Why symptoms of iron deficiency are often missed in young women and girls.

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By Linda Carroll

Doctors don't typically screen for it, but almost 40% of teenage girls and young women had low levels of the important mineral needed to make red blood cells, new research shows.

An underdiagnosed deficiency of an essential mineral may be contributing to fatigue, brain fog and concentration problems in almost 1 in 4 adolescent girls and young women in the United States.

Almost 40% of American teenage girls and young women had low levels of iron, an important mineral needed to make red blood cells, a study published this week in JAMA found. It's the first research to look at iron deficiency in young women and adolescent girls.

For the study, researchers at the University of Michigan Medical School pulled data on girls and women ages 12-21 collected over the last 20 years from the National Health and Nutrition Examination Survey, part of the Centers for Disease Control and Prevention. They found 6% of the survey's sample had iron-deficiency anemia.

The findings weren't a surprise to pediatric hematologist-oncologist Dr. Angela Weyand, the lead author, and an associate professor of pediatrics at the University of Michigan Medical School in Ann Arbor. She often gets referrals from pediatricians and primary care physicians who suspect their patients might have an iron deficiency. She wondered how common the problem was.

“I hypothesized that I was just seeing the tip of the iceberg and unfortunately that is true,” Weyand said.

The CDC recommends a blood test for anemia every five to 10 years for women of reproductive age, but doctors don’t typically screen for iron deficiency. Weyand and her colleagues haven’t yet checked to see if iron deficiency is on the rise or has been consistently high for the last two decades.

What are symptoms of iron deficiency?

Often girls and young women don’t realize that what they’re feeling is a sign of an iron deficiency because the symptoms can be subtle or can be dismissed as being due to other problems like poor sleep, she said.

According to Weyand, symptoms of iron deficiency include:

- Fatigue.
- Cold extremities.
- Hair loss.
- Brittle nails.
- Cognitive issues like brain fog.
- Decreased athletic performance.
- Shortness of breath with exertion.
- Junk food cravings.
- Headache, lightheadedness.
- Sleep disorders.

Menstruation was a risk factor, although a quarter of the girls who hadn't started their periods yet had iron deficiency, the data showed. Women and girls lose a lot of iron when they have heavy periods, but even when bleeding is in the normal range, iron stores can be depleted, Weyland said.

Those with low iron levels are often not discovered because doctors often test only for anemia, rather than the level of ferritin, a blood protein that contains iron and is a marker for stored iron, she said.

Think of ferritin as an indicator of how much is in your “iron savings account,” said Dr. Rachel Bercovitz, an associate professor of pediatrics at Northwestern University’s Feinberg School of Medicine and an attending hematologist at the Ann & Robert Lurie Children’s Hospital of Chicago. She was not involved in the new research.

“The iron we take in every day goes into a checking account where it’s used to make new blood cells and other things that need iron,” she said. “If any is left over, it goes into the savings account. If you’re living from paycheck to paycheck with iron, you may not be able to keep up and have a surplus for when you’re having your period.”

Many of the symptoms girls experience are related to the impact of iron deficiency on hemoglobin, a protein in the blood. “Iron is the key ingredient in hemoglobin and essentially red blood cells are bags of hemoglobin that carry oxygen to tissues," Bercovitz said. "When there’s not enough iron, fewer red blood cells are made, which is why you see symptoms like dizziness, headache, shortness of breath and fatigue.”

Those symptoms can be a big problem for teenagers, said Dr. Allison Wheeler, an associate professor in the department of pathology, microbiology and immunology at the Vanderbilt University Medical Center. Wheeler was not involved in the new research.
“There are significant consequences especially in the adolescent age cohort where fatigue and poor concentration can lead to poor school performance,” she said. “And poor athletic performance can lead to changes in how girls think about exercise.”

Many women and girls with heavy periods — which experts blame for especially low ferritin levels — don't know it's not normal because of stigma and discomfort talking about their periods, Bercovitz said. "People don't tend to talk about how many times a day they're changing pads or if they're having leakage overnight," she said. "They're not talking with friends and sometimes not even with family members."

What's a normal period and what's heavy?
It's hard to draw an exact line. "But, if you're changing your pad or tampon more often than every four to six hours, or if you have to sleep on a towel or use overnight pads plus period underwear because you leak, that's heavy," Bercovitz said.

There are a number of ways to keep your iron stores at a healthy level.
"You can add leafy green vegetables or meat to your diet," she said. "Even cooking in a cast iron skillet can increase the iron in your food. If you're still not getting enough iron in your diet, then iron supplementation would be a good idea."

Other foods high in iron include:

- Eggs.
- Seafood, such as tuna or sardines.
- Tofu.
- Beans.

Studies have shown that an iron supplement every other day works for people with mild iron deficiency and anemia. Taking them three days a week rather than every day will lead to fewer side effects, such as abdominal pain or a bad taste in the mouth.
"Some people have abdominal pain. The supplements can also cause constipation and occasionally diarrhea. Some people experience nausea, which is why it's important to take them with food," Bercovitz said.

She advises not taking the supplements with calcium-rich foods because calcium can block the absorption of iron.

"You can increase the amount of iron absorbed by taking supplements with a cup of orange juice," Bercovitz added.

Another approach is to use birth control pills or other methods that can reduce bleeding during menstruation.

Because doctors typically do not measure ferritin, women need to advocate for themselves, Wheeler said.

"There's a lot of stigma around menstrual bleeding and it's important that we talk about it in detail," she added. "And it's important that we as physicians listen to and trust our patients."

Key Points

Physician's Guide to Oral Iron Supplements Iron Deficiency

- Taking iron with food impairs absorption by 40-66%.
- Taking quantities of iron every day up-regulates a system involving hepcidin that blocks iron absorption for about 24 hours. It may be best to take iron every other day.
- Taking iron more than once a day has limited positive benefit and may make digestive symptoms worse.
- The best dosage at least for women seems to be about 40-80mg per dose. Take the iron on an empty stomach with about 500mg of vitamin C.
- Hemoglobin usually increases within 2-3 weeks of starting iron. Therapeutic doses should increase hemoglobin levels by 0.7-1.0 g/dL per week.
- Adequate iron is reflected in a serum ferritin of 100ug/L.
- Oral iron supplements must dissolve rapidly in the stomach so that the iron can be absorbed in the duodenum and upper jejunum.
- Do not use enteric coated iron as these may not dissolve in the stomach.
- Vitamin C enhances iron absorption by forming a chelate with ferric iron at an acid pH that remains soluble at the alkaline pH of the duodenum.
- Avoid caffeinated beverages, especially tea when you take the iron. Minimize calcium containing foods and beverages when you take the iron. The same is true of calcium supplements. Again, it might be best to take the iron on an empty stomach.
- Avoid antacids and acid blockers when taking iron.
- Consider taking betaine HCL when you take the iron to ensure acidification of the stomach.
- The average male has about 1000mg of stored iron in the body- enough for about 3 years. The average female, 300mg- enough for about 6 months.
- Males of average height have about 4000mg of iron total in the body. Females have about 3500 mg.

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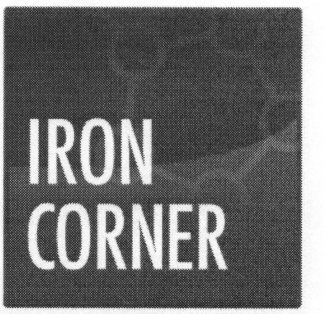

Physician's Guide to Oral Iron Supplements

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Introduction

Anemia is a common medical problem that is frequently diagnosed and treated by family physicians. Iron deficiency, the most common cause of anemia, may be treated with oral iron supplements, or less frequently with parenteral iron. Supplements are especially important when an individual is experiencing clinical symptoms of iron deficiency anemia. The goal of providing oral iron supplements is to supply sufficient iron to restore normal iron stores and replenish hemoglobin deficits. Oral supplements are most cost effective and may be only form of iron in resource-poor settings. Oral supplements are usually preferred method in children and adolescents. Use of oral iron avoids need for intravenous access and a monitored infusion setting.

Doctor William Ershler, formerly a hematologist at the National Institute of Health stated, "Once a physician has determined a diagnosis of iron deficiency anemia, searching for the cause of that anemia is as important, if not more important, than correcting the anemia. Initiating a work-up to get to the cause of the diagnosis may uncover a potentially curable cancer before it progresses. Referral to a gastroenterologist or hematologist may be necessary if the etiology of the anemia is not easily detectable."

In order for oral iron therapy to effectively resolve iron deficiency anemia, patients must receive and absorb an adequate dose of elemental iron. Since most oral iron preparations are non-prescription, physicians must provide their patients with adequate education to ensure that they are choosing the right iron, taking it at the right time, and minimizing the common side effects that can often lead to discontinuation of therapy.

For adults who are not pregnant, the Centers for Disease Control and Prevention (CDC) recommends 50-60 mg of oral elemental iron twice daily for three months for the therapeutic treatment of iron deficiency anemia.[1] However, this dosing regimen has recently been questioned. Iron supplements of 60 mg Fe as $FeSO_4$ increase hepcidin for up to 24 hours and are associated with lower iron absorption on the following day.[2] The data showed that fractional absorption in iron-depleted women is highest at low iron doses (40-80 mg) and that acute, consecutive -day dosing results in decreased iron bioavailability. Twice daily supplementation seems to have limited additional effect compared with daily administration and may increase gastrointestinal side-effects. In fact, alternate-day schedules of iron administration may maximize fractional absorption, increase dosage efficacy, reduce gastrointestinal exposure to unabsorbed iron and ultimately improve tolerance of iron supplements.[3,4]

Over-the-Counter Iron Supplements Contain Varying Amounts of Iron (examples)

Iron Supplement	Tablet Size	Elemental Iron

Ferrous fumarate	325 mg	108 mg
Ferrous sulfate	325 mg	65 mg
Ferrous gluconate	325 mg	35 mg
Iron bisglycinate		25 mg
Iron Protein Succinylate	300 mg	18 mg

Iron Supplements

There are a large number of iron preparations available with various amounts of iron, iron salts, complexes, combinations, and dosing regimens. They are available in regular tablets and capsules, liquid and drops, coated and extended release tablets and capsules. Oral iron preparations are available in both ferrous and ferric states. The most commonly available oral preparations include ferrous sulfate, ferrous gluconate and ferrous fumarate. All three forms are well absorbed but differ inelemental iron content. Ferrous sulfate is the least expensive and most commonly used oral iron supplement.[6] Studies have shown that Iron bisglycinate and iron protein succinylate are associated with less gastrointestinal intolerance than ferrous sulfate, gluconate and fumarate for a comparable dose of elemental iron but are more expensive.[5]

Compliance and Effectiveness

According to Ershler, "It is very important to follow up with your patients after starting oral iron therapy. Compliance is a huge problem; many patients simply cannot take oral iron. Asking patients specific questions about how, when, and how often they take their iron therapy coupled with a laboratory work-up will help determine compliance. Patients who are unable to complete a course of oral iron can be treated with an intravenous iron agent. The newer IV irons are safe and effective and an excellent alternative for these patients."

The effectiveness of iron supplementation is determined by measuring laboratory indices, including reticulocyte count, hemoglobin and ferritin levels. The reticulocyte hemoglobin content in picograms is an early indicator of a response to iron therapy, increasing within a few days of initiating therapy. Hemoglobin usually increases within 2-3 weeks of starting iron supplementation. Therapeutic doses of iron should increase hemoglobin levels by 0.7-1.0 g/dL per week. Reticulocytosis occurs within 7-10 days after initiation of iron therapy.[7] Serum ferritin level is a more accurate measure of total body iron stores. Adequate iron replacement has typically occurred when the serum ferritin level reaches 100 µg/L. If patients with iron deficiency anemia do not begin to respond to iron supplementation within a few weeks, the patient should be re-evaluated for blood loss, noncompliance or poor absorption.

One common reason for iron therapy treatment failure is ineffective iron intake. This could be due to non-compliance, under-dosing, or a failure to absorb iron from the supplement. Iron uptake and absorption may be impaired by malabsorption states, as well as the concomitant use of medications and ingestion of foods that inhibit iron absorption.[7] Some of the factors that affect the absorption of iron supplements are listed in the next section.

Factors that Affect the Absorption of Iron Supplements

Oral iron supplements must dissolve rapidly in the stomach so that the iron can be absorbed in the duodenum or upper jejunum. Enteric-coated reparations and long-acting supplements may be ineffective, since they do not dissolve in the stomach.[5]

Ascorbic acid is an enhancer of iron absorption and can reverse the inhibiting effects of substances such as tea and calcium. Ascorbic acid facilitates iron absorption by forming a chelate with ferric iron at acid pH that remains soluble at the alkaline pH of the duodenum.[8]

To minimize side effects, iron supplements are often taken with food. This may decrease iron absorption by as much as 40-66%.[7]

Food and drug interactions may reduce the efficacy of oral iron.

The primary reason for failure of iron therapy is poor compliance, often related to the frequent gastrointestinal side effects of oral iron. In those circumstances in which ongoing comorbid conditions are absent, blood loss mitigated, and lack of significant gastrointestinal side effects manifest, oral iron is very inexpensive, safe and effective. However, a recent meta-analysis covering thousands of patients treated with oral iron reported an incidence of 70% of significant gastrointestinal side effects associated with decrements in adherence.[9]

Physicians can help minimize the risk of treatment failure through the proper selection and dosing of iron supplements along with educating patients on strategies to maximize iron absorption, manage side effects, and improve compliance. Effective iron supplementation can help patients to relieve the symptoms of iron deficiency anemia, improve quality of life and improve their well-being.

There is a growing body of evidence supporting superior outcomes with intravenous iron, especially in the chronic kidney disease and chronic heart failure populations. One should not hesitate to move to intravenous iron early

as an alternative treatment when gastrointestinal intolerance, a poor response or non-adherence to oral iron is encountered. In many cases, one can expect an improved, faster, more convenient and less toxic outcome.[10]

Foods and Drugs that Impair Iron Absorption

- Taking oral iron with food reduces absorption
- Caffeinated beverages (especially tea)
- Calcium containing foods and beverages
- Calcium supplements
- Antacids
- H-2 receptor blockers

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