FPIN's Clinical Inquiries

Oral vs. Intramuscular Vitamin B_{12} for Treating Vitamin B_{12} Deficiency

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Clinical Question

How effective is oral vitamin B_{12} supplementation compared with intramuscular supplementation in patients with vitamin B_{12} deficiency?

Evidence-Based Answer

For normalizing serum vitamin B_{12} levels, oral and intramuscular vitamin B_{12} supplementation are equivalent after one to four months. (Strength of Recommendation [SOR]: C, disease-oriented evidence, systematic review of two randomized controlled trials [RCTs], and two additional RCTs.) For increasing vitamin B_{12} levels, oral supplementation at 2,000 mcg per day is more effective than intramuscular supplementation at 1,000 mcg per day; however, 1,000 mcg per day orally is equivalent to 1,000 mcg per day intramuscularly. (SOR: C, disease-oriented evidence, RCTs.) Oral vitamin B_{12} is also effective at maintaining normalization of vitamin B_{12} levels. (SOR: C, disease-oriented evidence, one case series.)

Evidence Summary

A 2018 Cochrane review examined three parallel RCTs from Turkey, the United States, and India of patients with vitamin B_{12} deficiency.[1] The trials compared oral vitamin B_{12} with intramuscular cyanocobalamin supplementation. Patients 39 to 72 years of age (44% women; N = 153) who had serum vitamin B_{12} levels less than 200 pg per mL (147.56 pmol per L) were included. Evaluated outcomes were vitamin B_{12} levels (two RCTs) and normalization of vitamin B_{12} levels (two RCTs). Study limitations included poor quality of randomization and blinding protocols.

A 2020 noninferiority RCT (n = 283) examined the effects of oral vs. intramuscular vitamin B_{12} in patients from Spain who were older than 65 years with vitamin B_{12} deficiency (defined as a level less than 211 pg per mL [155.68 pmol per L]).[2] The average age of participants was 75 years, and 58.3% were women. The intramuscular treatment regimen was 1 mg per day of cyanocobalamin on alternate days for two weeks, then 1 mg per week during weeks 3 to 8, and 1 mg per month during weeks 9 to 52. The oral regimen was 1 mg per day of cyanocobalamin for eight weeks, followed by 1 mg per week during weeks 9 to 52. The primary outcome was treatment success, defined as normalization of vitamin B_{12} serum concentration (greater than 211 pg per mL) measured at eight, 26, and 52 weeks. There was no significant difference in normalization of vitamin B_{12} levels between the oral and intramuscular arms by intention-to-treat analysis at eight weeks (4.8%; $P = .124$), 26 weeks (–3.2%; $P = .470$), and 52 weeks (–6.8%; $P = .171$).

Clinical Inquiries provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (https://www.cebm.net).

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A 2017 prospective, nonblinded, randomized trial from Switzerland, excluded from the 2018 Cochrane review, compared oral cyanocobalamin therapy with intramuscular hydroxocobalamin therapy in 37 patients (mean age = 49.5 years; 60.5% women) with vitamin B_{12} deficiency (less than 200 pg per mL).[3] The oral group received 1,000 mcg of cyanocobalamin per day through an electronically monitored punch card (99.6% adherence by pill count), and the intramuscular group received 1,000 mcg of hydroxocobalamin weekly for four weeks. There was no significant difference in the primary outcome of normalization of vitamin B_{12} levels at 28 days between the intramuscular and oral groups (100% vs. 84.2%; $P > .05$).

A 2003 prospective case series involved patients with vitamin B_{12} deficiency (n = 50) who were receiving 1,000 mcg of intramuscular hydroxocobalamin every three months.[4] The investigators evaluated the effect of changing from intramuscular to oral vitamin B_{12} supplementation on vitamin B_{12} levels. Patients were recruited from a general practice in the United Kingdom and were 31 to 90 years of age, and 66% were women. After patients received the final hydroxocobalamin injection, their vitamin B_{12} levels were monitored at weeks 2, 4, 8, and 12, and then every 12 weeks. When serum vitamin B_{12} levels were measured at the 25th percentile (418 pg per mL [308.40 pmol per L]) of the reference range (180 to 1,132 pg per mL [132.80 to 835.19 pmol per L]), patients were switched to 1,000 mcg of oral cyanocobalamin per day. Study duration was six to 18 months in 48 patients and up to three months in two patients. Patients were monitored to determine if there was need to restart intramuscular supplementation, which was defined as a vitamin B_{12} level below 275 pg per mL (202.90 pmol per L). Serum vitamin B_{12} levels at the start of oral therapy (median = 410 pg per mL [302.50 pmol per L]) increased and then plateaued at three months (median = 1,164 pg per mL [858.80 pmol per L]), with no patients meeting criteria to restart intramuscular supplementation. Ten patients (20%) dropped out, predominantly for social reasons.

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