy (eight ampoules of iron sucrose containing 50 mg elemental iron, each), the prescribing information, dosage guidelines, and two case report forms were provided to each of the practitioners by Zuventus Healthcare Limited. All therapeutic decisions were determined solely by the attending practitioner.

An advice to use minimum of 200 mg of iron sucrose (equivalent to four ampoules of Feronia IV) was given to the medical practitioners. The formula to assist the practitioner in calculating the required dose of iron sucrose for each individual woman, as stated in the dosage guideline was provided along with the medications is as follows:

$$\text{Iron requirement (mg)} = \text{Body weight (kg)} \times (\text{Target Hb in gm\%} - \text{Actual Hb in gm\%}) \times 2.4$$

In addition, 500 mg of elemental iron was to be administered, in case of chronic anemia, to build up the iron stores in the body [7].

Each practitioner had to complete the case report forms pertaining to individual woman's therapy outcome, including the rise in hemoglobin level from the baseline up to 4 weeks after initiation of therapy. Data collection was undertaken by the company representatives, who then submitted them to the medical department of Zuventus Healthcare Ltd.

Student's *t* test was used to compare the rise in hemoglobin level of the women after therapy with iron sucrose, and a value of less than 0.05 was considered to be statistically significant. Descriptive subgroup analysis was also performed after classifying the women based on the severity of anemia as per the WHO guidelines [11] into the following groups:

1. Mild anemia (Hb 10–10.9 g/dL)
2. Moderate anemia (Hb 7–9.9 g/dL)
3. Severe anemia (Hb less than 7 g/dL)

Results

A total of 145 case report forms were returned by the practitioners. Appropriately filled CRFs with valid entries were available for 143 women representing the study population.

Demographic Data

The demographic data of 143 women assessed during the study are shown in Table 1. The mean age of the study population was 28.38 ± 7.07 years (SD) with a range from 20 to 76 years. As per the WHO classification for severity of anemia, 61.54 % of study population represented moderate anemia, while 38.46 % had severe anemia. The entire study population was further divided into pregnant women with anemia and anemia associated with conditions other than pregnancy.

Anemia Associated with Pregnancy

Out of the 143 women, 118 were diagnosed as anemia associated with pregnancy. Among these women 17 (14.41 %), 34 (28.81 %), 37 (31.36 %) were in the first,

Table 1 Demographic data of the study population

	Total $N = 143$	Pregnant women $N = 118$	Women with other conditions $N = 25$
Age (Years)			
Mean ± SD	28.38 ± 7.07	27.06 ± 4.73	35.35 ± 11.95
Range	20–76	20–41	22–76
Severity of anemia			
Moderate	88 (61.54 %)	75 (63.56 %)	13 (52 %)
Range (gm %)	7–9.8	7–9.8	7–9
Severe	55 (38.46 %)	43 (36.44 %)	12 (48 %)
Range (gm %)	3–6.9	3.2–6.9	3–6.9

second, and third trimesters, respectively, whereas 25.42 % did not disclose the trimester status of their pregnancy.

Anemia Associated with Conditions other than Pregnancy

Among the 143 women, 25 were diagnosed to have anemia associated with conditions other than pregnancy. 48 % ($n = 12$) of these women had severe chronic iron deficiency anemia while others had associated conditions responsible for causing anemia. The associated conditions were post-partum hemorrhage (4 %), uterine fibroids (20 %), dysfunctional bleeding (4 %), tubercular endometritis with metromenorrhagia (4 %), menorrhagia (16 %), and incomplete abortion (4 %).

Efficacy Assessment

There was an overall rise in hemoglobin level from baseline of 6.90–9.33 gm % after 30 days, depicting a mean rise of 2.43 gm %. The highest rise in hemoglobin level with the use of iron sucrose was 5.5 gm % in three patients. A rise of

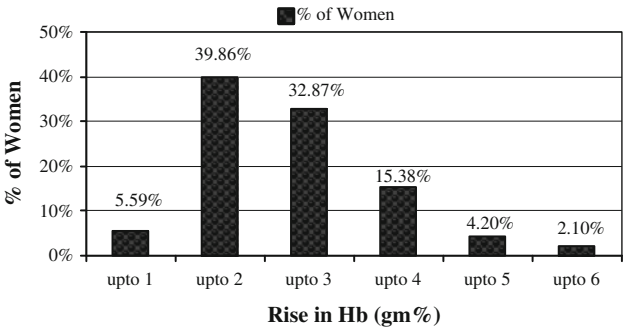

Fig. 1 Rise in Hb levels in the study population

6 gm % Hb was also observed in one patient, which, however, was in conjunction with three units of blood transfusion. The changes in Hb levels in the overall study population are tabulated in Table 2. The overall rise in Hb level after 30 days of treatment was found to be statistically significant in all the groups with P value less than 0.0001. The Hb rise in the study population is depicted in Fig. 1.

Hb Rise Versus Dose of Iron Sucrose Used

A correlation based on the dose of iron sucrose used and the corresponding mean rise in Hb is given in Table 3. Use of 800 mg and above of iron sucrose was associated with a mean Hb rise of 3.27 gm %. A single dose of 200 mg of iron sucrose was administered to 71 pregnant women, in whom the mean rise in Hb was 2.05 gm %. The rise in Hb level in pregnant women taking 200 mg of iron sucrose as per the trimester of pregnancy is given in Table 4.

Safety Assessment

Use of iron sucrose showed infrequent, self-limited side-effects in up to 4.19 % of the total study population.

Table 2 Change in hemoglobin level before and after treatment

Category	Sub-category	N	Hb at baseline (gm %)		Hb at follow up (gm %)		Rise in Hb (gm %)	
			Mean ± SD	Range of Hb	Mean ± SD	Range of Hb	Mean ± SD	Range of Hb
Women with anemia	Total	143	6.90 ± 1.40	3–9.8	9.33 ± 1.49	5–12.5	2.43 ± 1.07[a]	0.5–6
	Pregnant	118	6.98 ± 1.35	3.2–9.8	9.28 ± 1.45	5–12.5	2.31 ± 1.00[a]	0.5–5.05
	First trimester	17	6.75 ± 1.25	4–8.20	9.10 ± 1.31	7–11.6	2.35 ± 1.13[a]	0.8–5
	Second trimester	34	7.34 ± 1.40	4.1–9.8	9.67 ± 1.15	6.8–12.5	2.33 ± 1.25[a]	0.5–5.05
	Third trimester	37	7.07 ± 1.40	3.20–9.20	9.36 ± 1.72	5–12.40	2.29 ± 0.84[a]	1–4
	Other than pregnancy	25	6.52 ± 1.62	3–9	9.53 ± 1.70	5–12	3.02 ± 1.21[a]	0.9–6
Severity of anemia	Moderate	88	7.78 ± 0.65	7–9.8	10.04 ± 0.94	8.2–12.5	2.25 ± 0.92[a]	0.5–5
	Severe	55	5.48 ± 1.07	1.07–6.9	8.19 ± 1.52	1.5–11.5	2.71 ± 1.22[a]	0.9–6
Con-comitant medication	With oral iron	26	7.22 ± 1.13	3.3–8.9	9.43 ± 1.30	5.5–11.8	2.21 ± 0.9[a]	0.6–3.9
	Without oral iron	117	6.83 ± 1.45	4–9.8	9.30 ± 1.53	7–12.5	2.48 ± 1.10[a]	1.2–5.5

[a] P value < 0.0001

Table 3 Correlation between the dosage of iron sucrose used and the rise in Hb level

Dosage used (mg)	*N*	Rise in Hb (gm %) [Mean ± SD]
Up to 200	92	2.21 ± 1.06
300–800	41	2.74 ± 0.97
Above 800	6	3.27 ± 1.07

The reported side-effects were pain at the site of injection (1.4 %), nausea (2.1 %) and fever (0.7 %).

Concomitant Therapy

The concomitant medication groups taken by the patients are shown in Fig. 2. Administration of vitamins, minerals, and protein supplements were common among pregnant women.

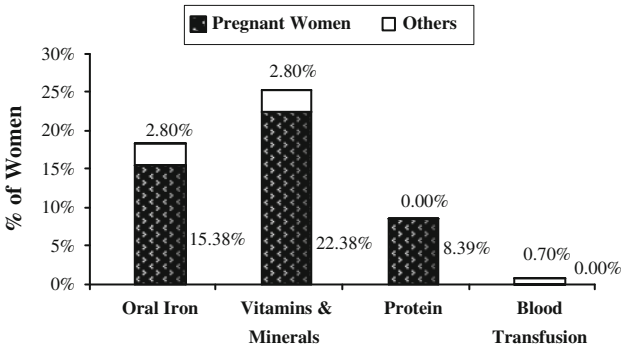

Fig. 2 Concomitant treatment used in the study population

Discussion

This post-marketing surveillance study was initialized to monitor the rise in hemoglobin level in women with iron deficiency anemia. The observed study population included anemic women who were either pregnant or had medical conditions other than pregnancy, attending the gynecologists' clinic. The study clearly illustrates that intravenous iron sucrose complex is effective in significantly raising the hemoglobin (Hb) level in anemic women. Depending on the selected total dose, Hb increases between 0.5 and 6 gm % were observed after 4 weeks. The rapid and profound response can be directly attributed to the high amount of iron that could be delivered directly to the hemopoietic tissues which in turn restores iron reserves. Previous studies of iron sucrose administration in pregnant women found a mean rise in Hb between 1.51 and 5.3 gm % [8, 10]. Our study observed a similar rise in Hb ranging from 0.5 to 5.05 gm % in pregnant women. Iron supplementation is generally not recommended during the first trimester of pregnancy, but in this study, it was found that 14.41 % of the pregnant women were in their first trimester of pregnancy. The rise in hemoglobin in this group of patients was found to be 2.53 ± 1.13 gm % from baseline of 6.75 ± 1.25 to 9.10 ± 1.31 gm % after 1 month of iron sucrose treatment.

The statistically significant increase in hemoglobin levels observed even in women with other gynecological conditions, paves the way for other potential indications, such as anemia discovered late in the pregnancy or in patients who have low iron reserves and present a risk of hemorrhage during peripartum, such as in multiple pregnancy or over distention of the uterus, in the hope of avoiding a transfusion.

During our observation mild side-effects were observed only in 4.19 % of the study population, while no serious adverse reactions were reported. The literature documents that intravenous iron sucrose is reasonably well tolerated (35 % of patients have mild side effects) with a low incidence of serious adverse reactions (0.03–0.04 %) [12].

In conclusion, our post-marketing experience reinforces the observations made in the previously conducted studies about Iron sucrose being a safe and effective therapy in the rapid reversal of iron deficiency anemia in obstetric and gynecological settings, especially in iron-deficient women who are unable to obtain an adequate rise in hemoglobin rapidly by the oral iron supplementation.

Table 4 Changes in Hb level in pregnant women taking a dose of 200 mg of iron sucrose

Trimester of pregnancy	*N*	Hb at baseline (gm %)		Hb at follow up (gm %)		Rise in Hb (gm %)	
		Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range
All	71	7.09 ± 1.34	3.2–9.74	9.14 ± 1.40	5–12.5	2.05 ± 0.99	0.5–5.05
First	10	7.14 ± 1.08	5–8.2	9.11 ± 1.10	7.3–11	1.97 ± 1.25	0.8–5
Second	22	7.34 ± 1.43	4.1–8	9.56 ± 1.06	7.5–12.5	2.22 ± 1.36	0.6–5.05
Third	25	7.06 ± 1.49	3.9–9.2	9.02 ± 1.70	5.2–10.5	1.96 ± 0.59	1.3–3
Not stated	14	6.71 ± 1.08	4.10–8	8.70 ± 1.43	6–11.2	1.99 ± 0.73	1.2–4.2

Acknowledgment The authors would like to thank the Group Product Manager, Mrs. Dolanchapa Bastya, for the managerial and logistic support offered. The authors also gratefully acknowledge the active participation of the doctors in the ASHA trial.

References

1. Beard JL. Effectiveness and strategies of iron supplementation during pregnancy. Am J Clin Nutr. 2000;71:1288S–94S.
2. Baker WF Jr. Iron deficiency in pregnancy, obstetrics, and gynaecology. Haematol Oncol Clin N Am. 2000;14:1061–77.
3. Allen LH. Anaemia and iron deficiency: effects on pregnancy outcome. Am J Clin Nutr. 2000;71:1280S–4S.
4. Sharma A, Patnaik R, Garg S, et al. Detection and management of anaemia in pregnancy in an urban primary health care institution. Indian J Med Res. 2008;128:45–51.
5. American College of Obstetricians and Gynaecologists (ACOG). Anaemia in pregnancy. Washington (DC): American College of Obstetricians and Gynaecologists (ACOG); 2008. p. 7 (ACOG practice bulletin; no. 95).
6. Kumar A, Jain S, Singh NP, et al. Oral versus high dose parenteral iron supplementation in pregnancy. Intl J Gynaec Obstet. 2005;89:7–13.
7. Bashiri A, Burstein E, Sheiner, et al. Anaemia during pregnancy and treatment with intravenous iron: review of the literature. Eur J Obstet Gynaecol Reprod Biol. 2003;110:2–7.
8. al-Momen AK, al-Meshari A, al-Nuaim L, et al. Intravenous iron sucrose complex in the treatment of iron deficiency anaemia during pregnancy. Eur J Obstet Gynaecol Reprod Biol. 1996;69:121–4.
9. Perewusnyk G, Huch R, Huch A, et al. Parenteral iron therapy in obstetrics: 8 years experience with iron-sucrose complex. Br J Nutr. 2002;88:3–10.
10. Bayoumeu F, Subiran-Buisset C, Baka NE, et al. Iron therapy in iron deficiency anaemia in pregnancy: intravenous route versus oral route. Am J Obstet Gynaecol. 2002;186:518–22.
11. Reveiz L, Gyte GM, Cuervo LG. Treatments for iron-deficiency anaemia in pregnancy. Cochrane Database Syst Rev. 2007; CD003094.
12. Goddard AF, James MW, McIntyre AS, et al. Guidelines for the management of iron deficiency anaemia. Br Soc Gastroenterol. 2005; 1–6. http://www.bsg.org.uk/pdf_word_docs/iron_def.pdf. Accessed 9 July 2005.