

Systematic Review and Pragmatic Clinical Approach to Oral and Nasal Vitamin B12 (Cobalamin) Treatment in Patients with Vitamin B12 Deficiency Related to Gastrointestinal Disorders

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At a glance:

- A daily dose of 1 mg vitamin B12 (B12) supplementation is effective for the normalization of serum B12 levels and for the treatment of clinical manifestations of B12 deficiency associated with gastrointestinal (GI) disorders.
- Oral B12 replacements generally are an adequate alternative to intramuscular (i.m.) B12 injections, except for in cases of severe neurological manifestations of B12 deficiency or critically low blood levels of B12, where i.m. supplementation is preferred.

Introduction & Background

GI disorders, for example pernicious anemia (= Biermer's disease), gastrectomy, and food-cobalamin malabsorption (FCM), due to atrophic gastritis, chronic carriage and *H. pylori* infection, long-term treatment with proton pump inhibitors, chronic alcoholism, and partial and exocrine pancreatic insufficiency, can lead to or be associated with B12 deficiency. B12 deficiency is commonly treated parenterally, but oral and nasal routes of B12 supplementation have

been developed. For these treatments, cyano- or hydroxycobalamin in the form of pills, tablets, or oral solutions are administered. 1-5% of free or crystalline cobalamin is absorbed via passive diffusion along the entire GI tract.

The aim of this systematic review was to investigate the efficacy and safety of oral and nasal cobalamin supplements in the treatment of patients with cobalamin deficiency associated with GI disorders.

Materials & Methods

The systematic literature search was conducted on two databases, using defined search terms. Included were clinical trials, guidelines, and review articles that were conducted on adult and elderly participants. Additionally, studies were collected from reference lists, Cochrane library, and ISI web of knowledge. Lastly, data from international meetings, commercial websites and educational books was included.

Results

413 articles were reviewed and 39 were included in the systematic review. Discussed disorders were FCM, pernicious anemia, B12 deficiency associated with veganism or vegetarianism, total gastrectomy after Roux-en-Y gastric bypass, and Crohn's disease. Only one study about nasal B12 treatment was included.

Randomized Controlled Trials (RCTs) and systematic reviews showed that there was no difference, or a benefit of oral supplements compared to i.m. injections in the treatment of B12 deficiency related to GI disorders. Doses between 1 mg and 2 mg per day for three to four months improved hematological and neurological parameters, for example paresthesia, ataxia, memory loss, cognitive function, sensory neuropathy, or vibration sense, associated with B12 deficiency in patients with GI disorders. One RCT showed that the dose necessary to normalize mild B12 deficiency was more than 200 times higher than the daily dietary allowance, so > 0.5 mg per day.

Prospective studies showed improvements in hematological parameters such as increased hemoglobin (Hb), decreased mean corpuscular volume (MCV), and increased serum B12 in patients with B12 deficiency and FCM after oral B12 treatment with 3 to 5 mg per day for three months. Furthermore, prospective studies and an analysis of data from a reference academic center showed that in patients with FCM and pernicious anemia, treatment with 0.125 to 1 mg of daily oral B12 corrected B12 levels in all patients, hematological abnormalities in most patients, and improved clinical parameters in one-third to 50% of patients. Even a smaller oral mean daily dose of 0.5 mg B12 showed efficacy for the treatment of B12 deficiency after a median follow-up of up to more than 4 years.

For the treatment of marginal B12 deficiency in vegetarian or vegan patients daily oral B12 supplementation of 50 μ g (= 350 μ g per week) was superior to a single dose of 2 mg per week.

1 mg of daily oral B12 supplementation was as effective as i.m. B12 treatment after six months for the improvement of hematological markers, namely a decrease in methylmalonic acid and homocysteine, of B12 deficiency in patients after Roux-en-Y Gastric Bypass surgery. Furthermore, 1 mg of daily oral B12 for a mean period of 65 months and after a follow up of 24 months increased B12 levels in total gastrectomy patients with B12 deficiency.

94.7% of patients with Crohn's disease normalized their B12 levels with 1 mg of oral B12 per day. After a follow-up of 3 years the oral route was effective in 81.7% of these patients.

In all studies, adverse events, namely skin allergy reactions after oral B12 supplementation, were only reported in rare cases.

Discussion & Conclusions

This study showed the efficacy of oral B12 supplementation for the treatment of B12 deficiency related to GI disorders, for example, FCM, malabsorption associated with chronic inflammatory bowel disease, and pernicious anemia. The authors suggest a practical clinical approach for the oral treatment of B12 deficiency as follows: 1000 μ g oral cyanocobalamin supplementation per day for life in case of pernicious anemia; and 1000 μ g per day for 1 month, then 125 to 1000 μ g per day, until B12 deficiency is corrected in cases of FCM and intake deficiency. For the treatment of patients with severe neurological manifestations of B12 deficiency or critically low B12 blood levels, i.m. B12 replacement should be preferred.

Individual considerations have to be made when choosing between oral and i.m. B12 treatment for a patient, for example the adherence to oral medications, personal preference, or contraindications such as coagulopathy after i.m. B12 injection. Oral B12 supplementation has the benefits of less discomfort, inconvenience, and cost compared to monthly i.m. injections. Further research is needed for the evaluation of nasal B12 treatments in patients with B12 deficiency.



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