Alternate-day versus consecutive-day oral iron supplementation in iron-depleted women: a randomized double-blind placebo-controlled study

Project 570

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Background

Guidelines to treat iron deficiency recommend daily provision of oral iron, but this may decrease fractional iron absorption and increase side effects. Our study aim was to compare consecutive day versus alternate day iron supplementation.

Methods

In a double-masked, randomized, placebo-controlled trial, young Swiss women (n=150; serum ferritin ≤30µg/L) were assigned to: daily 100mg iron for 90 days, followed by daily placebo for another 90 days (consecutive-day group) or the same daily dose of iron and placebo on alternate days for 180 days (alternate-day group). Primary outcomes, at equal total iron doses, were serum ferritin and incidence of gastrointestinal side effects; secondary outcomes were iron deficiency prevalence and serum hepcidin. Compliance and side effects were recorded daily using a specifically-designed mobile application. Data were analyzed using mixed models and longitudinal prevalence ratios (LPR).

Findings

The study period was Nov 24, 2021 to August 10, 2022; 75 women were assigned to each group and included in the intention-to-treat analysis. Capsule adherence and daily side effect reporting was >97% in both groups. At equal total iron doses, comparing consecutive-day and alternate-day groups, median serum hepcidin was 3·0nM (IQR 2·0–5·0) versus 1·9nM (1·4–2·9)(p<0·0001), median serum ferritin was 43·8µg/L (31·7–58·2) versus 44·8µg/L (33·8–53·6)(p=0·83), iron deficiency prevalence was 5·5% versus 3·0%(p=0·46), and the LPR for gastrointestinal side effects on days of iron intake was 1·56 (95%CI:1·38,1·77; p<0·0001).

Conclusion

Compared to consecutive day dosing of iron, alternate day dosing had comparable efficacy but triggered fewer gastrointestinal side effects.