

Iron dosing frequency

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Clinical question

How does once-daily (QD) iron dosing compare with dosing every second day (QOD) or twice weekly (BIW)?

Bottom line

Once-daily dosing of iron results in similar or slightly better hemoglobin (Hb) levels (about 3 g/L) than QOD or BIW dosing during a 3-month period. Daily dosing increases serum ferritin levels similarly or by up to 12 µg/L better. Intermittent dosing reduces adverse events (like abdominal pain) by up to 30% (absolute).

Evidence

Five RCTs from Europe, India, and Iran (mean age 14-22; 50-100 mg of elemental iron) found the following:

- In 40 females taking ferritin (≤ 25 µg/L) QD for 14 days or for 28 days QOD,¹ base Hb levels of both groups were around 130 g/L and increased by 4 g/L. Serum ferritin levels increased by 15 µg/L (QD) and by 10 µg/L (QOD); not statistically different ($P = .06$).
- In 24 females taking ferritin (≤ 15 µg/L) either QD or BIW for 90 days,² Hb levels increased from about 124 g/L by 6 g/L (QD) and by 8 g/L (BIW); not statistically different. Serum ferritin levels increased by 16 µg/L (QD) versus 4 µg/L (BIW); statistically different.
- In 203 females with anemia taking iron either QD or BIW for 12 weeks,³ Hb levels increased approximately from 91 g/L by 32 g/L (QD) and by 29 g/L (BIW); statistically different.⁴
 - Abdominal pain (41% vs 5%), nausea (11% vs 1%), and vomiting (6% vs 0%) increased with QD dosing; statistically different, according to authors.
- In 223 females with anemia treated with iron and folic acid either QD for 3 months or BIW for 1 year,⁵ Hb levels increased approximately from 97 g/L by 23 g/L (QD) and by 31 g/L (BIW); statistics not reported. Serum ferritin levels in both groups increased by about 20 µg/L.
 - Adverse events: 39% versus 18% (BIW). Nausea, vomiting, and constipation were the most common.
 - All dropouts: 12% versus 4% (BIW); not statistically different ($P = .053$).
- In 204 females (49% with anemia) given 50 mg of iron either QD or BIW for 3 months,⁶ Hb levels increased 7.4 g/L (QD) versus 8.5 g/L (BIW); not statistically different.⁴ Serum ferritin levels increased more with daily iron dosing (numbers not provided).

Context

- Limitations: lack of blinding,^{1-3,5,6} short¹ and imbalanced follow-up between groups,^{1,5} and poor randomization.^{1,5}
- Trials show a trade-off with intermittent iron (QOD or BIW), leading to slightly lower improvement in Hb (≤ 3 g/L) and ferritin (12 µg/L) levels, but have fewer adverse events, which might promote adherence.

Implementation

A main barrier to effective iron replacement is nonadherence (up to 70% cases⁷) due to dose-dependent gastrointestinal side effects. Less frequent dosing improves tolerability,^{1,3,5} but therapy duration might be longer than with QD dosing owing to lower Hb level increases. Ferrous gluconate or sulfate versus fumarate have been suggested for improved adherence.^{8,9} Consolidation therapy for 3 months is recommended upon iron deficiency correction to replenish stores.¹⁰ Optimal iron replacement formulation, frequency, and duration should be discussed with patients to optimize treatment efficacy and adherence. 

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Competing interests
None declared

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