Evaluation of the Use of Intravenous Iron Supplements in an Obstetrics and Gynecology Department

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Abstract

Background: The use of intravenous (IV) iron sucrose was approved for the obstetric and gynecologic (OBGYN) population at our mother–child teaching hospital in 2006 for intolerance or nonresponse to oral iron supplements, contraindication to intramuscular (IM) iron, and rapid increase of the hemoglobin desired in iron-deficient patients. **Objectives:** (a) To describe the indications and doses of IV iron sucrose used in OBGYN, (b) to assess monitoring, and (c) to describe the adverse effect profile. **Methods:** A retrospective study of patients admitted to the OBGYN wards with at least one prescription of IV iron from January 1, 2006, to March 31, 2010, was conducted. A standardized data collection sheet was used to record data. **Results:** A total of 164 prescriptions of IV iron were reviewed in 128 women. The indications for IV iron were anemia before delivery ($n = 76$), intolerance or no response to oral iron ($n = 61$), or intolerance or contraindication to IM iron ($n = 27$). Fourteen doses (9%) were appropriate, and the others were too low. Prior to prescription, ferritin or serum iron levels were assessed in 31% of women and hemoglobin electrophoresis in nearly all of Black or Asian women. One-week follow-up hemoglobin levels were measured after 66 prescriptions (40.2%). Adverse effects, mostly pain at the injection site, were reported in 18 (11%) occasions. **Conclusions:** IV iron is prescribed in OBGYN patients to obtain a rapid hemoglobin increase or when oral iron is not tolerated or inefficacious. The dose prescribed is generally too low, baseline essential testing often omitted, and appropriate follow-up monitoring incomplete. IV iron is well tolerated.

Keywords

intravenous iron, pregnancy, gynecology, postpartum

Introduction

Anemia is frequent in women of all ages. According to the World Health Organization (WHO), the global prevalence of anemia is 41.8% in pregnant women and 30.2% in nonpregnant women.¹ Iron deficiency is one of the common causes of anemia even in industrialized countries (22% for pregnant women and 10% for nonpregnant women).¹ In pregnancy, the risk factors for iron deficiency include low intake of iron, poor iron absorption, and increased iron requirements. Outside of pregnancy, anemia may be secondary to heavy blood loss during menstruation and acute or chronic infections.²

Anemia is defined as hemoglobin below 110 g/L in the first and last trimesters of pregnancy and below 105 g/L in the second trimester of pregnancy, whereas below 120 g/L in nonpregnant women.^{3,4} Severe anemia is defined at below 70 g/L. A hemoglobin level below 40 g/L is an emergency and should be treated immediately.⁴

In pregnancy, severe anemia has been linked to increased maternal mortality especially due to hemorrhage in the

postpartum period.⁵ Also, low antenatal hemoglobin concentrations are a risk factor for postpartum hemorrhage, thus increasing the risk of blood transfusions and prolonged hospitalizations.⁶ It may affect negatively the fetus by increasing the incidence of growth retardation, preterm birth, and perinatal mortality.⁷ Less severe anemia in pregnant and nonpregnant women is also associated with fatigue and decreased productivity.⁴

According to the WHO, the benefits of treating iron deficiency are substantial by restoring health and, thus, decreasing negative consequences of anemia on women.

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The standard treatment of iron deficiency anemia is oral iron supplements, which are easily available and inexpensive. However, they are not always taken as prescribed due to digestive complaints such as nausea and constipation and due to forgetfulness.^{8,9}

In case of severe nausea and vomiting, when a rapid increase in hemoglobin is desired or when oral iron therapy was not tolerated or efficient, intramuscular (IM) and intravenous (IV) iron are often prescribed.

IM iron (iron dextran) may be associated with allergic reactions, can be painful, and is contraindicated in some patients with hemostatic disorders. IV iron dextran is also associated with potentially dangerous allergic reactions. Iron sucrose, a newer salt of IV iron, is also available in Canada. This formulation is usually better tolerated and causes fewer hypersensitivity reactions.¹⁰ Although several equations can be used to calculate the appropriate dose of IV iron, it is usually calculated using hemoglobin deficit and lean body weight.¹¹

In 2003, IV iron sucrose was added to our hospital drug formulary for pediatric use. In 2006, its use was broadened to include the obstetrics and gynecology population.

The objectives of this study were to describe the indications and doses of IV iron used in our obstetrics and gynecology ward, to evaluate if appropriate monitoring was done, and to describe the adverse effect profile.

Methods

Design

This retrospective, descriptive, and observational study was conducted at the Centre hospitalier universitaire (CHU) Sainte-Justine in Montreal, Quebec, Canada. It is a large mother and child hospital with an obstetrics and gynecology department oriented toward high-risk pregnancies. In 2006, the use of IV iron sucrose in the obstetric and gynecologic population was approved in the following situations:

- Intolerance or nonresponse to oral iron supplements
- Contraindication to IM iron
- Rapid increase of the hemoglobin desired in iron-deficient patients (eg, anemic women who were to have a surgery or a caesarean section within 2 weeks)

The subjects were all women attending or admitted to the obstetrics and gynecology wards who were prescribed IV iron sucrose between January 2006 and April 2010. Women were identified through the pharmacy computerized record. A standardized form was used to collect demographic and medical data, reasons for administering IV iron, doses of IV iron, and adverse effects. We also noted hemoglobin follow-up results. We considered that optimal timing to check hemoglobin levels were at least after 1 week since reticulocytosis is observed after 7 to 10 days

Table 1. Population Demographics.

Characteristic	Result
Age (years)	
Mean $\pm$ SD	31 $\pm$ 5.8
Median (min-max)	30.9 (15-47)
Race, n (%)	
Non-Hispanic white	65 (50.8%)
Black	33 (25.8%)
Hispanic	8 (6.3%)
Asian	6 (4.7%)
Other or unknown	16 (12.5%)
Timing of administration of IV iron ^a (n = 135)	
Pregnancy	47
Postpartum	78
Gynecology	10

Abbreviations: IV, intravenous; SD, standard deviation.

^aSix women received IV iron during pregnancy and after delivery, and 1 woman got IV iron during 2 different pregnancies.

after treatment.^{11,12} The protocol was approved by the *Direction des Affaires Universitaires* of CHU Ste-Justine.

Statistical Analyses

Descriptive analyses were used to present the indications, the doses, and adverse effect profile. Mean hemoglobin levels before and after IV iron (24, 48, 72 hours and 1 week after IV iron) were compared with a paired Student *t* test.

Results

During the study period, the charts of 128 women were reviewed for 164 prescriptions of IV iron. IV iron was prescribed to 43 pregnant women, 75 women in the postpartum period, and 10 gynecological patients. Six women received IV iron during pregnancy and after delivery, and 1 woman received IV iron during 2 different pregnancies for a total of 135 episodes of IV iron administration.

The population demographics are presented in Table 1. The mean age was 31 years (± 5.8). The majority of the women were Caucasians (51%). For pregnant women, mean gestational age at the beginning of treatment was 31.1 weeks (20-39 weeks).

Most women were prescribed IV iron to obtain a rapid hemoglobin increase (47%). Other indications of IV iron are described in Table 2.

All Asian and 97% of Black women who were anemic were investigated with a hemoglobin chromatography (Table 3). In our population, ferritin, serum iron, and vitamin B₁₂ levels were only routinely indicated in pregnant women to identify other potential causes of anemia because most were considered nonresponders to oral iron supplementation. Other patients included were anemic due to acute bleeding either after a delivery or a surgery.

Table 2. Indications for IV Iron (N = 164).

Indication	n (%)
Rapid hemoglobin increase desired	76 (47%)
Intolerance or no response to oral iron therapy	61 (37%)
Intolerance or contraindication to IM iron (mainly coagulation anomalies)	27 (16%)

Abbreviations: IM, intramuscular; IV, intravenous.

Table 3. Workup and Follow-Up.

Pre-IV Iron Workup	Percentage With Workup
Hemoglobin chromatography ^a	
Asian (n = 6)	100%
Black (n = 33)	97.0%
Maghreb or Middle-East (n = 4)	50%
Indian subcontinent (n = 4)	50%
Hispanics (n = 8)	50%
Non-Hispanic White (n = 65)	11%
First Nations (n = 2)	0%
Unknown (n = 6)	0%
Post-IV iron prescription follow-up ^b	
One-week hemoglobin follow-up (all prescriptions, N = 164)	66 (40.2%)
Pregnancy ^a (n = 62)	38 (61.7%)
Postpartum (n = 91)	25 (27.5%)
Gynecologic patients (n = 11)	3 (27.3%)

Abbreviation: IV, intravenous.

^aOne sickle cell disease, 6 sickle cell traits, 2 HbAC, and 4 minor thalassemias among Black women.

^bPercentage was calculated with the total number of IV iron prescriptions.

Ferritin levels were measured in 24 (55.8%) pregnant women; 76% of these women had a ferritin level below 15 µg/L. Serum iron and vitamin B₁₂ levels were measured in 23 (53.5%) and 28 (65.1%) of pregnant women, respectively. Fourteen of the 28 vitamin B₁₂ levels were low and all these pregnant women were treated.

Overall, 1-week hemoglobin levels were measured in 40.2% of each prescription of IV iron in our study (Table 3). Earlier hemoglobin levels after 24, 48, and 72 hours were measured after 85 (51.8%), 68 (41.5%), and 51 (31.1%) doses, respectively.

Table 4 presents the hemoglobin levels before and after IV iron. IV iron was administered to women with hemoglobin ranging between 53 and 102 g/L (mean = 76 ± 12 g/L). One week after IV iron, hemoglobin results varied from 69 and 119 g/L (mean = 92 ± 11 g/L), which represents a mean variation of 22.5% (−15.0% to 109%). Mean hemoglobin levels only significantly increased between pre- and post-IV iron administration at 72 hours ($P < .0001$); increases were not statistically different at 24 and 48 hours and at 1 week

posttreatment ($P > .05$). It should be noted that 21 women were transfused before receiving IV iron and 9 women received blood transfusions once IV iron had started (discontinuing the administration of IV iron). Similar 1-week hemoglobin results were obtained with subanalyses on patients who did not receive blood transfusions (data not shown).

IV Iron Doses

In the entire cohort, the mean total dose prescribed was 500 mg (100-1500 mg); in pregnant women, the mean dose was slightly higher (630 mg [100-1500 mg]). We used the following equation based on the patient weight and hemoglobin deficit to calculate the appropriate IV iron dose (target hemoglobin of 110 g/L)¹⁰:

$$\text{Suggested dose (mg)} = \text{Weight}_{\text{before pregnancy}} (\text{kg}) \times (110 - \text{Hb (g/L)}) \times 0.24 + 500 \text{ mg (for iron stores)}$$

In our study, when using the equation above, only 14 prescriptions were appropriate (9%), the other ones were too low. The mean ± SD difference between the suggested dose and the prescribed dose was -580.9 ± 400.4 mg ($-49.92 \pm 31.84\%$). Similar 1-week hemoglobin results were obtained in our subanalyses after the appropriate prescriptions and the reminder of the prescriptions, 94.6 ± 13.7 and 92.7 ± 11.6 g/L, respectively.

Adverse Effect Profile

Overall 11% of women had at least one adverse effect with IV iron. Table 5 describes the adverse effects reported. Most adverse reactions reported were localized at the IV site; we did not observe any anaphylactic shock, allergic reaction, or any severe drug adverse reaction.

Incomplete Treatments

The dose administered was lower than the prescribed dose in 46 prescriptions (28.0%). The main reasons for incomplete treatments were hospital discharge, 10 (22.2%); delivery, 6 (13.3%); IV access infiltrated or pain at IV site, 6 (13.3%); no IV access available, 5 (11.1%); transfusions, 3 (6.7%); adverse drugs reaction (other than IV access), 3 (6.7%); and for other reasons or for an unknown reason, 14 (30.4%). Of these, hemoglobin follow-up at 1 week was done after 20/46 (43.5%) prescriptions of IV iron.

Discussion and Conclusion

Iron deficiency anemia is the most frequent form of anemia in pregnancy and is also commonly diagnosed in nonpregnant

Table 4. Hemoglobin Levels Pre- and Post-IV Iron^a.

Hemoglobin Levels	Predose (n = 164)	Postdose			
		24 Hours (n = 85)	48 Hours (n = 68)	72 Hours (n = 51)	1 Week (n = 66)
Mean $\pm$ SD (g/L)	76 $\pm$ 12	75 $\pm$ 13	77 $\pm$ 14	85 $\pm$ 14	92 $\pm$ 11
Percent change ^b	NA	-1.32	1.32	11.8	21.1
Median (min-max) (g/L)	77 (53-102)	73 (54-108)	75 (52-116)	84 (63-111)	93 (69-119)
Percent change ^b	NA	-5.19	-2.59	9.09	20.8

Abbreviations: IV, intravenous; NA, nonapplicable; SD, standard deviation.

^aTwenty-one women were transfused before IV iron. Nine women received blood transfusions once IV iron had started (discontinuing the administration of IV iron).

^bCompared with predose.

Table 5. Adverse Effects Reported With the Use of Intravenous Iron.

Adverse Effects (n = 162 ^a)	n (%)
Burning sensation or pain at IV site	8 (5%)
IV line infiltrated	4 (2%)
Cellulitis	2 (1%)
Induration at IV site	1 (1%)
Superficial phlebitis at IV site	1 (1%)
Other (dizziness, abdominal pain)	2 (1%)

Abbreviation: IV, intravenous.

^aTwo prescriptions were never administered.

women.¹ Serum ferritin levels is an easy way to diagnose iron deficiency although it can be affected by infection or inflammatory disorders. A hemoglobin result above 100 g/L would exclude iron deficiency in pregnancy and postpartum.¹³ Nearly all Black women were investigated for abnormal hemoglobin chromatography as recommended. Asian women were also tested for hemoglobinopathies and some for thalassemias. Investigation of anemia before IV iron administration was not complete in half of pregnancy cases. In order to optimize anemia treatment during pregnancy, in our practice, we strive to identify all other causes of anemia including iron, vitamin B₁₂, and folic acid deficiencies especially in women who were previously treated with oral iron.¹⁴ In our cohort, a vast majority of patients had been treated with oral iron before the starting IV iron.

IV iron sucrose is an alternative in case of oral iron intolerance or contraindication (oral or IM). IV iron sucrose is safe and usually well tolerated. Studies comparing IV iron to oral iron demonstrate equal or superior efficacy, a more rapid short-term repletion of iron stores.^{6,15} In certain studies it is also associated with less adverse effects.¹⁵ IV iron was well tolerated in our review, with only 11% of charts reporting adverse effects. No anaphylactic shock or other serious adverse effects were reported. Therefore, IV iron could be more liberally used if indicated. Although IV iron is more expensive, it may reduce duration of hospitalizations by increasing the well-being of the women.¹³ A more

rapid increase in hemoglobin may also reduce transfusions; our study was too small to investigate these outcomes.

According to our calculations using the chosen equation described previously, the doses prescribed were usually too low.¹⁶ With the equation that we used, any dose below 500 mg is automatically too low. Other equations and doses have been proposed by other authors,^{14,16} and the rate of adequate dose might have changed with a different equation or recommendation.¹⁰ Although several equations can be used to calculate the appropriate dose of IV iron, it is usually calculated using hemoglobin deficit and lean body weight.¹¹ The wide range of doses used in our study indicates that a standardized dosing recommendation is not routinely used in our institution.

We considered that optimal hemoglobin follow-up was after at least 1 week after treatment since reticulocytosis is observed after 7 to 10 days. One-week follow-up studies of hemoglobin levels were lacking in 60% of cases. One-week follow-up was more frequent in gynecological patients; postpartum follow-up were only performed in approximately one quarter of patients. Earlier monitoring between 24 and 72 hours was performed after 30% to 50% of doses; these results are not useful to measure IV iron efficacy but could be useful to assess blood loss.

The strengths of our study were that it evaluated a real clinical setting, describes actual practice, and it will serve as basis for improvement in clinical practice. Our sample size, the evaluations of the safety profile, and the use of a standardized data collection are also positive aspects of our study. However, the retrospective and noncomparative nature of our study introduces inherent biases making it difficult to draw any conclusion on efficacy, and some data might be incomplete. It would have been optimal to have data in patient satisfaction as well as neonatal outcomes.

In conclusion, IV iron sucrose is a well-tolerated alternative to oral or IM iron. Investigations of anemia in pregnancy could be more thorough, and in order to improve clinical practice, tools will be developed to improve prescribing and monitoring of IV iron.

Authors' Note

This project was presented as an abstract and short oral presentation form at the 67th Annual Clinical Meeting of the Society of Obstetricians and Gynecologists of Canada (June 21-25, 2011, Vancouver, British Columbia, Canada).

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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