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ARTICLE

Assessment of intravenous iron sucrose in the management of anemia in gynecological and obstetrical practice

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ABSTRACT

Keywords:

Anemia,
Iron Sucrose,
Hemoglobin,
Pregnancy.

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:** 77 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 mg to 1050 mg. In women who received 200 mg of the drug, the mean Hb rise was found to be 2.21 ± 1.06 gm%. 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.

Introduction

Iron deficiency continues to be the leading single-nutrient deficiency in the world, affecting the lives of more than 2 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 anaemic [3]. Indian studies have shown that in women attending antenatal clinics, the prevalence of anaemia 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 anaemia in pregnancy [4].

Current knowledge indicates that iron deficiency anaemia 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 anaemia 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 anaemia, 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 anaemia [6] thereby reducing the need for blood transfusion [7].

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Intravenous iron dextran, iron gluconate and iron sucrose have been considered for the correction of iron-deficiency anaemia 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 agent like iron sucrose; iron dextran and iron gluconate due to life threatening side effects are used hesitantly, whereas more confidence is building up on using iron sucrose in the clinical practice. This may be due to the fact that 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 anaemia, and other types of anaemia 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, multi-centric, 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 (8 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 200mg 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 anaemia, 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 four 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 anaemia as per the WHO guidelines [11] into the following groups:

1. Mild anaemia (Hb 10 to 10.9 g/dL)
2. Moderate anaemia (Hb 7 to 9.9 g/dL)
3. Severe anaemia (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 $28.38 \pm$ (SD) 7.07 years with a range from 20 to 76 years. As per the WHO classification for severity of anaemia, 61.54% of study population represented moderate anaemia while 38.46% had severe anaemia. The entire study population was further divided into pregnant women with anaemia and anaemia associated with conditions other than pregnancy.

Anaemia associated with pregnancy

Out of the 143 women, 118 were diagnosed as anaemia associated with pregnancy. Among these women 17 (14.41%), 34 (28.81%), 37 (31.36%) were in the first, second and third trimesters respectively, whereas 25.42% did not state the trimester of their pregnancy.

Anaemia associated with conditions other than pregnancy

Among the 143 women, 25 were diagnosed to have anaemia

Table 1: Demographic data of the study population.

		Total	Pregnant Women	Women with other conditions
		N=143	N=118	N=25
Age(Years)	Mean \pm SD	28.38 \pm 7.07	27.06 \pm 4.73	35.35 \pm 11.95
	Range	20-76	20-41	22-76
Severity of anaemia	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

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 \pm SD	Range of Hb	Mean \pm SD	Range of Hb	Mean \pm SD	Range of Hb
Women	Total	143	6.90 \pm 1.40	3-9.8	9.33 \pm 1.49	5-12.5	2.43 \pm 1.07 ^a	0.5-6
with Anaemia	Pregnant	118	6.98 \pm 1.35	3.2-9.8	9.28 \pm 1.45	5-12.5	2.31 \pm 1.00 ^a	0.5-5.05
	1 st Trimester	17	6.75 \pm 1.25	4 - 8.20	9.10 \pm 1.31	7-11.6	2.35 \pm 1.13 ^a	0.8 - 5
	2 nd Trimester	34	7.34 \pm 1.40	4.1 - 9.8	9.67 \pm 1.15	6.8 - 12.5	2.33 \pm 1.25 ^a	0.5-5.05
	3 rd Trimester	37	7.07 \pm 1.40	3.20 - 9.20	9.36 \pm 1.72	5 - 12.40	2.29 \pm 0.84 ^a	1 - 4
	Other than pregnancy	25	6.52 \pm 1.62	3-9	9.53 \pm 1.70	5-12	3.02 \pm 1.21 ^a	0.9-6
Severity of Anaemia	Moderate	88	7.78 \pm 0.65	7-9.8	10.04 \pm 0.94	8.2-12.5	2.25 \pm 0.92 ^a	0.5-5
	Severe	55	5.48 \pm 1.07	1.07-6.9	8.19 \pm 1.52	1.5-11.5	2.71 \pm 1.22 ^a	0.9-6
Con-comitant Medication	With Oral Iron	26	7.22 \pm 1.13	3.3-8.9	9.43 \pm 1.30	5.5-11.8	2.21 \pm 0.9 ^a	0.6-3.9
	Without Oral Iron	117	6.83 \pm 1.45	4-9.8	9.30 \pm 1.53	7-12.5	2.48 \pm 1.10 ^a	1.2-5.5

^ap value < 0.0001

associated with conditions other than pregnancy. Also, 48% (n=12) of these women had severe chronic iron deficiency anaemia while others had associated conditions responsible for causing anaemia. 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 gm% to 9.33 gm% after 30 days, depicting a mean rise of 2.43 gm%. Highest rise in hemoglobin level with the use of iron sucrose was 5.5 gm% in 3 patients. A rise of 6 gm% Hb was also observed in one patient, which however was in conjunction with 3 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 Figure 1.

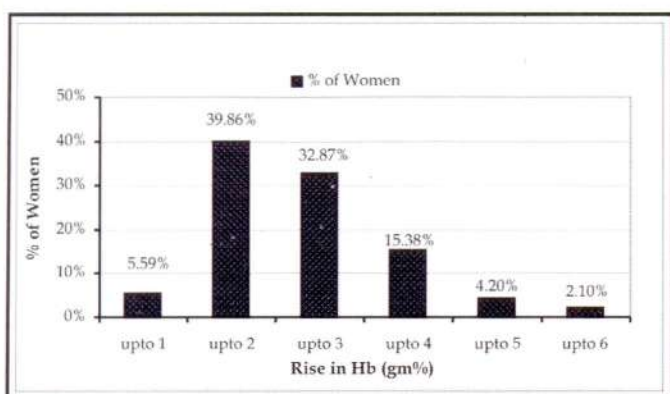


Figure 1. Rise in Hb levels in the study population.

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. 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 figure 2. Administration of vitamins, minerals and protein supplements were common among pregnant women.

Discussion

This post-marketing surveillance study was initialized to

Table 3: Correlation between the Dosage of Iron Sucrose used and the rise in Hb level.

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

Table 4: Changes in Hb level in pregnant women taking a dose of 200mg of Iron Sucrose.

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

monitor the rise in hemoglobin level in women with iron deficiency anaemia. The observed study population included anaemic 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 anaemic 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 in pregnant women found a mean rise in Hb between 1.51 to 5.3 gm% [8,10]. Our study observed a similar rise in Hb ranging from 0.5-5.05 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 gm% to 9.10 ± 1.31 gm% after one 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 anaemia 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 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. 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 in previously conducted studies about Iron sucrose being a safe and effective therapy in the rapid reversal of iron-deficiency anaemia 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.

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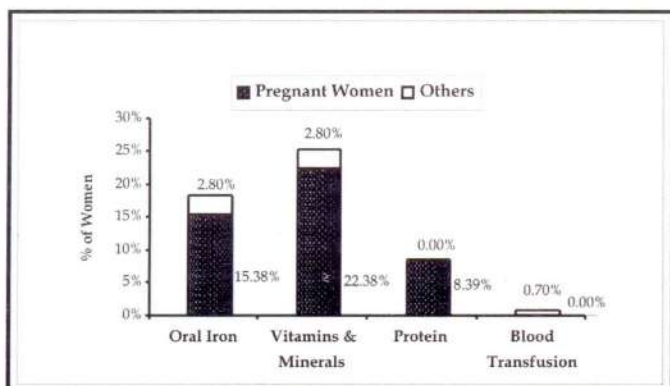


Figure 2. Concomitant treatment used in the study population.

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Pattnaik, Cuttack: Dr. Sunita Kale, K.Nagar: Dr. Sunita Khare, Delhi: Dr. Sunita SK, Mysore: Dr. V.S. Sukhiya, Nagpur: Dr. Varsha Parekar, Mumbai: Dr. Veena Laroia, Delhi: Dr. Zeenat Zaman, Islampur: Dr. Hiten Kalita, Assam.

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