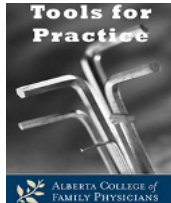


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## Iron dosing frequency: Is less more or just less?

**Clinical Question: How does once daily iron dosing compare with dosing every second day or twice weekly?**

**Bottom Line: Once daily dosing of iron yields similar or slightly better hemoglobin ( $\sim 3$  g/L) versus twice weekly or alternate day over  $\sim 3$  months. Daily dosing increased ferritin similarly or up to 12 mg/L better. Adverse events (like abdominal pain) are reduced by up to 30% (absolute) with intermittent dosing. Research focused on females aged 14-22.**

### Evidence:

- 5 randomized controlled trials (RCT) from Europe, India, and Iran, mean age 14-22 given 50-100 mg of elemental iron.
  - 40 females with ferritin  $\leq 25\mu\text{g/L}$ , daily x14 days or alternating days x28 days.<sup>1</sup>
    - Hemoglobin started  $\sim 130\text{g/L}$ : both groups increased 4g/L.
    - Ferritin increased:  $15\mu\text{g/L}$  versus  $10\mu\text{g/L}$  (alternating day dosing), not quite statistically different ( $p=0.06$ ).
  - 24 females with ferritin  $\leq 15\mu\text{g/L}$ , daily or twice/week x90 days.<sup>2</sup>
    - Hemoglobin started  $\sim 124\text{g/L}$ : increased 6g/L versus 8g/L (twice/week dosing), not statistically different.
    - Ferritin increased:  $16\mu\text{g/L}$  versus  $4\mu\text{g/L}$  (twice/week dosing), statistically different.
  - 203 anemic females, daily or twice/week x12 weeks.<sup>3</sup>
    - Hemoglobin started  $\sim 91\text{g/L}$ : increased  $\sim 32\text{g/L}$  versus  $\sim 29\text{g/L}$  (twice/week dosing), statistically different.<sup>4</sup>
    - Abdominal pain (41% versus 5%), nausea (11% versus 1%), and vomiting (6% versus 0%) increased with daily dosing (statistically different, by authors).
  - 223 anemic females, daily x3 months or twice/week x1 year.<sup>5</sup>
    - Hemoglobin started  $\sim 97\text{g/L}$ : increased  $\sim 23\text{g/L}$  versus  $\sim 31\text{g/L}$  (twice/week dosing), statistics not reported.
    - Ferritin: both groups increased  $\sim 20\mu\text{g/L}$ .
    - Total adverse events higher in once daily (39%) versus twice/week dosing (18%). Nausea, vomiting, and constipation most common.
    - All dropouts: 12% versus 4% (twice/weekly), not quite statistically different ( $p=0.053$ ).
  - 204 females (49% anemic), daily or twice/week x3 months.<sup>6</sup>

- Hemoglobin increased 7.4g/L versus 8.5g/L (twice/week), not statistically different.<sup>4</sup>
- Ferritin improved more with daily iron (numbers not provided).

**Context:**

- Overall limitations include lack of blinding,<sup>1-3,5,6</sup> imbalanced follow-up duration between study groups,<sup>1,5</sup> poor randomization,<sup>1,5</sup> and short follow-up.<sup>1</sup>
- Trials demonstrate a trade-off with intermittent iron (every second day or twice/week): leading to slightly lower improvement in hemoglobin ( $\leq 3$  g/L) and ferritin (12  $\mu$ g/L) but less adverse events that may promote adherence.

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**Disclosures:**

Authors do not have any conflicts of interest to declare.

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