

Acid-suppressing medications associated with vitamin B12 deficiency

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Use for 2 or more years of proton pump inhibitors and histamine 2 receptor antagonists (two types of acid-inhibiting medications) was associated with a subsequent new diagnosis of vitamin B12 deficiency, according to a study appearing in the December 11 issue of *JAMA*.

"Vitamin B12 deficiency is relatively common, especially among older adults; it has potentially serious [medical](#) complications if undiagnosed. Left untreated, vitamin B12 deficiency can lead to dementia, neurologic damage, anemia, and other complications, which may be irreversible," according to background information in the article. Proton pump inhibitors (PPIs) and histamine 2 [receptor antagonists](#) (H2RAs) suppress the production of gastric acid, which may lead to malabsorption of vitamin B12, and they are among the most commonly used pharmaceuticals in the United States. However, few data exist about any association between long-term exposure to these medications and vitamin B12 deficiency in large population-based studies.

Jameson R. Lam, M.P.H., of Kaiser Permanente, Oakland, Calif., and colleagues evaluated the relationship between the use of acid-suppressing prescription medications and vitamin B12 deficiency within the Kaiser Permanente Northern California population. The researchers identified 25,956 patients having new diagnoses of vitamin B12 deficiency between January 1997 and June 2011 and 184,199 patients without B12 deficiency, and compared their exposure to acid inhibitors as observed via electronic pharmacy, laboratory, and diagnostic databases.

Among patients with a new diagnosis of vitamin B12 deficiency, 3,120 (12.0 percent) were dispensed a 2 or more years' supply of PPIs, 1,087 (4.2 percent) were dispensed a 2 or more years' supply of H2RAs (without any PPI use), and 21,749 (83.8 percent) had not received prescriptions for either PPIs or H2RAs. Among control patients, 13,210 (7.2 percent) were dispensed a 2 or more years' supply of PPIs, 5,897 (3.2 percent) were dispensed a 2 or more years' supply of H2RAs (without any PPI use), and 165,092 (89.6 percent) had not received prescriptions for either PPIs or H2RAs.

Receiving 2 or more years' supply of PPIs and H2RAs was associated with increased risk for vitamin B12 deficiency. Doses more than 1.5 PPI pills/day were more strongly associated with vitamin B12 deficiency than were doses less than 0.75 pills/day.

The researchers found that the magnitude of the association was stronger in women and younger age groups with more potent acid suppression (PPIs vs. H2RAs), and that the association decreased after discontinuation of use. There was no significant trend with increasing duration of use.

"We cannot completely exclude residual confounding [factors besides the drugs] as an explanation for these findings, but, at minimum, the use of these medications identifies a population at higher risk of B12 deficiency, independent of additional risk factors. These findings do not recommend against acid suppression for persons with clear indications for treatment, but clinicians should exercise appropriate vigilance when prescribing these medications and use the lowest possible effective dose. These findings should inform discussions contrasting the known benefits with the possible risks of using these medications," the authors conclude.

More information: [DOI: 10.1001/jama.2013.280490](https://doi.org/10.1001/jama.2013.280490)

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