# Parenteral Iron Sucrose Therapy for Moderate and Severe Iron-Deficiency Anemia in Pregnancy

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**ABSTRACT**

**OBJECTIVE:** In this study, we aimed to analyze the effectiveness of parenteral iron sucrose use in our pregnant patient population.

**STUDY DESIGN:** The medical records of all anemic pregnant patients hospitalized at our tertiary hospital for parenteral iron sucrose therapy were reviewed retrospectively between January 2014 and April 2015. Paired samples t-test was used for comparing means of continuous variables.

**RESULTS:** The results of 117 pregnant women (1.3% of anemic patients) were available for the analysis. Four (3.4%) patients had severe and 113 (96.6%) patients had moderate anemia. The median gestational age for iron sucrose administration was 31.1 weeks (26.8-34.3). The mean hemoglobin, hematocrit and ferritin levels before and after delivery were 10.8±1.3 gr/l; 9.9±1.3 gr/l, 33.5±4.0; 30.8±4.0 and 89.6±0.7 µg/L; 98.1±0.9 µg/L, respectively. All but two (1.8%) patients had elevated hemoglobin levels after iron sucrose therapy. When hemoglobin and hematocrit levels were compared between before iron sucrose therapy and before delivery, there was a 2.8 g/l and 7.8% increase in the mean hemoglobin and hematocrit levels, respectively and this difference was statistically significant (p=0.000 and p=0.000, respectively). No severe or life-threatening hypersensitivity reaction was reported.

**CONCLUSION:** In this study, we found out that intravenous iron sucrose therapy for iron deficiency anemia is feasible, effective and has a good safety profile.

**Keywords:** Iron deficiency anemia, Pregnancy, Oral iron, Iron sucrose

***Gynecol Obstet Reprod Med 2016;22(3) 125-128 DOI:10.21613/GORM.2016.501***

## Introduction

Anemia is defined as a decrease in the amount of red blood cells (RBC) or hemoglobin levels. Although pregnancy itself is associated with a modest decrease in hemoglobin levels (i.e., dilutional anemia of pregnancy), in pregnancy, hemoglobin levels below 11 gr/dL in the first and third trimesters and below 10.5 gr/dL in the second trimester is defined as frank anemia by the Centers for Disease Control and Prevention (CDC) (1). Iron-deficiency is the major cause of anemia and prevention and treatment of iron-deficiency anemia is critically important.

Oral iron treatment for iron-deficiency anemia is considered as the first line treatment in pregnancy. It is inexpensive and effective unless irregularly taken; however, patients' compliance with oral iron therapy is frequently low due to poor tolerability and necessity of a long lasting treatment (2). Parenteral iron therapy is gaining popularity among low tolerant patients due to its fast and effective action (3,4).

In this study, we aimed to analyze the effectiveness of parenteral iron sucrose use in our pregnant patient population.

## Material and Method

This is a retrospective analysis of anemic pregnant patients who were treated with parenteral iron sucrose (Venofer, Vifor International Inc., St. Gallen, Switzerland) at Etlik Zubeyde Hanim Womens' Health and Teaching Hospital. The Institutional Review Board approved the study. The medical records of anemic pregnant patients, who received parenteral iron sucrose therapy between January 2014 and April 2015, were reviewed by two researchers (SE and BY).

In our study, iron-deficiency anemia was diagnosed when the hemoglobin level was below 11 gr/dL in the first and third trimesters or below 10.5 gr/dL in the second trimester; mean cell volume was lower than 75 fl and the serum ferritin level was lower than 30 ng/mL in the absence of the other causes of anemia. Pregnant patients with hemoglobin levels of 6-11 gr/dL were included in the study if the anemia was iron deficiency anemia and the patient was either intolerant or did not respond to oral iron therapy despite regular use. Patients having iron-de-

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*Submitted for Publication:* *14.10.2016*
*Accepted for Publication:* *20.10.2016*

ficiency anemia with hemoglobin levels below 6 gr/dL or symptomatic (severe fatigue, palpitations, tachycardia, shortness of breath) patients with hemoglobin levels greater than 6 gr/dL were candidates for RBC transfusion and those were excluded. After informed consent for intravenous iron therapy was taken, the patients were hospitalized. The iron sucrose dosage was calculated according to the following formula:

Total iron deficit [mg] = body weight [kg] x [target Hb (usually taken as 11 gr/dL)-actual Hb] [g/dL] x 2.4 + depot iron (usually taken as 500) [mg] (5).

The total amount of iron sucrose to be administered (in mL) was calculated by total iron deficit (mg) divided by 20 mg/mL.

Iron sucrose was diluted only in sterile 0.9% sodium chloride solution as 100 mg iron (5 ml iron sucrose) in maximum 100 ml sterile 0.9% sodium chloride solution and for stability reasons, dilutions to lower iron sucrose concentrations was not allowed. As infusion, maximum tolerated single dose per day given, not more than once per week was: 500 mg iron (25 ml iron sucrose) in at least 3 ½ hours for patients above 70 kg and 7 mg iron / kg body weight in at least 3 ½ hours for patients of 70 kg and below. If the total dose to be administered was greater than the maximum tolerated single dose per day, the remaining dose was administered one week later.

Various data were extracted from the medical charts of the women. Demographic and patient characteristics, past obstetrical history and recent pregnancy characteristics were recorded. Statistical analysis was performed with the SPSS (version 13.0 for Windows; SPSS, Chicago, IL, USA). Distribution of the variables was tested with one-sample Kolmogorov-Smirnov test. Descriptive statistics for parametric variables and nonparametric variables were expressed as mean ± standard deviation and median (interquartile range), respectively. Paired samples was used for comparing means of continuous variables. In order to investigate the effect of iron sucrose therapy on hemoglobin and hematocrit levels, levels before iron sucrose administration and before delivery was chosen to see temporal changes. Statistical tests were considered significant at the 95% level.

## Results

The demographics of the study is presented in table 1. During the study period, the prevalence of iron deficiency anemia in our high-risk pregnant patient population was 21.6%. Flow-chart of the study is presented in the Figure-1. A total of 117 pregnant women (1.3% of anemic patients) were available for the analysis. Thirty-one (26.5%) and 86 (73.5%) patients were in the second and third trimester of the pregnancy, respectively. The mean maternal age was 26.6 ± 5.2. The median and interquartile ranges for gravida, parity and live children were 2 (1-3), 1 (0-2) and 1 (0-1), respectively. Four (3.4%) of the patients had severe and 113 (96.6%) of the patients had moderate anemia. The median gestational age for iron sucrose administration was 31.1 weeks (26.8-34.3). The mean hemoglobin, hematocrit and ferritin levels before iron sucrose therapy were 8.0±0.6 gr/l (minimum 6.4 gr/l and maximum 9.7 gr/l), 25.7±2.0 and 12.3±0.9 µg/L, respectively. The median number of iron sucrose ampoules used per patient was 9.1 (6-12). 99 (85%) patients needed more than 1 day of iron sucrose therapy. The mean hemoglobin, hematocrit and ferritin levels before and after delivery were 10.8±1.3 gr/l; 9.9±1.3 gr/l, 33.5±4.0; 30.8±4.0 and 89.6±0.7 µg/L; 98.1±0.9 µg/L, respectively. 75 (64.1%) patients were delivered by spontaneous vaginal delivery. The median gestational age of delivery was 39.2 (38.2-40.2). The median birth weight was 3330 grams (2850-3640) and the median duration from iron sucrose administration to delivery was 7.4 (4.1-11.5) weeks. When hemoglobin and hematocrit levels were compared between before iron sucrose therapy and before delivery, there was a 2.8 g/l and 7.8 % increase in the mean hemoglobin and hematocrit levels, respectively and the difference was statistically significant (p= 0.000 and p=0.000, respectively) (Table 2). All but two (1.8%) patients had elevated hemoglobin levels after iron sucrose therapy (Figure 2). Before delivery, the number of patients in the moderate and mild anemia and non-anemia groups was 30 (25.7%), 28 (23.9%) and 59 (50.4%), respectively. Therefore, 49.6% of our cohort was still anemic (<11 gr/dL) in the pre-delivery period. When hemoglobin increase was compared between pre-treatment hemoglobin level groups, we found no difference (p=0.11) (Figure 3). Five patients (4.3%) reported mild hypersensitivity reaction to intravenous iron in the form of mild itching at the infusion site. No severe or life-threatening hypersensitivity reaction was reported.

*Table 1: Demographics of the study*

| Characteristics | Value* |
|---|---|
| Mean Maternal Age | 26.6±5.2 |
| Median Parity | 1 (0-2) |
| Mean Hemoglobin Levels before Iron Sucrose therapy (g/dL) | 8.0±0.6 |
| Median Duration From Iron Sucrose Administration To Delivery (weeks) | 31.1 (26.8-34.3) |
| Median Gestational Age Of Delivery | 39.2 (38.2-40.2) |
| Median Birth Weight (grams) | 3330 (2850-3640) |
| Median Duration From Iron Sucrose Administration To Delivery | 7.4 (4.1-11.5) |

**Data expressed as mean ± standard deviation or median (range)*

*Table 2: Changes in hemoglobin, hematocrit and ferritin levels**

| | Before venofer therapy | Pre-delivery | p |
|---|---|---|---|
| Hemoglobin gr/L (mean±S.D.) | 8.0±0.6 | 10.8±1.3 | 0.000 |
| Hematocrit | 25.7±2.0 | 33.5±4.0 | 0.000 |
| Ferritin µg/L (mean±S.D.) | 12.3±0.9 | 89.6±0.7 | 0.000 |

**Paired samples t-test was used to compare means*

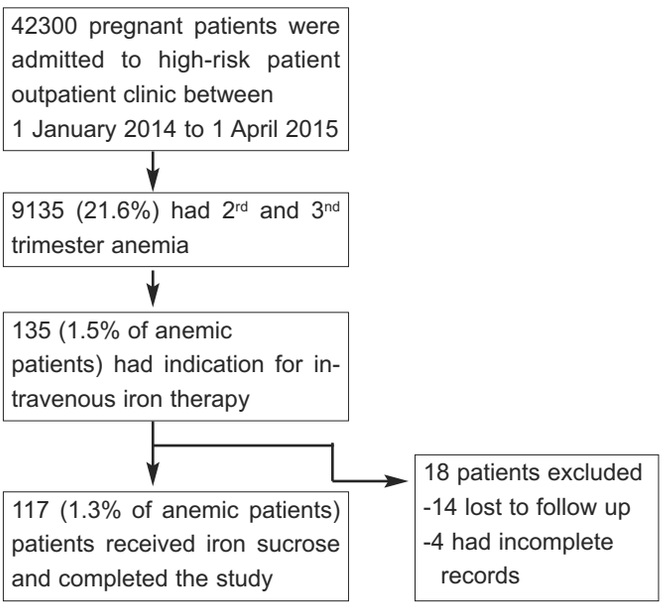


*Figure 1: Flow chart of the study*

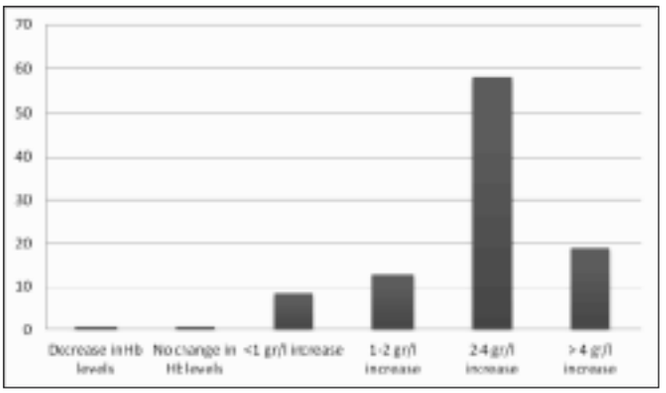


*Figure 2: Comparison of predelivery and pre-treatment hemoglobin levels*

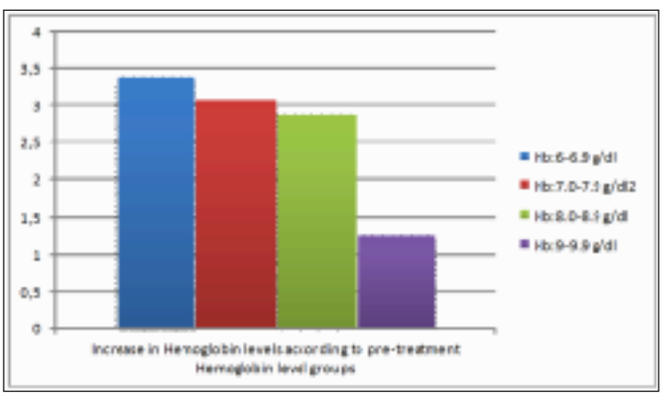


*Figure 3: Increase in hemoglobin levels according to pre-treatment hemoglobin level groups*

## Discussion

Iron therapy is the mainstay of iron-deficiency anemia treatment and intravenous iron is increasingly used when oral therapy is not effective or well tolerated. In this study, we found that intravenous iron therapy is effective in iron restoration and anemia treatment with few side effects.

Iron deficiency and iron-deficiency anemia are serious public health problems. The prevalence of anemia and severe anemia in pregnancy (defined as hemoglobin levels less than 7 gr/dl) is 38% and 0.9%, respectively and most of these cases are caused by iron deficiency anemia (6). Severe iron-deficiency anemia has been associated with an increased risk of low birth weight, maternal mortality, neonatal mortality and preterm birth. Since iron is essential for the normal erythrocyte turnover and most women either do not have adequate iron stores or do not meet the requirement of iron for red blood cell mass expansion during pregnancy, iron is generally prescribed as a prenatal multivitamin or supplement. In pregnancy, high progesterone levels result in slow bowel movements, which leads to bloating and constipation. Because of this, up to 70% of pregnant taking oral iron report adverse events (7). Moreover, in order to treat anemia and back up body iron stores, a long course of oral iron therapy is needed.

Due to the therapeutic challenges of oral iron therapy, intravenous iron emerged as an alternative tool for treatment of iron deficiency. High-molecular-weight iron dextran was the first iron product for intravenous use: however, this was associated with an elevated risk of anaphylactic reactions, which discouraged the physicians to use it. Recently new intravenous iron products with better safety profiles were launched to the market. Iron sucrose, which is a dextran free product and has a satisfying safety profile without a need for a test dose (unless the patient has a history for drug allergies), has become the leading intravenous iron compound in the market (8,9). When compared with oral iron for pregnant women with severe iron deficiency anemia, intravenous iron sucrose resulted in significantly higher mean hemoglobin and ferritin levels and those patients treated with iron sucrose achieved maximum hemoglobin levels in half the time (10-13). Al-Momen et al. compared the efficacy of intravenous iron sucrose with oral iron in 52 patients (10). The increase in hemoglobin and ferritin levels found in their study was similar to our results and also they reported no serious side effects. In Perewusnyk et al. study, all patients treated with iron sucrose were cured

for anemia but in our study, two patients (1.8%) failed to show an increase in hemoglobin levels (14). In our study, five (4.3%) patients reported mild itching at the infusion site but none required medication. Similar to our results, Abhilashini et al. reported that 2% of their cohort had pruritus (15).

As a result, we found that intravenous iron sucrose therapy for iron deficiency anemia is feasible, effective and has a good safety profile. The retrospective cohort design of the study is the main limitation but the high number of pregnant patients is the main strength. Before delivery, almost half of the patients were still in the anemia range. Our study group had moderate and severe anemia and there was a substantial increase in hemoglobin levels and accordingly, we consider the therapy as effective. However, prospective randomized trials may give further insights on the effectiveness of iron sucrose in the treatment of anemia in pregnancy.

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