Categories of Oral Iron

Summary

There is great interest in the development of compounds better tolerated than iron salts; numerous compounds have been proposed (eg, sucrosomial iron, heme iron polypeptide, iron containing nanoparticles), but studies are limited. Sucrosomial iron has been tested in patients with CKD, but the mechanism of absorption and the real benefits are uncertain. In the same condition, the phosphate binder iron ferric citrate simultaneously corrects both hyperphosphatemia and iron deficiency; its double effect is being tested in a clinical trial in CKD. A phase 3 trial of ferric maltol provided positive results on iron deficiency anemia in inflammatory bowel diseases. Rigorously designed clinical trials are needed to confirm the efficacy of these iron preparations.

Iron Salts

Ferrous sulfate, ferrous fumarate, and ferrous gluconate are the iron salt formulations most commonly prescribed for treatment of iron deficiency anemia in otherwise healthy patients, given their general availability, and low cost. However, expect a discontinuation or non-compliance rate of as high as 30-40% due to gastrointestinal side effects. In patients with co-morbid conditions associated with inflammation and an increase in hepcidin, ferrous sulfate (as well as other iron salts and, to a great degree, oral iron in general) will be ineffective. An increase in the dose of oral iron in an effort to increase absorption will only result in increased gastrointestinal toxicity.

Ferrous sulfate is generally ineffective in the immediate post-surgical setting due to post-surgical inflammation, and may contribute to a prolongation in post-operative ileus.

Carbonyl Iron and Polysaccharide-iron Complex

Carbonyl iron is available in the U.S. as Feosol with Carbonyl Iron. This is not an iron salt, but rather microparticles of elemental iron. It requires an acidic environment in the stomach for the microparticles to dissolve and form a hydrochloride salt.

It does not appear to offer a significant advantage over ferrous sulfate other than less poisoning potential in children. Niferex is a polysaccharide iron complex consisting of ferric iron complexed to hydrolyzed starch. It is promoted to cause less GI irritation, but the claim is unproven.

Heme Iron

A heme iron polypeptide is commercially available and marketed in the United States as *Proferrin ES* or *Proferrin Forte* (combined with 1 mg of folate and therefore requiring a prescription). This product is made from hemoglobin extracted from cow red blood cells.

Data suggest that heme iron is better tolerated and better absorbed than iron salts. However, like other oral iron supplements, bioavailability of the iron moiety is limited in patients with inflammation and elevated hepcidin levels.

Heme iron is an excellent alternative to ferrous sulfate in otherwise healthy patients with iron deficiency, who are intolerant to iron salts. It is significantly more expensive.

Iron Amino Acid Chelates

These iron products consist of a conjugate of ferrous iron with an amino acid, typically glycine. Products marketed in the United States include *Easy Iron, Gentle Iron,* and *Ferrochel* (combined with calcium, vitamin B12, vitamin C, and folate).

There are some data suggesting higher bioavailability than iron salts in otherwise healthy, iron deficient patients. The iron amino acid chelates appear less likely to cause gastrointestinal intolerance than the iron salts and represent another (and only modestly more expensive) alternative to ferrous sulfate.

IRON CORNER

Iron Protein Succinylate (IPS)

These iron products are a form of ferric iron bound with a chemically modified protein (casein) via succinylation that stabilizes the complex. IPS is insoluble at low pH and becomes soluble in the duodenum due to hydrolysis of the protein moiety at the higher pH in the duodenum. Studies have shown a significantly lower rate of adverse events compared to ferrous fumarate, ferrous sulfate, ferrous gluconate and ferrous glycine.[1] Efficacy may be superior to the ferrous salts as well. A number of formulations are available without prescription in the United States including Ferrets IPS, Ironsorb, and Iron Protein Plus.

Novel Irons

Microencapsulated iron pyrophosphate

Microencapsulated iron pyrophosphate in liposomal form is a novel advancement in management of iron deficiency anemia. This salt is "generally recognized as safe (GRAS)" by United States Food and Drugs Administration (USFDA) Code of Federal Regulation. Furthermore, European Food Safety Authority (EFSA) has also declared iron pyrophosphate to be a safe food additive.[1,2] Comparatively to conventional oral iron salts, microencapsulated liposomal iron has the highest bioavailability. It leads to quicker increase in serum hemoglobin levels, its taste has better palatability, and it doesn't have unwanted effects such as heartburn, GI upset, and constipation.

Sucrosomial Iron Chemical

Sucrosomial iron is an oral iron preparation consisting of ferric pyrophosphate protected by a phospholipid bilayer membrane made up of primarily a sunflower lecithin.[1] Preclinical data have shown that sucrosomial iron retains the iron in the sucrosome when in stomach acid, which allows intact sucrosomes to reach the small intestine where they are absorbed. A randomized open-label trial evaluated oral sucrosomial iron in non dialysis dependent patient with iron deficiency anemia.[3] Patients were randomized 2:1 to receive oral sucrosomial iron 30 mg/d for 3 months or IV ferrous gluconate 125 mg/wk to a total dose of 1000 mg, with follow-up of 4 months. The study indicated that short-term oral sucrosomial iron was as effective as IV ferrous gluconate at correcting anemia, with a favorable tolerability profile. Sucrosomial iron also has been evaluated in several other clinical settings, including IDA associated associated with pregnancy, inflammatory bowel disease, celiac disease, cancer, and bleeding.[3,4]

Recommended References

Pergola PE, Fishbane S, Ganz T. Novel Oral Iron Therapies for Iron Deficiency Anemia in Chronic Kidney Disease. *Adv Chronic Kidney Dis*. 2019;26(4):272-291. doi:10.1053/j.ackd.2019.05.002

Girelli, D., Ugolini, S., Busti, F. *et al.* Modern iron replacement therapy: clinical and pathophysiological insights. *Int J Hematol* **107,** 16–30 (2018). https://doi.org/10.1007/s12185-017-2373-3

Hussain U, Zia K, Iqbal R, *et al.* (May 07, 2019) Efficacy of a Novel Food Supplement (Ferfer®) Containing Microencapsulated Iron in Liposomal Form in Female Iron Deficiency Anemia. *Cureus* 11(5): e4603

Additional References

1. Cancelo-Hidalgo MJ, Castelo-Branco C, Palacios S, *et al.* Tolerability of different oral iron supplements: a systematic review. *Curr Med Res Opin*. 2013;29(4):291-303. doi:10.1185/03007995.2012.761599

2. Pasricha SR, Tye-Din J, Muckenthaler MU, Swinkels DW. Iron deficiency. *Lancet.* 2020 Dec 4:S0140-6736(20)32594-0

3. Brilli E., Romano A *et al* Sucrosomial technology is able to promote ferric iron absorption: pre-clinical and clinical evidences. *Blood.* 2016; 128: 3618

4. Pisani A.,Riccio E.*et al*. Effect of oral liposomal iron versus intravenous iron for treatment of iron deficiency anaemia in CKD patients: a randomized trial. *Nephrol Dial Transpl.* 2015; 30: 645-652

5. Elli L. Ferretti F. Branchi F. *et al.*Sucrosomial iron supplementation in anemic patients with celiac disease not tolerating oral ferrous sulfate: a prospective study.*Nutrients.* 2018; 10: 330

6. Parisi F, Berti C. *et al*. Effects of different regimens of iron prophylaxis on maternal iron status and pregnancy outcome: a randomized control trial. *J Matern Fetal Neonatal Med.* 2017; 30: 1787-1792

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