

## Physician's Guide to Oral Iron Supplements

### 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.

### 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

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.<sup>1</sup> However, this dosing regimen has recently been questioned. Iron supplements of 60 mg Fe as FeSO<sub>4</sub> increase hepcidin for up to 24 hours and are associated with lower iron absorption on the following day.<sup>2</sup> 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.<sup>3,4</sup>

### 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 in elemental iron content. Ferrous sulfate is the least expensive and most commonly used oral iron supplement.<sup>6</sup> 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.<sup>5</sup>

## 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.<sup>7</sup> 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.<sup>7</sup> 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 preparations and long-acting supplements may be ineffective, since they do not dissolve in the stomach.<sup>5</sup>

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.<sup>8</sup>

## 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

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

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.<sup>9</sup>

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.

# IRON CORNER

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.<sup>10</sup>

## References

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