

Proton Pump Inhibitor and Histamine 2 Receptor Antagonist Use and Vitamin B₁₂ Deficiency

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Abstract

Importance Proton pump inhibitors (PPIs) and histamine 2 receptor antagonists (H₂RAs) suppress the production of gastric acid and thus may lead to malabsorption of vitamin B₁₂. However, few data exist regarding the associations between long-term exposure to these medications and vitamin B₁₂ deficiency in large population-based studies.

Objective To study the association between use of PPIs and H₂RAs and vitamin B₁₂ deficiency in a community-based setting in the United States.

Design, Setting, and Patients We evaluated the association between vitamin B₁₂ deficiency and prior use of acid-suppressing medication using a case-control study within the Kaiser Permanente Northern California population. We compared 25 956 patients having incident diagnoses of vitamin B₁₂ deficiency between January 1997 and June 2011 with 184 199 patients without B₁₂ deficiency. Exposures and outcomes were ascertained via electronic pharmacy, laboratory, and diagnostic databases.

Main Outcomes and Measures Risk of vitamin B₁₂ deficiency was estimated using odds ratios (ORs) from conditional logistic regression.

Results Among patients with incident diagnoses of vitamin B₁₂ deficiency, 3120 (12.0%) were dispensed a 2 or more years' supply of PPIs, 1087 (4.2%) were dispensed a 2 or more years' supply of H₂RAs (without any PPI use), and 21 749 (83.8%) had not received prescriptions for either PPIs or H₂RAs. Among patients without vitamin B₁₂ deficiency, 13 210 (7.2%) were dispensed a 2 or more years' supply of PPIs, 5897 (3.2%) were dispensed a 2 or more years' supply of H₂RAs (without any PPI use), and 165 092 (89.6%) had not received prescriptions for either PPIs or H₂RAs. Both a 2 or more years' supply of PPIs (OR, 1.65 [95% CI, 1.58-1.73]) and a 2 or more years' supply of H₂RAs (OR, 1.25 [95% CI, 1.17-1.34]) were associated with an increased risk for vitamin B₁₂ deficiency. Doses more than 1.5 PPI pills/d were more strongly associated with vitamin B₁₂ deficiency (OR, 1.95 [95% CI, 1.77-2.15]) than were doses less than 0.75 pills/d (OR, 1.63 [95% CI, 1.48-1.78]; *P* = .007 for interaction).

Conclusions and Relevance Previous and current gastric acid inhibitor use was significantly associated with the presence of vitamin B₁₂ deficiency. These findings should be considered when balancing the risks and benefits of using these medications.