

# 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  $\geq$  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<sub>12</sub> 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](mailto: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 Health Care System  
University of Washington  
Seattle, Washington, USA*

## Reference

1. Harju E. Clinical pharmacokinetics of iron preparations. *Clin Pharmacokinet.* 1989;17:69-89.