Iron deficiency and iron deficiency anemia in pregnancy

A. Kinga Malinowski MD MSc, Ally Murji MD MPH

■ Cite as: CMAJ 2021 July 26;193:E1137-8. doi: 10.1503/cmaj.210007

1 Iron deficiency and iron deficiency anemia are common during pregnancy and are associated with adverse outcomes Prenatal iron deficiency occurs in more than 30% of pregnancies in Canada.¹ It has been linked with low birth weight, small for gestational age size, preterm birth, need for blood transfusion for the mother, postpartum hemorrhage².³ and long-term neurocognitive effects in childhood.⁴

2 Symptoms are often dismissed as normal during pregnancy Symptoms include fatigue, weakness, dizziness, irritability, decreased stamina, hair loss and dyspnea, all of which are often attributed to the physiologic changes of pregnancy. Consequently, many patients go untreated, which increases maternal, fetal and neonatal health risks.^{3,5}

Table 1: Oral and parenteral iron preparations*					
Generic name	Brand name	Daily or alternate day dosing	Dose, mg	Elemental iron, mg/tab	Daily estimated cost, \$†
Oral iron					
Ferrous gluconate	Floradix, Floravit	1 to 2 tabs	300	35	0.10
Ferrous sulfate	Ferodan, Ferrotrate	1 tab	300	60	0.20
Ferrous fumarate	Palafer, EuroFer	1 tab	300	100	0.25
Ferrous bisglycinate	Ferrochel, CanPrev	1 tab	25	25	0.30
Polysaccharide iron complex	Feramax	1 tab	150	150	0.75
Heme iron polypeptide	OptiFerA, Proferrin	2 to 3 tabs	398	11	2.40
Parenteral iron					
Iron sucrose	Venofer	200–300 mg in a single dose over 2 h§		-	375
Ferric derisomaltose‡	Monoferric	500–1500 mg in a single dose over 30 to 60 min§		-	450-900

 * List does not include all available formulations.

†Cost will vary depending on geographic location and place of purchase; costs determined by Dr. Nastaran Ostad, Perinatal Pharmacist, Sinai Health System (personal communication, 2021).
‡Not yet approved for use in pregnancy; studies including pregnant and breastfeeding women are ongoing.
§Total parenteral iron replacement dose based on Ganzoni formula, which can then be divided into several doses based on individual product monographs for maximum per single dose): total iron dose (mg) = weight (kg) × [target hemoglobin – actual hemoglobin (g/dL)] × 2.4+iron stores (mg) [where iron stores for adults should consist of 500 mg]; to convert hemoglobin in g/L to g/dL, divide by 10.

Ferritin and hemoglobin should be routinely assessed at the initial and 28-week prenatal visits⁵

Ferritin < 30 ug/L is diagnostic for iron deficiency. Higher ferritin values in patients with inflammation or infection do not exclude iron deficiency.⁵ Anemia during pregnancy is diagnosed when the patient's hemoglobin level is < 110 g/L⁶ (with some suggesting hemoglobin < 105 g/L in the second trimester);² postpartum, it is diagnosed at hemoglobin levels < 100 g/L.⁵

Oral iron is the first-line treatment

Oral ferrous iron medications should contain 40–100 mg of elemental iron^{5,7} and be taken daily or every other day to mitigate adverse effects (Table 1).⁵ Enteric-coated or sustained-release products are not as well absorbed (i.e., onset of action is distal to the duodenum).5 To maximize absorption, patients should take oral iron with vitamin C (250-500 mg) on an empty stomach if tolerated, 1 hour before or 2 hours after calcium, proton pump inhibitors, antacids, thyroxine, tea, coffee, milk, soy and eggs.8 Response to oral iron should be evaluated by measuring the hemoglobin level 2-4 weeks after treatment begins.^{5,7} Treatment should continue for at least 3 months after the hemoglobin level normalizes until 6 weeks postpartum.5,7

5 Parenteral iron is safe and effective from the second trimester onward

Parenteral iron rapidly achieves the target hemoglobin with few adverse effects, and should be considered after the first trimester for patients with intolerance to oral therapy; a poor response (hemoglobin increase of < 10 g/L 2 wk after starting treatment or < 20 g/L after 4 wk); moderate-to-severe iron deficiency anemia (hemoglobin < 80 g/L); or iron deficiency anemia occuring within 4–6 weeks of anticipated delivery.⁷ A hematologist should be consulted if the patient has a hemoglobinopathy, such as thalassemia or sickle cell disease.

References

- Tang G, Lausman A, Abdulrehman J, et al. Prevalence of iron deficiency and iron deficiency anemia during pregnancy: a single centre Canadian study. Blood 2019;134(Suppl 1):3389.
- Young MF, Oaks BM, Tandon S, et al. Maternal hemoglobin concentrations across pregnancy and maternal and child health: a systematic review and meta-analysis. Ann NYAcad Sci 2019:1450:47-68.
- Peña-Rosas JP, De-Regil LM, Dowswell T, et al. Daily oral iron supplementation during pregnancy. Cochrane Database Syst Rev 2012;12:CD004736.
- 4. Georgieff MK. Iron deficiency in pregnancy. Am J Obstet Gynecol 2020;223:516-24.
- Pavord S, Daru J, Prasannan N, et al. UK guidelines on the management of iron deficiency in pregnancy. Br J Haematol 2020;188:819-30.
- Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System (WHO/NMH/NHD/ MNM/11.1). Geneva: World Health Organization; 2011. Available: https://www. who.int/vmnis/indicators/haemoglobin.pdf (accessed 2021 Jan. 3).
- Muñoz M, Pena-Rosas JP, Robinson S, et al. Patient blood management in obstetrics: management of anaemia and haematinic deficiencies in pregnancy and in the post-partum period: NATA consensus statement. *Transfus Med* 2018;28:22-39.
- Auerbach M. Patient education: Anemia caused by low iron in adults (beyond the basics). UpToDate; 2021 [updated 2021 Feb. 21].

Competing interests: A. Kinga Malinowski reports consulting and speaker fees for Pfizer and Alexion. Ally Murji reports consulting and speaker fees from Abbvie, Bayer and Pfizer.

This article has been peer reviewed.

Affiliations: Department of Obstetrics & Gynaecology (Malinowski, Murji), Sinai Health System; University of Toronto (Malinowski, Murji), Toronto, Ont.

Content licence: This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY-NC-ND 4.0) licence, which permits use, distribution and reproduction in any medium, provided that the original publication is properly cited, the use is noncommercial (i.e., research or educational use), and no modifications or adaptations are made. See: https://creativecommons.org/licenses/by-nc-nd/4.0/

Correspondence to: A. Malinowski, ann.malinowski@sinaihealth.ca

CMAJ invites submissions to "Five things to know about ..." Submit manuscripts online at http://mc.manuscriptcentral.com/cmaj