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Iron Salts

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Drug Levels and Effects

Summary of Use during Lactation

Iron is a normal component in human milk. Daily oral iron intake from prenatal vitamins or other multimineral supplements does not affect milk iron levels. Higher daily oral iron dosing has a minimal effect on milk iron levels and is not expected to cause harm to the breastfed infant if needed to treat the mother's anemia, but it is not an adequate substitute for direct infant iron supplementation to prevent or treat infant anemia.

Drug Levels

Iron is normally present in human breastmilk, with higher concentrations in hindmilk.[1] One-third of milk iron is found in the fat fraction bound to metalloproteins in the outer membrane of fat globules. Most of the remainder is in the whey fraction bound mostly to lactoferrin, but also to other proteins such as transferrin and to smaller ligands. About 10% of milk iron is bound to casein.[2] Quantities are highest in colostrum, and they decrease as lactation progresses. Reported average milk iron levels in the first postpartum week are about 1 mg/L, decreasing to a range of 0.4 to 0.9 mg/L during the first postpartum month, then 0.2 to 0.4 mg/L from 1 to 3 months, and 0.1 to 0.3 mg/L from 3 to 6 months.[1-4]

Mammary epithelial trace element active transporters regulate milk iron content and are believed to be responsible for insulating milk iron levels from changes in maternal iron status.[5] However, severe maternal malnutrition and anemia can lead to lower milk iron levels.

Maternal Levels. In a study of 75 postpartum women in India, the average milk iron level at 12 to 18 days postpartum was 0.69 mg/L in women with severe anemia, defined as a hemoglobin level ≤6 grams/dL during the third trimester, compared to 0.74 to 0.79 mg/L in those with less severe anemia, and 0.83 mg/L in those with hemoglobin ≥ 11grams/dL.[6]

A similar study in Cairo, Egypt reported an average milk level of 0.29 mg/L in malnourished, severely anemic mothers compared to 0.78 mg/L and 1.6 mg/L in mildly anemic and non-anemic mothers, respectively.[7]

A study of 212 non-malnourished and mostly non-anemic mothers in West Java, Indonesia identified a 1.9% and 0.4% change in milk iron concentration for every 1 gram/L change in maternal hemoglobin and 1 mcg/L change in serum ferritin, respectively, but milk iron levels were not associated with maternal dietary iron intake.[8] A lack of correlation between milk levels and maternal dietary iron intake has also been reported in similar studies.[9-11]

In 62 healthy and well-nourished, lactating mothers from Valencia, Italy taking 0 to 160 mg of supplemental elemental iron daily (exact doses not given), average milk iron levels were 0.57 mg/L and 0.5 mg/L on day 3 and day 15 postpartum, respectively. There was no linear relationship between iron dose and milk iron level.[1]

Forty-seven non-anemic, lactating mothers in Ankara, Turkey randomly received 80 mg elemental iron daily as ferrous sulfate or placebo beginning 10 to 20 days postpartum and continued for 4 months. Average milk iron levels changed from 0.58 mg/L at baseline to 0.37 mg/L at 4 months in the iron supplemented group, compared to 0.51 mg/L and 0.39 mg/L, respectively, in the placebo group. The difference in percent change from baseline between the two groups was not significant.[12]

Twenty-eight breastfeeding women in Rio de Janeiro, Brazil with normal baseline iron status who received oral iron supplements during pregnancy as part of their routine prenatal care were randomized to receive 40 mg elemental iron as ferrous sulfate or no iron, once daily beginning at 1 or 2 days postpartum and continuing for 3 months. Milk iron levels were approximately 1 mg/L in both groups at baseline. At 30 to 40 days postpartum, average milk iron levels were approximately 0.7 mg/L in both groups. At 90 to 100 days, milk levels were 0.7 mg/L in the supplemented group and 0.55 mg/L in the nonsupplemented group, but were not significantly different. However, the percentage of milk protein as lactoferrin was significantly higher in the supplemented group.[13] High milk lactoferrin has also been reported in populations with high dietary iron intake.[2] The clinical relevance of this observation is not established.

Among 145 healthy women between 20 and 60 days postpartum in Marilia, Brazil who donated breastmilk to a milk bank, those who reported taking an iron supplement during lactation had average milk iron levels of 0.3 mg/L compared to 0.4 mg/L in those who did not take an iron supplement. The exact doses of those in the iron group were not given.[14]

Thirty-two exclusively breastfeeding and well-nourished women in Warsaw, Poland who were 4 to 6 weeks postpartum provided 4 milk samples in a single day in addition to completing an extensive dietary history. Almost half of the participants reported taking a dietary supplement that contained a low dose of iron, around 30 mg or less daily. The average milk iron level in the entire group was 0.39 mg/L. Milk iron level was not correlated with the maternal supplemental iron dose, but was correlated with the total iron intake from food and supplement.[15]

Nineteen well-nourished but mildly anemic lactating mothers from Trujillo, Peru were given 100 mg elemental iron as ferrous sulfate once daily beginning on postpartum day 2. Average milk iron level was 0.90 mg/L at baseline and 0.38 mg/L at 30 days postpartum, compared to 0.8 mg/L and 0.35 mg/L, respectively in 10 other non-anemic lactating mothers who did not receive supplementation. Because no anemic control group was included in the study it is not clear if iron supplementation made a difference, although milk levels in the anemic group were not significantly different from the non-anemic group at 30 days which would indicate such an intervention is at least safe.[16]

Sixty-five healthy women in Copenhagen, Denmark with postpartum hemorrhage within 48 hours of delivery were randomized to receive oral or intravenous iron to improve hematopoietic recovery. Women randomized to the oral group received an average of 45 mg elemental iron daily (salt form not stated) in the first three days of the study as they transitioned from their prenatal vitamins to high-dose oral supplementation, and then 90 mg daily from day 4 to day 8. Milk was collected 2 to 4 days after iron initiation and again at 6 to 8 days. Average milk levels were 0.4 mg/L and 0.44 mg/L, respectively.[17]

In a U.S. study of 63 postpartum, lactating, mostly white, women taking a daily prenatal or multivitamin, those on a vegan or vegetarian diet had similar milk iron levels to those on an omnivore diet.[18]

Infant Levels. One-hundred thirty-one non-anemic, lactating mothers in Ankara, Turkey randomly received 80 mg elemental iron daily as ferrous sulfate or placebo beginning 10 to 20 days postpartum and continued for 4 months. Average serum iron levels in the iron group infants at 4 months was 0.4 mg/L compared to 0.46 mg/L in the placebo group.[19]

In a study of 1066 breastfeeding infants born to mothers living in rural Bangladesh who randomly received 30 mg or 60 mg elemental iron as ferrous fumarate once daily beginning during their second trimester and continuing postpartum, there were no differences in the frequency of infant anemia, or blood iron indices, at 6 months postpartum between the groups.[20]

Effects in Breastfed Infants

One-hundred thirty-one non-anemic, lactating mothers in Ankara, Turkey randomly received 80 mg elemental iron as ferrous sulfate daily or placebo beginning 10 to 20 days postpartum and continued for 4 months. Hematological indices and biochemical iron status values were no different between the two groups of infants at the end of the study.[19]

Effects on Lactation and Breastmilk

Iron-enriched human milk fortifier intended for preterm hospitalized infants increases milk microbial growth compared to iron-free fortifier under *in vitro* experimental conditions.[21] The clinical consequences of these findings have not been evaluated. Such studies tested milk iron concentrations in the range of 13 to 14 mg/L which were common for fortifiers in the countries where the studies were conducted. Currently available U.S. premature infant milk fortifier provides a much lower iron supplemental dose resulting in a milk iron level of 3 mg/L above the mother's underlying milk level.

Alternate Drugs to Consider

Ferric Carboxymaltose, Ferric Derisomaltose, Iron Sucrose

References

1. Silvestre MD, Lagarda MJ, Farré R, et al. A study of factors that may influence the determination of copper, iron, and zinc in human milk during sampling and in sample individuals. Biol Trace Elem Res 2000;76:217-27. PubMed PMID: 11049220.
2. Lönnerdal B. Iron and breastmilk. In: Stekel A, ed. Iron nutrition in infancy and childhood. New York: Raven Press; 1984:95-117.
3. Dorea JG. Iron and copper in human milk. Nutrition 2000;16:209-20. PubMed PMID: 10705077.
4. Trinta VO, Padilha PC, Petronilho S, et al. Total metal content and chemical speciation analysis of iron, copper, zinc and iodine in human breast milk using high-performance liquid chromatography separation and inductively coupled plasma mass spectrometry detection. Food Chem 2020;326:126978. PubMed PMID: 32413760.
5. Lönnerdal B. Trace element transport in the mammary gland. Annu Rev Nutr 2007;27:165-77. PubMed PMID: 17506666.
6. Kumar A, Rai AK, Basu S, et al. Cord blood and breast milk iron status in maternal anemia. Pediatrics 2008;121:e673-7. PubMed PMID: 18310187.
7. El-Farrash RA, Ismail EA, Nada AS. Cord blood iron profile and breast milk micronutrients in maternal iron deficiency anemia. Pediatr Blood Cancer 2012;58:233-8. PubMed PMID: 21548016.

8. Gibson RS, Rahmannia S, Diana A, et al. Association of maternal diet, micronutrient status, and milk volume with milk micronutrient concentrations in Indonesian mothers at 2 and 5 months postpartum. Am J Clin Nutr 2020;112:1039-50. PubMed PMID: 32844187.
9. Daniels L, Gibson RS, Diana A, et al. Micronutrient intakes of lactating mothers and their association with breast milk concentrations and micronutrient adequacy of exclusively breastfed Indonesian infants. Am J Clin Nutr 2019;110:391-400. PubMed PMID: 31152543.
10. Dror DK, Allen LH. Overview of nutrients in human milk. Adv Nutr 2018;9 (Suppl 1):278S-294S. PubMed PMID: 29846526.
11. Domellöf M, Lönnerdal B, Dewey KG, et al. Iron, zinc, and copper concentrations in breast milk are independent of maternal mineral status. Am J Clin Nutr 2004;79:111-5. PubMed PMID: 14684406.
12. Yalçin SS, Baykan A, Yurdakök K, et al. The factors that affect milk-to-serum ratio for iron during early lactation. J Pediatr Hematol Oncol 2009;31:85-90. PubMed PMID: 19194189.
13. Zapata CV, Donangelo CM, Trugo NMF. Effect of iron supplementation during lactation on human-milk composition. J Nutr Biochem 1994;5:331-7. doi:10.1016/0955-2863(94)90062-0
14. Mello-Neto J, Rondo PH, Oshiiwa M, et al. Iron supplementation in pregnancy and breastfeeding and iron, copper and zinc status of lactating women from a human milk bank. J Trop Pediatr 2013;59:140-4. PubMed PMID: 23070740.
15. Bzikowska-Jura A, Sobieraj P, Michalska-Kacymirow M, Wesołowska A. Investigation of iron and zinc concentrations in human milk in correlation to maternal factors: An observational pilot study in Poland. Nutrients 2021;13:303. PubMed PMID: 33494328.
16. Zavaleta N, Nombera J, Rojas R, et al. Iron and lactoferrin in milk of anemic mothers given iron supplements. Nutr Res 1995;15:681-90. doi:10.1016/0271-5317(95)00035-h
17. Holm C, Thomsen LL, Norgaard A, et al. Iron concentration in breast milk normalised within one week of a single high-dose infusion of iron in randomised controlled trial. Acta Paediatr 2017;106:256-60. PubMed PMID: 27883237.
18. Perrin MT, Pawlak R, Judd N, et al. Major and trace mineral composition of milk from lactating women following vegan, vegetarian and omnivore diets. Br J Nutr 2023;130:1005-12. PubMed PMID: 36562211.
19. Baykan A, Yalçın SS, Yurdakök K. Does maternal iron supplementation during the lactation period affect iron status of exclusively breast-fed infants? Turk J Pediatr 2006;48:301-7. PubMed PMID: 17290563.
20. Eneroth H, El Arifeen, S, Persson LA, et al. Maternal multiple micronutrient supplementation has limited impact on micronutrient status of Bangladeshi infants compared with standard iron and folic acid supplementation. J Nutr 2010;140:618-24. PubMed PMID: 20053938.
21. Taylor SN. ABM Clinical Protocol #29: Iron, zinc, and vitamin D supplementation during breastfeeding. Breastfeed Med 2018;13:398-404. PubMed PMID: 30016173.

Substance Identification

Substance Name

Iron Salts

CAS Registry Number

7439-89-6

Drug Class

Breast Feeding

Lactation

Milk, Human

Ferrous Compounds

Hematinics

Iron Compounds

Minerals