



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

102. IRON HOMEOSTASIS AND BIOLOGY

Efficacy of Vitamin C with Iron Supplementation in Iron Deficiency Anemia Patients: A Systematic Review and Meta-Analysis

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Background

Oral iron supplementation is one of the mainstays of treatment for iron deficiency anemia (IDA) but can be complicated by poor absorption. Vitamin C is hypothesized to increase the acidity of the GI tract and enhance the conversion of non-absorbable ferric iron (Fe³⁺) to its absorbable ferrous (Fe²⁺) state for improved absorption and is often prescribed with iron. However, whether vitamin C supplementation translates to clinically relevant differences, such as sufficient improvements in hemoglobin, remains unclear and a synthesis of available evidence is lacking. Therefore, the present systematic review and meta-analysis aims to compare oral iron with or without vitamin C supplementation in patients with IDA.

Methods

MEDLINE, EMBASE, Web of Science and Cochrane Central Register of Controlled Trials were searched from database inception to July 2023 for randomized controlled trials (RCTs) and non-randomized studies (NRSs) that investigated the use of oral iron supplements with vitamin C compared to oral iron supplements only in patients with IDA. Title & abstract, full text review and data extraction were conducted independently and in duplicate.

The primary outcome was the change in serum hemoglobin levels in g/dL. Secondary outcomes include change in serum ferritin, change in transferrin saturation, change in reticulocyte percentage, and incidence of adverse events including constipation, nausea/vomiting, GI upset and poor taste. The Mantel-Haenszel fixed effects model was utilized for the meta-analysis. The calculated effect sizes were represented by odds ratios (OR) and mean differences (MD) for binary endpoints and continuous endpoints, respectively, with 95% confidence intervals (CI).

Results

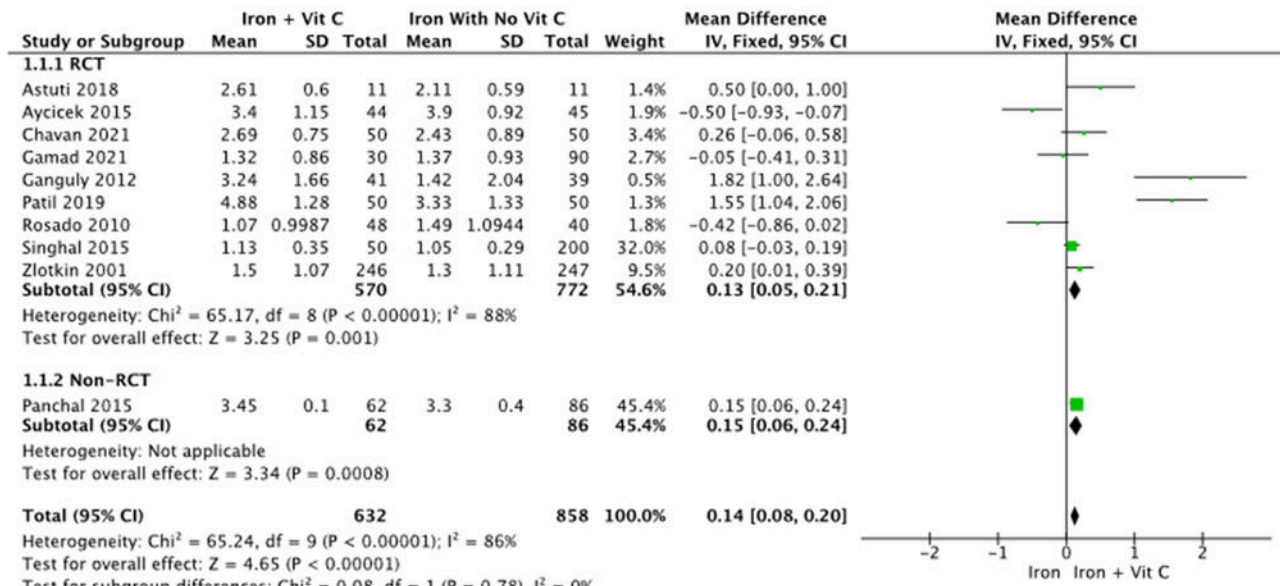
2231 studies were retrieved from electronic databases. 12 RCTs and one prospective cohort study comprising 2240 patients were included. There was a small but statistically significant increase in serum hemoglobin level (MD 0.14 g/dL [95%CI 0.08, 0.20]) and serum ferritin levels (MD 3.23 µg/L [95%CI 1.63, 4.84]) in the iron + vitamin C group compared to the iron only group. There was a greater reduction in serum transferrin saturation associated with vitamin C supplementation (MD -2.01% [95%CI -3.31, -0.71%]) but the pool of evidence consists of only two studies. Reticulocyte percentage (MD 0.22% [95%CI 0.08, 0.36]) was higher in the iron + vitamin C group than in the iron only group. There were no significant differences between the iron + vitamin C group and the iron only group in overall incidence of adverse effects (OR 0.71 [95%CI 0.50, 1.00]), constipation (odds ratio (OR) 0.83 [95%CI 0.35, 1.96]), or nausea/vomiting (OR 0.80 [95%CI 0.52, 1.24]). The risk of GI upset is lower in the iron + vitamin C group (OR 0.40 [95%CI 0.18, 0.92]). Nevertheless, only three primary studies reported on incidence of adverse events.

Conclusion

The addition of vitamin C to iron supplementation in the management of IDA was associated with a statistically significant, but likely clinically unimportant, increase in serum hemoglobin of 0.14 g/dL. Similarly, a statistically significant increase in serum ferritin levels by 3.23 µg/L was observed, but its clinical relevance remains uncertain. A strength of the present analysis is the number of RCTs included; however, its conclusions are limited by the heterogeneity of interventions (e.g. different formulations/dosage) across studies. Our results do not provide strong evidence for adding vitamin C to iron supplementation.

Disclosures Crowther: Bayer: Honoraria; Eversana: Consultancy; Syneos Health: Consultancy; Hemostasis Reference Laboratory: Consultancy; Precision Biologics: Consultancy; Astra-Zeneca: Consultancy; Pfizer: Honoraria; CSL Behring: Honoraria; Treasurer, American Society of Hematology: Membership on an entity's Board of Directors or advisory committees.

Figure 1. Change in Serum Hemoglobin [g/dL] in Oral Iron Supplementation With or Without Vitamin C



Abbreviations (from left to right, top-down): SD, standard deviation; CI, confidence interval; RCT, randomized controlled trial.

Table 1. Summary of Findings

Outcome	Iron + Vitamin C	Iron With No Vitamin C	Effect Size	Number of Studies in Systematic Review (Total Sample Size n=2240)
Primary Outcome				
Change in serum hemoglobin levels [g/dL]	N/A	N/A	MD = 0.14 (95% CI: 0.08 to 0.20; p < 0.01; I ² = 86%)	10 (n=1490)
Secondary Outcomes				
Change in serum ferritin levels [µg/L]	N/A	N/A	MD = 3.23 (95% CI: 1.63 to 4.84; p < 0.01; I ² = 95%)	9 (n=1682)
Change in transferrin saturation [%]	N/A	N/A	MD = -2.01 (95% CI: -3.31 to -0.71; p < 0.01; I ² = 51%)	2 (n=560)
Change in reticulocyte percentage [%]	N/A	N/A	MD = 0.22 (95% CI: 0.08 to 0.36; p < 0.01; I ² = 94%)	3 (n=620)
Adverse Events Outcomes				
Incidence of all adverse events [events/total sample]	76/680	113/820	OR = 0.71 (95% CI: 0.50 to 1.00; p=0.05; I ² = 0%)	3 (n=1500)
Incidence of constipation [events/total sample]	19/300	30/320	OR = 0.83 (95% CI: 0.35 to 1.96; p=0.66; I ² = 0%)	3 (n=620)
Incidence of nausea/vomiting [events/total sample]	45/300	58/360	OR = 0.80 (95% CI: 0.52 to 1.24; p = 0.32; I ² = 40%)	3 (n=660)
Incidence of GI upset [events/total sample]	12/80	25/140	OR = 0.40 (95% CI: 0.18 to 0.92; p = 0.03; I ² = 0%)	2 (n=220)
Incidence of poor taste [events/total sample]	N/A	N/A	Not estimable	0

Abbreviations (from left to right, top-down): N/A, not applicable; MD, mean difference; CI, confidence interval; OR, odds ratio; GI, gastrointestinal.

Figure 1

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