Research Article

A prospective study of adverse effects and compliance of intravenous iron sucrose for the treatment of severe anemia in ante- and post-natal women

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ABSTRACT

Background: Anemia is a leading cause of maternal death in the world. About half of it occur in southeast Asia and among them, 80% occur in India. Nowadays, intravenous (IV) iron sucrose is started for the therapy of severe anemia. **Objective:** This study was done to evaluate the adverse effect and compliance of IV iron sucrose injections in ante- and post-natal women. **Materials and Methods:** Totally 406 patients having hemoglobin between 4 and 7 g/dL were included in the study. IV iron sucrose was started as per the national guidelines. At every follow-up visit, patients were examined and asked about adverse effects. The number of patients lost to follow-up was recorded, and the patients were contacted on phone about adverse effects. Recorded data were entered in MS Excel 2016. Chi-square test was used for analysis, and the results were published as percentage. **Results:** The most common adverse effect experienced by women was swelling at injection site (8.87%) followed by muscle/joint pain (2.7%) and pruritus (2.7%). Anaphylaxis was observed in <0.5% of the patients. Multiparous women and postnatal women were less compliant to treatment. **Conclusion:** IV iron sucrose is very safe, and the adverse effects are minimal. Compliance is less in multipara and postnatal women as compared to primipara women. Hence, proper counseling is needed mainly for multipara and postnatal women to improve their compliance to treatment.

KEY WORDS: Iron Deficiency Anemia; Iron Sucrose; Compliance; Adverse Effects

INTRODUCTION

Anemia is a condition in which the number of red blood cells or their oxygen-carrying capacity is insufficient to meet physiologic needs, which vary by age, sex, altitude, smoking, and pregnancy status. There are various form of anemia. Among them, iron deficiency anemia is the most common.[1] Its prevalence is almost 20-50% in the world.[2] The prevalence of anemia in India is the highest in the world.[3]

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Anemia is an important risk factor for pregnancy. The causes for anemia in pregnancy include increased demand during pregnancy, poor diet, repeated pregnancies, and pre-existing anemia.[4] TheWHO defines anemia as hemoglobin (Hb) level <11 g% and hematocrit level <33% in pregnancy.[5] It is also one of the most common reasons for maternal death in the world.[6] In Southeast Asian countries, anemia contributes about half of the maternal deaths in the world and 80% of it occur in India.[7] In Gujarat, 60.8% of the pregnant women are anemic and 3.8% have severe anemia.[8]

Early detection and proper management of iron deficiency anemia can lead to substantial reduction in preterm labor, pre-eclampsia, infection, hemorrhage, intrauterine growth restriction, low birth weight, undernutrition in childhood and adolescent, and improvement in adult height. Thus, it can lead to decrease in maternal mortality ratio and infant mortality rate.[9]

The provision of iron supplements to women is one of the most widely practiced public health measures. If anemia occurs even after applying these measures, the traditional treatment includes oral iron, parentral iron, and blood transfusion.[9] Among them, oral iron is associated with side effects, non-compliance, and takes a long time to correct anemia and many times poor compliance by patients. The second option is preparation such as iron dextran and iron sorbitol which are administered parenterally. They are associated with anaphylactic reactions. The third and last option is blood transfusion. It is associated with cross-reactions and viral infections and also not possible at primary health centers and community health center (CHC) level where blood bank is not available.[9]

On the other hand, an alternate therapeutic agent such as intravenous (IV) iron sucrose which is used to treat anemia due to chronic renal failure in the USA from decades has very less side effects.[10] It can be used for the rapid correction of anemia or restoring iron stores. Because of these advantages, iron sucrose is used to treat maternal anemia in Middle Eastern countries in the last decade.[11] After watching its success, few years ago, the Government of India had decided to start iron sucrose IV infusion to treat the iron deficiency anemia in pregnant women.[12]

As iron sucrose is started only few years ago in India, the information about compliance of patients about it is not much explored. In the same way, not many researches are available about its adverse effect in pregnant and postnatal women with a large sample size, so this study was chosen with a view to check compliance of patients and any adverse effect.

Objective

This study was conducted with an objective to determine an iron sucrose compliance and safety in the treatment of iron deficiency anemia in ante- and post-natal women.

MATERIALS AND METHODS

This prospective study was carried out at CHC, Prantij, Gujarat, from August 2015 to July 2016. All pregnant and postnatal women who came to obstetric clinic having Hb between 4 and 7 g/dL were included in the study. Totally 438 patients attended the clinic during the study period. Patients not giving consent, having any known hematological disease other than iron deficiency anemia, known hypersensitivity to iron, history or need of blood transfusion, and history of chronic medical disorders were excluded from the study. Hence, a total of 406 patients were included in the study.

Before beginning the therapy, patients' phone numbers were recorded and a tablet of albendazole (400 mg) was given to each patient.

Patients' Hb assessment was carried out before enrollment. Dose of IV iron sucrose was calculated by formula given below:

"Total iron dose (in mg): {2.4 × body weight in kg × Hb% deficient (11-actual Hb%)} + 500"

The total dose of iron sucrose in mg was given in divided doses on alternate days up to 3 times a week. About 200 mg iron sucrose was diluted in 100 ml of isotonic sodium chloride solution (normal saline) to be given over a period of half an hour during each dose. Patients were monitored for half an hour after every infusion for any adverse effect. Test dose was not given, but anaphylactic kit was kept ready.

Follow-ups were done after 1 week and after 2 weeks of treatment. The number of patients not coming to follow-up were recorded. They were contacted on phone and the reason for not coming was found.

Statistical analysis

The recorded data were analyzed by MS Excel 2016, and results were published in percentages used Chi-square test.

RESULTS

Among the total 406 pregnant women who participated in the study, majority (50%) were in the age group of 20-25 years. Women from general caste comprised 77.3%. Gravidity-wise distribution shows that 32% of the women were having second gravida followed by 29.1% of the women who were in the first gravida (Table 1).

Table 1: Distribution of study participants according to age, caste, and gravidity

	Number of participants (*n*=406)	Percentage
Age group		
18-20	56	13.8
20-25	203	50.0
26-30	111	27.3
30-35	31	07.6
Caste		
Gen	314	77.3
SC	69	17.0
ST	22	05.4
Gravidity		
1st	118	29.1
2nd	130	32.0
≥3	106	26.1
PNC	52	12.8

PNC: Postnatal Care

The most common adverse effect experienced by women was swelling at injection site (8.87%) followed by muscle/joint pain (2.7%) and pruritus (2.7%). About half of the swelling at injection site (4%) were because of rapid infusion or misplaced (not in vein) IV catheter/needle by sisters. Anaphylaxis was observed in only two patients which is <0.5%. Adverse effects were less at the time of subsequent doses (Table 2).

Higher percentage of multipara women (65.7%) interrupted iron sucrose treatment between 3 and 6 doses which is statistically significant (Table 3).

DISCUSSION

Mean age of the study participants was 24.3 ± 3.81 years. Gastrointestinal tract (GIT) adverse effects (nausea, vomiting, and diarrhea) were not experienced by any of the study participants. Incidence of some adverse effects such as blurring of vision, vertigo, muscle pain/joint pain, pruritus, and anaphylaxis decreased on subsequent doses, while the incidence of swelling at injection site and delayed hypersensitivity increased. Out of the 406 participants, 226 (55.66%) interrupted treatment between 3 and 6 doses while 102 (25.12%) received complete six doses.

In a study conducted by Patel et al. in 110 antenatal and postnatal women, 89 (80.73%) women did not experience any adverse effect after taking required doses of IV iron sucrose.[12] Uma et al. in their study of 36 pregnant women observed minor side effects in few cases (pain at injection site- one, metallic taste- three, headache- one, and warm tingling sensation-two cases) while majority of the patients were free of side effects (80.56%).[5] A study of safety and efficacy of iron sucrose in 76 pregnant women carried out by Huilgol et al. reported minimal adverse effects with only two patients complained of pain at the injection site and only one had rigor.[4] Our study also shows similar results demonstrating no adverse effects in 80.54% women after the 1st dose and in 83.49% women after subsequent doses.

Perewunsnyk et al. studied 400 women who received a total of 2000 ampoules of iron sucrose. Minor general adverse effects including a metallic taste, flushing of the face, and burning at the injection site occurred in 0.5% of the cases.[13] The high tolerance of the drug has been partly attributed to slow release of iron from the complex and also due to the low allergenicity of sucrose. Till date, one death has been reported with IV iron sucrose injection.[14] The explanation given for this was because of very slow infusion (1-2 h). The cause of death may be free radicals released from the iron sucrose. The injection should be given within 15-20 min or up to 200 mg can be given as slow IV push over 2-3 min.

This study involved 406 ante- and post-natal women, so sample size was adequate. Pre-treatment with antihelminthic could rule out worm infestation in all participants. IV iron sucrose was given in CHC where regular monitoring of adverse effects was carried out by on-duty medical staff.

IV iron sucrose becomes the therapeutic mainstay for severely iron-deficient mothers when they are unable to take oral preparations.[15] In practice, physician often face poor compliance, justified by digestive side effects leading to worsening of anemia. In these cases, parenteral iron sucrose of administration is indicated.[16] Many of the pregnant women who are anemic do not tolerate oral iron or have adverse effects with other parenteral iron preparations. Blood transfusion for the management of anemia in pregnancy has many problems such as availability, spread of infection, cost, and blood transfusion reactions.[17] In this context, iron sucrose has a very important role because of its efficacy and safety. The cost of iron sucrose compared with other modalities of treatment is affordable. Iron sucrose therapy

Table 2: Adverse effects felt by participants

Adverse effect	After 1st dose (*n* =406)	After subsequent doses (*n*=406)
GIT effect	0	0
Nausea		
Vomiting		
Dyspepsia		
Constipation	00	00
Diarrhea	00	00
Blurred vision	03	01
Vertigo	11	07
Muscle pain/joint pain	14	08
Swelling at injection site	35	37
Pruritus	14	08
Anaphylaxis	02	0
Delayed hypersensitivity	0	06

GIT: Gastrointestinal tract

Table 3: Number of participants interrupt the treatment before completion

	Primigravida	Multigravida	Postnatal	Total
Stop before 3 doses	06	20	42	68
Stop between 3 and 6 doses	71	155	10	226
Received 6 doses	41	61	00	102
Total	118	236	52	406

Chi-square=179.87, df=4, *P*<0.01

in the treatment of anemia in pregnancy reduces maternal mortality and morbidity to a significant level.

Recommendation

IV iron sucrose should be used for moderate-to-severe anemia without any fear of side effect if not contraindicated. Multigravida patients and postnatal women should be properly counseled about the need of iron and effects of anemia to improve their compliance and follow-up.

CONCLUSION

IV iron sucrose is safe and has minimal rate of side effects. It is also well tolerated by patients. One important finding is that women with 1st gravidity are more conscious as compared to multi- and post-natal for complete therapy and follow-up.

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