TO P.O. B₁₂ OR NOT TO P.O. B₁₂?

Vitamin B₁₂ (cobalamin) is a coenzyme for various metabolic functions, including fat and carbohydrate metabolism and protein synthesis. It plays an important role in hematopoiesis and maintaining the integrity of the neural system. Deficiency of cobalamin is a common problem, especially among the elderly. If untreated or suboptimally treated, this deficiency can lead to macrocytic anemia and serious neuropathies. Traditionally, vitamin B₁₂ supplements have been administered parenterally but there is a growing body of evidence favoring the use of oral and sublingual formulations of vitamin B₁₂.

Cobalamin Absorption:
Knowledge of the routes of cobalamin absorption is necessary to understand the rationale for giving cobalamin orally particularly in the treatment of pernicious anemia. The classic pathway is a complex uptake mechanism that involves the binding of cobalamin to intrinsic factor produced by the stomach and the transfer of this complex into and across intestinal epithelial cells via a specialized transport system in the terminal ileum. This system has an absorption efficiency of about 60%.

However, there is a secondary pathway that involves passive diffusion across the intestinal wall independent of either intrinsic factor or an intact ileum. About 1% of a large oral dose (> 300 mcg) of cobalamin will be absorbed via this mechanism. Therefore, oral supplementation with 300 mcg or more of cobalamin should easily meet or exceed the daily requirements of 2 – 3 mcg.

Causes of Cobalamin Deficiency:
1. Dietary Insufficiency: Vitamin B₁₂ is a water-soluble vitamin found primarily in meat and dairy products. Other than in strict vegetarians, inadequate intake of vitamin B₁₂ is rare.
2. Decreased absorption: This occurs in persons with a deficiency of intrinsic factor (pernicious anemia), persons with certain gastric dysfunctions (e.g., hypochlorhydria), and possibly long-term use of acid suppressive drugs.
3. Inadequate Utilization: Vitamin B₁₂ is bound to the transport protein, transcobalamin II, that rapidly delivers the vitamin to sites of utilization and storage. In persons with a deficiency in transcobalamin II, this process is inhibited.

The Evidence for Oral Administration:
In a Swedish study published in 1968, 64 patients with pernicious anemia were treated with 1000 ug of oral vitamin B₁₂ daily for several years. None of the patients relapsed or had a low serum cobalamin level. Following this study, oral cobalamin became an alternative first-line treatment for B₁₂ deficiency in Sweden and has been widely used in that country for the past thirty years. Currently, approximately 40% of Swedish patients with pernicious anemia are maintained on oral vitamin B₁₂ therapy.

Over the last decade, several studies in North America have also reported favorable results with high dose oral B₁₂ therapy. One of these was a randomized, controlled trial conducted in New York. For a period of four months, patients deficient in cobalamin were administered either 2000 ug of oral B₁₂ daily or 1000 ug of IM cyanocobalamin on days 1, 2, 7, 10, 14, 21, 31, 61, and 90. At four months, 18 of 18 patients receiving oral therapy versus 7 of 14 patients receiving injections achieved serum cobalamin levels greater than 200 pg/mL, considered to be the threshold level for metabolic evidence of cobalamin deficiency. The researchers concluded that large daily oral doses of vitamin B₁₂ were as effective as a standard parenteral regimen in producing hematologic and neurologic responses and possibly superior in increasing serum cobalamin levels after four months.
Application to Practice:
In North America, cobalamin deficiency, including pernicious anemia, food-cobalamin malabsorption in the elderly and vegetarianism, is commonly treated with parenteral vitamin B\textsubscript{12}. (11) The recommended regimen for pernicious anemia is daily injections (i.m. or deep s.c.) of 100 \textmu g of cyancobalamin for 5 – 10 days to saturate B\textsubscript{12} stores in the body and resolve clinical manifestations of the deficiency, then 100 – 200 \textmu g monthly until normalization of the hemoglobin and hematocrit and 100 \textmu g monthly thereafter to maintain remission. (12,13)

There are several drawbacks to parenteral administration including pain on injection, difficulty in patients with a tendency to bleed or in very thin patients, and the inconvenience and cost of frequent visits to health professionals for injections. (3,11) In a study conducted in Ontario during 1995 and 1996, researchers estimated that switching elderly patients receiving cobalamin injections to high-dose oral therapy would save the provincial healthcare system between $2.9 and $17.6 million (depending on the number of vitamin-injection visits avoided). (14)

Daily oral doses of 300 \textmu g to 2000 \textmu g and higher have been used successfully to treat pernicious anemia with no evidence of toxicity. (15) Evidence from published studies indicates that 1000 \textmu g daily produces satisfactory long-term results while, in some patients, 500 \textmu g daily results in only borderline cobalamin concentrations. (16) Serum B\textsubscript{12} concentrations should be monitored closely, especially during the first months of therapy, to ensure efficacy and compliance. (15) For treatment of elderly people with vitamin B\textsubscript{12} deficiency not related to pernicious anemia, 100 \textmu g daily orally has been shown to normalize B\textsubscript{12} levels within one month. (10)

Parenteral administration remains the treatment of choice for hospitalized patients, for patients unable to take medications by mouth, or with diarrhea or vomiting, patients with severe neurological symptoms, and when compliance to a daily dosage regimen is a concern. (4)

Sublingual Cobalamin:
The effectiveness of sublingual B\textsubscript{12} replacement therapy has also been studied. In a prospective open-labelled study of 18 patients with cobalamin deficiency, sublingual cobalamin (2000 \textmu g daily) was found to be an effective, safe and convenient treatment. The researchers concluded that sublingual B\textsubscript{12} supplementation provides rapid restoration of serum cobalamin concentrations and therefore should be considered as an alternative method of administering B\textsubscript{12}. (15)

Conclusion:
Oral and sublingual vitamin B\textsubscript{12} supplements appear to be safe, effective and cost-saving alternatives for the treatment and maintenance of mild to moderate B\textsubscript{12} deficiency.

References: Available upon request

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References:


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