Low-dose iron supplementation was effective in older patients with iron-deficiency anemia

Rimon E, Kagansky N, Kagansky M, et al. **Are we giving too much iron? Low-dose iron therapy is effective in octogenarians.** Am J Med. 2005;118:1142-7.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Geriatrics ★★★★★☆☆ Hematol/Thrombo ★★★★★★☆

QUESTION

In older patients with iron-deficiency anemia, can low-dose iron supplementation safely replace conventional doses of iron?

METHODS

Design: Randomized controlled trial.
Allocation: Unclear allocation concealment.*
Blinding: Unblinded.*
Follow-up period: 60 days.
Setting: A geriatric ward in a hospital in Rehovot, Israel.
Patients: 90 patients ≥ 80 years of age (mean age 85 y, 59% women) who were admitted to hospital with a diagnosis of anemia (hemoglobin level 80 to 119 g/L [5.0 to 7.4 mmol/L]) and ferritin levels < 40 ng/mL. Exclusion criteria were vitamin B_{12} deficiency, severe systemic illness, cancer, renal failure, iron therapy or blood transfusion within the previous week, celiac disease, active known gastrointestinal blood loss, or acute infection.
Intervention: Elemental iron, 15 mg (n = 30), 50 mg (n = 30), or 150 mg (n = 30) per day. Low iron doses (15 and 50 mg) were given as liquid ferrous gluconate in a simple syrup. The conventional iron dose (150 mg) was given as 1 tablet of 500 mg of ferrous calcium citrate taken 3 times/d.
Outcomes: Change from baseline in hemoglobin and ferritin levels and adverse effects.
Patient follow-up: 75 patients (83%) completed the study.

MAIN RESULTS

Serum hemoglobin and ferritin levels increased in all 3 groups, with no differences in increase among them (Table 1). Patients who received 150 mg of daily iron had a greater rate of all adverse effects than patients who received 15 mg (Table 2) and a greater rate of nausea and vomiting and black stools than patients who received 50 mg ($P < 0.05$). Abdominal discomfort, diarrhea, constipation, darkened stools, and black stools were more common in the 50-mg group than in the 15-mg group ($P < 0.05$).

CONCLUSIONS

In older patients with iron-deficiency anemia, increases in hemoglobin levels did not differ between those receiving low-dose (15 or 50 mg/d) and conventional-dose (150 mg/d) iron supplementation. The lowest dose was associated with fewest adverse effects.

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For correspondence: Dr. E. Rimon, Kaplan Medical Center, Rehovot, Jerusalem, Israel. E-mail efraim_r@clalit.org.il.

*See Glossary.

Table 1. 15, 50, and 150 mg/d of elemental iron for iron-deficiency anemia at 60 days†

Outcomes	Mean values (baseline)		
	15 mg	50 mg	150 mg
Hemoglobin (g/dL)	11.3 (10.0)	12.3 (10.9)	11.6 (10.2)
Ferritin (ng/mL)	60.2 (19.8)	61.4 (25.1)	66.3 (22.2)

†Increase from baseline was significant for all 3 groups and did not differ between groups.

Table 2. Adverse effects of 15 vs 150 mg/d of elemental iron for iron-deficiency anemia at 60 days‡

Outcomes	15 mg	150 mg	RRR (95% CI)	NNT (CI)
Abdominal discomfort	20%	70%	71% (43 to 87)	2 (2 to 4)
Nausea or vomiting	13%	67%	80% (53 to 92)	2 (2 to 4)
Diarrhea	13%	70%	81% (56 to 93)	2 (2 to 4)
Constipation	0%	23%	100% (50 to 100)	5 (3 to 10)
Darkened stools	44%	91%	52% (30 to 70)	3 (2 to 5)
Black stools	0%	67%	100% (83 to 100)	2 (2 to 3)

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

Rimon and colleagues showed that the conventional dose of iron supplementation (150 mg/d) was associated with more side effects and discontinuations than low-dose iron supplementation (15 mg/d). However, the increase in hemoglobin levels at 60 days of follow-up was similar in the low- and conventional-dose iron supplementation groups.

Some caution should be exercised with respect to the results because the 150-mg dose was administered as ferrous calcium citrate tablets, which may have more side effects and lower proportional absorption than the liquid ferrous gluconate used for the 15-mg and 50-mg doses (1). However, the 50-mg group had more side effects and discontinuations than the 15-mg group, suggesting that the side effects were primarily related to the dose of iron rather than the formulation.

Although more patients discontinued treatment in the 150-mg group (27%) than in the 15-mg group (6.7%), the mean increase in hemoglobin level was similar in the 2 groups. Thus, this increase may be higher in patients who comply with the 150-mg dose than in those who comply with the 15-mg dose. It is also unclear what difference would be observed between the 2 groups if the study was continued for 4 to 6 months, which may be necessary to correct anemia. At the end of the study, the mean hemoglobin level was still low in all 3 groups (although improved from study initiation).

This study expands clinicians' options for iron supplementation in older patients. Iron supplementation can be started at 15 mg/d and increased if there is inadequate response in hemoglobin levels (since some patients may have lower rates of iron absorption). Or a conventional dose (150 mg/d) can be started and then reduced if patients have substantial side effects.

George Ioannou, MD, MS
Cara Debley, MD
VA Puget Sound Heath Care System
University of Washington
Seattle, Washington, USA

Reference

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