The Use of Parenteral Iron Therapy for the Treatment of Postpartum Anemia

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Abstract

Rates of postpartum hemorrhage have been increasing in Canada over the last 10 years, with postpartum iron deficiency anemia as the most common consequence. Postpartum anemia is treated with oral iron supplementation and/or blood transfusion. Recent studies have evaluated the use of parenteral iron as a better tolerated treatment modality. Compared with oral iron supplements, parenteral iron is associated with a more rapid rise in serum ferritin and hemoglobin and improved maternal fatigue scores in the postpartum period. It may also decrease rates of blood transfusion. Parenteral iron may be considered in select clinical situations for the treatment of postpartum anemia.

Résumé

Les taux d'hémorragie postpartum ont connu une hausse au Canada depuis les 10 dernières années, la manifestation d'une anémie ferriprive postpartum en étant la conséquence la plus courante. L'anémie postpartum est prise en charge au moyen d'une supplémentation orale en fer et/ou d'une transfusion sanguine. De récentes études ayant évalué l'utilisation de fer parentéral ont indiqué qu'il s'agissait d'une modalité de traitement mieux tolérée. Par comparaison avec les suppléments oraux de fer, le fer parentéral est associé à une hausse plus rapide des taux sériques de ferritine et d'hémoglobine, en plus de mener à une amélioration des scores de fatigue maternelle au cours de la période postpartum. Le fer parentéral pourrait également mener à une diminution des taux de transfusion sanguine. Son utilisation pourrait être envisagée dans certaines situations cliniques particulières, aux fins de la prise en charge de l'anémie postpartum.

J Obstet Gynaecol Can 2015;37(5):439–442

Key Words: Postpartum anemia, intravenous iron, parenteral iron

Competing Interests: None declared.

Received on November 4, 2014

Accepted on November 10, 2014

A comprehensive study on temporal trends in postpartum hemorrhage in Canada from 2003 to 2010 was published in January 2014.[1] This study highlighted increased rates of postpartum hemorrhage in recent years, primarily as a result of atonic postpartum hemorrhage and increased rates of severe postpartum hemorrhage requiring blood transfusion, hysterectomy, uterine suturing, or ligation/embolization of pelvic arteries. The increases were observed across Canada, and analyses could not explain the increases by incorporating changes in maternal, fetal, or obstetrical factors. With continued increases in rates of postpartum hemorrhage, and with the influences associated with these increases still uncertain, the authors of that study identified the need for additional research to clarify etiology.[1]

The implications of rising postpartum hemorrhage rates are considerable. There is a risk of maternal mortality, and the maternal morbidity directly associated with postpartum hemorrhage can be significant; they include the consequences of loss of blood volume and hypotension such as acute renal failure, adult respiratory distress syndrome, coagulopathy, and shock. Symptoms of anemia in the postpartum period include dyspnea, lethargy, palpitations, and maternal infections, which may influence the ability to care for and bond with a newborn. In addition, there are longer term effects of postpartum hemorrhage related to postpartum anemia, including impaired quality of life, poor cognitive performance, emotional instability, increased risk for postpartum depression, and poor lactation[2–4]; these occur remote from delivery, and constitute a significant health problem in women of reproductive age.[2] Lactation also results in loss of iron via breast milk.

The World Health Organization categorizes anemia in pregnant women at sea level as mild (hemoglobin [Hb] concentration 100 to 109 g/L), moderate (Hb concentration 70 to 99 g/L) and severe (Hb concentration < 70 g/L).[5] Iron deficiency anemia is defined as a low Hb concentration

in combination with iron deficiency, and is characterized by a defect in Hb synthesis, resulting in abnormally small (microcytic) red blood cells with a decreased Hb content (hypochromic), resulting in reduced capacity of the blood to deliver oxygen. Iron stores may be measured using several indices, although serum ferritin and transferrin saturation are the most common. While postpartum anemia is typically seen subsequent to postpartum hemorrhage, it is most commonly associated with antepartum iron deficiency anemia combined with blood loss at delivery.[2] While there currently is no clear classification of postpartum anemia, it is generally described as an Hb concentration < 100 g/L at 24 to 48 hours after delivery.[6] Approximately 15% of women will have a blood loss > 500 mL at the time of delivery.[7] It is generally recommended that antepartum anemia caused by iron deficiency and postpartum anemia should be treated; treatment may consist of dietary and pharmacologic iron supplementation, and more rarely transfusion of blood products.

Iron is essential for normal Hb synthesis to maintain oxygen transport, as well as being necessary for metabolism and synthesis of DNA and enzymatic processes. Oral iron therapy is the treatment of choice for the majority of patients with iron deficiency anemia because of its effectiveness, safety, and low cost. A variety of oral iron supplements are currently available in Canada, including ferrous sulfate, ferrous gluconate, ferrous fumarate, and iron-polysaccharide complexes. Formulations using these types of elemental iron have a wide range of available dosages. Side-effects of oral supplementation are primarily gastrointestinal, and include nausea, vomiting, dyspepsia, constipation, diarrhea, or dark stools. While these effects are generally dose-related and (with the exception of dark stools) usually subside with continued therapy, these adverse effects often lead to poor patient compliance. In addition, oral iron is often not capable of replenishing severe iron deficiencies.

Antepartum anemia attributable to iron deficiency is most commonly treated with oral supplementation. Use of parenteral iron beyond the first trimester is reserved for patients with failure of a trial of oral iron, documented intolerance of iron, malabsorption of oral iron, or a requirement for fast repletion.[4,8] Oral iron supplementation with or without blood transfusion is the current preferred therapy for postpartum anemia; blood transfusions have been associated with the transmission of pathogens and transfusion reactions.[3]

Several solutions have been proposed to improve patient compliance and to aid in the treatment of postpartum anemia, including use of an oral supplement containing a low iron concentration, use of oral liquid iron, slow dose titration or oral supplementation, and the use of parenteral iron.[3] Several forms of parenteral iron are currently available, with iron dextran, iron sucrose, and sodium ferric gluconate the most commonly used in Canada. Iron dextran contains 50 mg of elemental iron per mL and can be administered by intravenous infusion or by intramuscular or subcutaneous injection.[9] A test dose of iron dextran should be given before infusion or injection, because approximately 4.4% of patients are at risk of anaphylaxis.[9] Second-generation, non-dextran forms of parenteral iron have a lower risk of anaphylaxis; iron sucrose contains 20 mg of elemental iron per mL and sodium ferric gluconate contains 12.5 mg of elemental iron per mL. Other parenteral forms of iron, such as ferric carboxymaltose, a third-generation parenteral iron, are not currently available in Canada. Parenteral iron has been shown to produce a faster and greater increase in Hb concentration than oral supplementation without the risks associated with a blood transfusion.[3,10]

Parenteral iron is emerging as an alternative treatment for significant postpartum anemia. A review of the literature identified three randomized controlled trials evaluating the efficacy of parenteral iron to treat postpartum anemia before discharge from hospital.[11–13] The studies involved the use of common formulations of parenteral iron and evaluated the outcomes of Hb and ferritin levels, among other indices.

Bhandal and Russell conducted a single centre RCT that compared administration of intravenous ferrous sucrose given on the second and fourth postpartum days with oral ferrous sulfate twice daily for a duration of six weeks in 44 women with a postpartum Hb level < 90 g/L (Table).[11] Intravenous ferrous sucrose was associated with a significantly faster rise in Hb concentration on postpartum days 5 and 14; Hb concentrations by postpartum day 40 were similar in the intravenous ferrous sucrose and oral iron groups (115 g/L and 112 g/L, respectively). Administration of intravenous ferrous sucrose was associated with significantly higher serum ferritin levels by postpartum day 40 than oral ferrous sulfate (42.2 μg/L and 15.0 μg/L, respectively, $P < 0.05$). No serious adverse events were observed.

Westad et al. reported results of a multicentre RCT in Norway involving 128 women. This study compared the effects of postpartum intravenous iron sucrose administered over three days, plus twice daily oral iron sulfate supplementation administered from the fourth postpartum week with the effects of twice daily oral iron sulphate supplementation administered from the first postpartum day (Table).[12] By the fourth postpartum week,

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