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Fatal anaphylactic reaction to iron sucrose in pregnancy

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Abstract

Iron-deficiency anemia in pregnancy can have serious deleterious effects for both mother and fetus. Parenteral iron therapy in iron-deficiency anemia is recommended in patients where oral iron therapy is ineffective due to malabsorption states and non-compliance. Compared to oral iron therapy, intravenous iron results in much more rapid resolution of iron-deficiency anemia with minimal adverse reactions. Iron sucrose has a favorable safety profile and is an alternative to other forms of parenteral iron therapy in correction of iron stores depletion. Immune mechanisms and iron agent releasing bioactive, partially unbound iron into the circulation, resulting in oxidative stress appears to cause severe adverse reactions. Although iron sucrose has a favorable safety profile in comparison to other parenteral iron preparations, this report highlights a fatal anaphylactic shock to iron sucrose in a pregnant woman with severe iron deficiency non-compliant to oral iron therapy.

KEY WORDS: Anaphylactic Reaction, fatal, iron sucrose, pregnancy

Introduction

Iron-deficiency anemia is common in pregnancy. Treatment of iron-deficiency anemia in pregnancy with oral iron therapy and blood transfusion has significant drawbacks. High dose of oral iron causes significant side effects; non-compliance is common. Intravenous iron produces a better hematological response than oral iron, including a faster increase in hemoglobin and faster replenishment of body iron stores and can provide an alternative to transfusion in profound iron deficiency anemia.^[1] All available iron preparations for parenteral use can cause short-term side-effects, including anaphylactic reaction. We report here a fatal anaphylactic reaction to iron sucrose in a pregnant woman with severe iron-deficiency anemia.

Case Report

A 20 years-old primigravida with seven months amenorrhea presented to the emergency department with giddiness and difficulty in breathing. The history of presenting complaints revealed that she had developed these complaints within few minutes of receiving first infusion of iron sucrose USP 5 ml injection (FERISE 5 brand of Intas Pharma Company) diluted in 100 ml normal saline for severe iron deficiency anemia in a primary health care centre. Parenteral iron therapy was initiated to her because she was noncompliant to oral iron and folic acid supplements. She had no history of allergies or significant past medical illness. On presentation, she was conscious, alert (Glasgow coma scale 15/15) and afebrile. Her pulse rate was 140/min, respiratory rate 28/min, oxygen saturation of 90% at room air and systolic blood pressure 70 mm of Hg. On physical examination, she had marked pallor in mucous membranes. Chest examination revealed bilateral diminished breath sounds; rest of the systemic examination was unremarkable. Her hemoglobin was 6.0 gm/dL, total leucocyte count 27900/μL, red

blood cell count 2.86 million/cmm, platelet count 570000/ μ L, International normalized ratio (INR) 1.13 and APTT 34.4 seconds. Arterial blood gas analysis was suggestive of hypoxia (pH 7.37, po₂ 66, pco₂ 44, HCO₃ 20 and po₂/Fio₂ 0.66 on 100% Fio₂). Chest radiograph showed bilateral infiltrates. She had normal urine analysis, serum electrolytes, renal, liver and thyroid function tests. She was treated with intravenous adrenaline, hydrocortisone, antihistaminics and H₂ blockers and transferred to the intensive care unit for ventilatory and inotropic support.

Despite intensive resuscitation attempts in the intensive care unit, the patient expired due to cardiac arrest within 24 hrs.

Discussion

Anemia in pregnant women is estimated to be between 39.9 to 43.8% globally and 43.9 to 52.5% in South-East Asia. It is generally estimated that half of the anemia cases in pregnancy are related to iron deficiency. The prevalence of iron-deficiency anemia in pregnant women is estimated to be between 35 and 75% in developing countries whereas in industrialized countries, the average prevalence is 18%.^[2,3] Parenteral iron therapy in iron-deficiency anemia is recommended in patients where oral iron therapy is ineffective due to mal-absorption states and noncompliance.^[1] Compared to oral iron therapy, intravenous iron results in much more rapid resolution of iron-deficiency anemia with minimal adverse reactions.^[4] Three commercial formulations; Iron dextran, sodium ferric gluconate complex and iron sucrose are currently available for intravenous iron therapy. All available iron preparations for parenteral use can cause short-term side-effects, such as metallic taste, back pain, nausea, vomiting, diarrhea, abdominal pain, hypotension and allergic or even anaphylactic reactions.^[5] Symptoms of anaphylaxis include dyspnea, chest pain, angioedema, urticaria with hypotension, and are generally immediate, sudden, and severe, typically occurring in conjunction with the first dose of parenteral iron.^[6] The systemic reaction observed in response to the first dose of intravenous iron preparations have not been found consistently to be IgE mediated and are therefore described as anaphylactic or anaphylactoid reaction.^[7]

The immunologic basis of allergic hypersensitivity to intravenous iron agents is not known. Iron dextran induced toxicity is believed to be due to hypersensitivity related to the dextran moiety, since iron dextran is associated with a higher risk for anaphylaxis or anaphylactoid reactions than newer IV iron products. Iron dextran had the highest reports of anaphylaxis, anaphylactoid reaction, urticaria, upper airway angioedema, while iron sucrose carried the lowest risk for these hypersensitivity reactions. The all-event reporting rates for iron dextran, sodium ferric gluconate, and iron sucrose were 29.2, 10.5, and 4.2 reports per million 100mg dose equivalents, respectively, while the all-fatal-event reporting rates were 1.4, 0.6, and 0.0 reports per million 100mg dose equivalents, respectively. Iron sucrose appears to have a favorable safety profile and is an alternative to other forms of parenteral iron therapy in correction of depletion of iron stores. Rare anaphylactic reactions with iron sucrose have been reported in 0.002% of cases.^[8,9]

In our patient, an adverse drug reaction occurring few minutes after infusion of first dose of iron sucrose suggests hypersensitivity reaction rather than an immediate dose related toxicity. Use of Naranjo probability scale indicated a probable relationship between the hypersensitivity reaction and iron sucrose as the causal drug. Since serum IgE or tryptase levels were not obtained, we are not able to establish whether this reaction was an anaphylaxis or an anaphylactoid reaction.

In conclusion, clinicians should be alert to the possibility of this fatal adverse effect in patients receiving parenteral iron sucrose. A public health initiative aimed at reducing the number of severe adverse reactions to parenteral iron would require a rational use of this drug and a mandatory test dose before the first infusion.

Footnotes

Source of Support: Nil

Conflict of Interest: No

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