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## Q/ Is high-dose oral B<sub>12</sub> a safe and effective alternative to a B<sub>12</sub> injection?

### EVIDENCE-BASED ANSWER

**A/** YES. Both high-dose oral B<sub>12</sub> and injected B<sub>12</sub> raised low vitamin B<sub>12</sub> levels and improved hematologic parameters and neurologic symptoms in short-term studies (3-4 months) predominantly involving patients with conditions

associated with intestinal malabsorption (strength of recommendation: **A**, randomized controlled trials [RCTs]).

Both forms are well tolerated. Oral B<sub>12</sub> is less expensive.

### Evidence summary

Two open-label RCTs compared oral and intramuscular (IM) therapy for vitamin B<sub>12</sub> deficiency.<sup>1,2</sup> Both studies enrolled patients from hospital-based clinics—not primary care centers. Most patients (63 of 93 total) had conditions associated with intestinal malabsorption, including 7 patients with pernicious anemia and 3 with ileal resection. Both trials excluded patients with celiac and inflammatory bowel disease.

#### Oral therapy works as well as injections and costs less

One RCT compared the effects of oral B<sub>12</sub> with IM therapy in 60 patients (mean age 62 years) with B<sub>12</sub> deficiency and megaloblastic anemia.<sup>1</sup> Investigators gave patients in each group equivalent doses of cobalamin: 1000 mcg daily for 10 days, weekly for 4 weeks, and then monthly to complete a 90-day course.

The mean hemoglobin increased significantly in both the oral and IM groups (from 8.4 to 13.8 g/dL,  $P < .001$  for oral therapy; from 8.3 to 13.7 g/dL,  $P < .001$  for IM therapy), as did mean serum B<sub>12</sub> levels (from 73 to 214 pg/mL,  $P < .001$ , oral; and from 70 to 226 pg/mL,  $P < .001$ , IM). Neurologic symp-

toms (sensitive peripheral neuropathy, alteration of cognitive function, loss of sense of vibration) either cleared or improved markedly in both groups within one month (7 of 9 patients with oral therapy and 9 of 12 patients with IM treatment;  $P$  value not given).

Oral therapy cost less (\$80 vs \$220 per patient) and neither group reported adverse effects.<sup>1</sup>

#### B<sub>12</sub> therapy changes hematologic parameters

The second RCT compared oral with IM B<sub>12</sub> therapy in 33 patients (mean age 72 years) with newly diagnosed B<sub>12</sub> deficiency.<sup>2</sup> Investigators randomized patients to receive either oral cyanocobalamin (2000 mcg daily) for 120 days or IM cobalamin (1000 mcg) on Days 1, 3, 7, 10, 14, 21, 30, 60, and 90.

At 4 months, both groups had improved significantly from baseline in all metabolite measures and achieved a normal serum cobalamin level. The higher-dose oral therapy raised cobalamin levels more than IM therapy (from 93 to 1005 pg/mL,  $P < .0005$  with oral therapy vs from 95 to 325 pg/mL,  $P < .0005$  with IM treatment). Oral therapy increased cobalamin levels above 300 pg/mL in all pa-

tients; only half the patients treated with injections reached that level.

B<sub>12</sub> therapy also significantly changed hematologic parameters from baseline even though the patients in the study didn't have anemia. Mean corpuscular volume, for example, decreased from 100 to 90 fL with oral therapy and 102 to 97 fL with IM therapy ( $P < .005$  for each). Neurologic symptoms (memory loss, paresthesias, ataxia) either cleared or improved markedly in all patients. Investigators compared all parameters against baseline values but didn't directly compare oral with IM therapy. The trial didn't assess safety outcomes.<sup>2</sup>

### Recommendations

Canada's British Columbia Medical Association and Ministry of Health recommend oral replacement of B<sub>12</sub> (1000-2000 mcg/d) for most cases of vitamin B<sub>12</sub> deficiency, including pernicious anemia. For patients with neurologic symptoms, they recommend an initial B<sub>12</sub> injection (1000 mcg IM) followed by oral replacement.<sup>3</sup>

The US Centers for Disease Control and Prevention recommends either oral (1000 mcg daily) or parenteral B<sub>12</sub> replacement. They advise giving parenteral therapy either subcutaneously (to reduce the burning sensation) or IM (1000 mcg per week for 8 weeks, then monthly for life).<sup>4</sup> **JFP**

### References

1. Bolaman Z, Kadikoylu, G, Yukselen, et al. Oral versus intramuscular cobalamin treatment in megaloblastic anemia: a single-center prospective, randomized, open-label study. *Clin Ther*. 2003;25:3124-3134.
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