

Dear Dave

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If you have a clinical question email it to
dave@bpac.org.nz



Can Proton Pump Inhibitors cause vitamin B₁₂ deficiency?

As yet there are no clear guidelines on routine monitoring for vitamin B₁₂ status in people taking long term acid suppressant drugs. For people who have been taking proton pump inhibitors (PPIs) for more than 3–4 years, especially the elderly, it would be a reasonable precaution to occasionally check vitamin B₁₂ status particularly if there are associated signs and symptoms. This also probably applies to people taking long term H2RAs.

Who is Dave?

Pharmaceutical Programme Manager
Dave Woods is a graduate of Manchester University (B.Sc. [Hons]) and the University of Otago (MPharm). Dave has extensive experience in hospital pharmacy, drug information, rational use of drugs and quality assurance. He has published on a range of subjects and holds editorial positions for several international journals.

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Vitamin B₁₂ requires gastric acid and pepsin to release it from its protein bound form in food and allow binding with intrinsic factor. PPIs do not reduce the secretion of intrinsic factor, but reduced acid secretion may lead to vitamin B₁₂ malabsorption.

Several studies have demonstrated that omeprazole can reduce vitamin B₁₂ absorption^{1,2}. The effects of long-term PPI administration on vitamin B₁₂ status has been examined in a number of studies but these are of variable design and quality, making firm conclusions difficult. Most studies have been relatively short (1–4 years) which may be of insufficient duration to deplete body stores of vitamin B₁₂ and reflect a deficiency. There is also the difficulty in separating out the underlying pathology as a possible cause of reduced vitamin B₁₂ concentrations and most of the longer term studies have been performed in people with Zollinger-Ellison Syndrome (ZE), which may not be applicable to people with other conditions.

Conflicting results

For these reasons the results of studies are conflicting. A small study³ in 34 patients with peptic ulcer disease and a prospective study in patients with ZE (Maton, 1989) found no significant change in vitamin B₁₂ concentrations with chronic PPI treatment over 1–4 years. However, Termanini et al⁵ found that vitamin B₁₂ concentrations were reduced in 11% of patients with ZE who had two concentrations measured at least five years apart. A recent case control study⁶ showed that chronic (≥12 months) use of PPIs and H2RAs was associated with a significantly increased risk of vitamin B₁₂ deficiency (OR 4.45; 95% CI 1.47–13.34) in patients aged 65 years and older with a variety of reasons for acid suppressant use. The elderly are already at increased risk of B₁₂ deficiency due to the increased prevalence of atrophic gastritis and reduced acid secretion. The latter two studies have identified the possibility that the elderly may be at increased susceptibility of PPI induced vitamin B₁₂ deficiency.

H2RAs as well?

The long term use of H2RAs (e.g. ranitidine, famotidine) has also been associated with vitamin B₁₂ deficiency⁶. The evidence is weaker and it could be expected that the effect on vitamin B₁₂ absorption is less as acid suppression is of a shorter duration.

References

1. Schenk BE, Festen HPM, Kuipers EJ, et al. Effect of short and long-term treatment with omeprazole on the absorption and serum levels of cobalamin. *Alimentary Pharmacol Therap.* 1996;10:541-45
2. Saltzman JR, Kemp JA, Golner BB, et al. Effect of hypochlorhydria due to Omeprazole treatment or atrophic gastritis on protein bound vitamin B₁₂ absorption. *J Amer Coll Nutr* 1994;13:584-91
3. Koop H, Bachem MG. Serum iron, ferritin, and vitamin B₁₂ during prolonged omeprazole therapy. *J Clin Gastroenterol.* 1992;14(4):288-92
4. Maton PN, Vinayek R, Frucht H, et al. Long-term efficacy and safety of omeprazole in patients with Zollinger-Ellison syndrome: a prospective study. *Gastroenterology.* 1989;97(4):827-36
5. Termanini B, Gibril F, Sutliff VE, et al. Effect of long-term gastric acid suppressive therapy on serum vitamin B₁₂ levels in patients with Zollinger-Ellison syndrome. *Am J Med* 1998;104(5):422-30
6. Valuck RJ, Ruscin JM. A case control study on adverse effects: H2 blocker or proton pump inhibitor use and risk of vitamin B₁₂ deficiency in older adults. *J Clin Epidemiol* 2004;57:422-428