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The Management of Iron Deficiency Anemia in Obstetrics and Gynecology

Anemia is an extremely common condition, in both developed and undeveloped countries. Data from the (World Health Organization) WHO Vitamin and Mineral Nutrition Information System for 1993-2005[1], estimated the global anemia prevalence as 24.8 %, affecting 1.62 billion people. Of those affected, 41.8 % occurred in pregnant women and 30.2 % in non-pregnant women. This equates to 677 million pregnant women and 489 million non-pregnant women worldwide.[1] In a more recent study from the Bill and Melissa Gates Foundation of the eight causes of chronic disease affecting more than 10% of the world's population, iron deficiency anemia affected the greatest number of people – 2.36 billion individuals worldwide.[2] The effects of anemia are an independent risk factor for morbidity, and mortality in both the mother and fetus.[3]

Causes of Iron Deficiency Anemia

The most common cause of iron deficiency anemia (IDA) in pre-menopausal women is menstrual blood loss. In post-menopausal women, blood loss from the gastrointestinal tract is more common.

Symptoms of Iron Deficiency Anemia

- Easy fatigability.
- Decreased functional capacity and exercise tolerance
- Depression
- Cold intolerance.

More troublesome symptoms include

- Restless legs syndrome.
- Eating disturbances such as pagophagia, a form of pica causing a pathological craving for ice. Such eating disturbances are often misrecognized leading to missed opportunities to detect anemia earlier.

Consequences of Anemia

The consequences of anemia are protean irrespective of gender, or age; some of the adverse outcomes are:[3]

- Decreased cognitive function.
- Decreased concentration and attention.
- Increased incidence of preterm delivery.
- Intrauterine growth retardation.
- Intrauterine fetal demise.
- Increased maternal and fetal infection risk.
- Disturbed post-partum maternal–infant interaction.
- Delayed growth and development.

More worrisome is a recent report by Congdon et al[4], that studied longitudinal outcomes of long-term effects of iron deficiency at birth on the neural correlates of recognition, memory and cognition in children and concluded, not only do iron deficient neonates have delayed growth and development but a statistically significantly increase in the number of cognitive and behavioral abnormalities up to ten years after iron repletion.[4]

Pregnancy

During pregnancy, physiologic changes such as hemodilution result in plasma volume expansion, estimated to be approximately 40-50% until the 30th week of gestation. In addition, a 20-30% increase in red blood cell mass is observed. This decrement in measured hemoglobin is complicated by iron deficiency at a time when there is increased maternal and fetal erythropoiesis. The preferential transfer of maternal iron to the fetus to meet red blood cell synthesis requirements, leads to further iron depletion. During delivery blood loss ranging from 250 mls to greater than 1000 mls further exacerbates the deficient state. With a blood loss at delivery of 250 mls, the total iron needed for an average pregnancy is 1,000 mg. This increases to approximately 1,375 mg with a 1,000 ml blood loss at delivery. When one considers that 30-40% of women have depleted iron stores at the beginning of pregnancy, the absolute need for iron supplementation during pregnancy becomes clear.

Postpartum

A hemoglobin level of less than 10 g/dl is seen as clinically significant post-partum anemia.[5] This is a combination of blood-loss anemia and pre-existing iron deficiency anemia. The nadir of the postpartum hemoglobin is typically reached about 48 hours after delivery. Serum ferritin cannot be used to assess iron stores since levels may be "false normal" or "false elevated" for the first few weeks after delivery. An

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accurate determination of residual iron stores can be assessed about 6 weeks or more after delivery, but isn't necessary when significant anemia is present since iron deficiency may be assumed.[4] Coexisting comorbidities such as multiparity, obesity, anemia during pregnancy, and age < 20 years, may delay recovery.[6,7] Socioeconomic factors, especially malnutrition, have a complex interplay in the development of post-partum anemia, supported by data from the Special Supplemental Nutrition program for women, infants and children's study. Of nearly 60, 000 participants, 27% overall, 40% of Hispanic, and 48% of African Americans were found to be anemic between 4-26 weeks postpartum, despite having normal hemoglobin levels during pregnancy.[6]

Heavy Uterine Bleeding

In premenopausal women, when menstrual blood loss exceeds 80 milliliters per cycle or lasts for more than 7 days, iron deficiency develops over time. In postmenopausal women, the prevalence varies widely, often due to multiple factors which include nutritional deficiencies such as folate or vitamin B12, gastrointestinal iron losses and anemia due to chronic inflammation.

Treatment

Irrespective of etiology the recognition of anemia and prompt attempts to identify and correct the problem are key to eliminating the symptoms associated with iron deficiency and decreased hemoglobin and rule out potentially dangerous causes, particularly in pot-menopausal women, such as undiagnosed malignancy. Iron supplementation should be individualized with special attention given to correcting hemoglobin to normal levels and replenishing iron stores.

Oral Iron

Oral iron is the current first line standard for mild anemia down to 9.5 g/dl or so, however, 70% of those to whom it is prescribed report significant gastrointestinal perturbation markedly limiting adherence. In such cases and when more severe anemia is present or when rapid correction is required, intravenous iron is preferred. Complete replacement dosing can now be administered in 15- 60 minutes. To date no serious adverse events have been reported in gravidas. In pregnant patients intolerant of, or unresponsive to, oral iron therapy, intravenous iron should be administered to rapidly meet the body's demands without the difficult gastrointestinal toxicities of nausea, vomiting, colicky abdominal pain, diarrhea and constipation.

IV Iron

There are currently five intravenous iron formulations approved for use in the USA. Low molecular weight iron dextran, sodium ferric gluconate, iron sucrose, ferumoxytol and ferric carboxymaltose, when administered according to recommended guidelines are all safe and effective. There are currently no data on ferumoxytol use in gravidas.

Breymann et al, in a study of 1 gram of iron sucrose administered in five divided doses to greater than 500 women of gestational age 16 weeks and older with a diagnosis of IDA, concluded this formulation was safe and efficacious for use in pregnancy and the post partum perio, supporting existing published data.[9]

Ayub et al, studied 100 women of gestational age greater than 12 weeks with a confirmed diagnosis of IDA and concluded that complete replacement dosing in a single setting, with low molecular weight iron dextran is an effective and safe method .[10]

This is supported in a recent publication by Auerbach et al, which evaluated the safety and efficacy of the rapid administration of 1 gram of low molecular weight iron dextran in 1 hour. In this study, 164 infusions in 157 pregnant women (second and third trimester), observed only four adverse reactions which resolved without intervention. These findings were consistent with the remaining study population.[11]

All currently available intravenous iron products are probably comparable in safety and efficacy though they differ in the amount of unbound iron and in their administration protocols and elimination kinetics. Cost and convenience to the patient regarding their administration should be taken into consideration when choosing a formulation. There are limited data regarding their administration in pregnancy regardless of which formulation is chosen.

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Reveiz et al, in the Cochrane database review of treatment of IDA in pregnancy, concluded that intravenous iron administration was superior to oral iron in achieving improvement in hemoglobin levels. Nonetheless unsubstantiated concerns about possible adverse effects such as thrombosis and allergic reactions were noted.[12] These concerns have not been supported, however, by published data over the last 5 -7 years.

In conclusion, anemia, and in particular IDA, has a prevalence that may exceed 30-40% in some populations with a negative impact on quality of life, increased morbidity and mortality, and an association with poor fetal outcomes. Its early recognition and treatment is a global issue and should be a high priority.

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