

## Acid-Suppressing Drugs Linked to Vitamin B12 Deficiency and Dementia

By Catherine Saint Louis

People who use certain acid-suppressing drugs for two years or longer are at increased risk of vitamin B12 deficiency, which can lead to anemia, neurological problems or dementia, researchers reported on Tuesday.

The drugs in question are called proton-pump inhibitors, or P.P.I.'s, and histamine 2 receptor antagonists, and they are available by prescription and over the counter under brand names like Prevacid, Prilosec and Nexium. Nearly 157 million prescriptions were written for P.P.I.'s alone last year.

“People who are taking these medications are more likely than the average person to be vitamin B12 deficient, and it’s a potentially serious problem,” said Dr. Douglas A. Corley, senior author of the new study, published in *The Journal of the American Medical Association*. “This raises the question of whether people taking these medications for long periods should be screened for vitamin B12 deficiency.”

Dr. Corley has received funding from Pfizer, which makes a P.P.I. called Protonix.

He and his colleagues at Kaiser Permanente in Oakland, Calif., examined the medical records of 25,956 adults who received vitamin B12 deficiency diagnoses between 1997 and 2011, comparing them with 184,199 patients without B12 deficiency during that period.

Patients who took P.P.I.'s for more than two years were 65 percent more likely to have a vitamin B12 deficiency, the researchers found. Higher doses of P.P.I.'s were more strongly associated with the vitamin deficiency, as well.

Twelve percent of patients deficient in vitamin B12 had used P.P.I.'s for two years or more, compared with 7.2 percent of control patients. The risk of deficiency was less pronounced among patients using H2RA's long term: 4.2 percent, compared with 3.2 percent of nonusers.

The new study is the largest to date to demonstrate a link between taking acid suppressants and vitamin B12 deficiency across age groups. Earlier small studies focused primarily on the elderly.

Robert J. Valuck, a professor of pharmacy at the University of Colorado in Aurora, was surprised that the association in the new report was strongest in adults younger than age 30. “It’s not safe to assume vitamin B12 deficiency is only an issue in the elderly,” he said.

Currently, “awareness of B12 deficiency with the use of P.P.I.'s is very low,” said Dr. T.S. Dharmarajan, the vice chairman of medicine at the Wakefield campus of Montefiore

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Medical Center in the Bronx, who was not involved in the research. “If physicians read the study, a lot of B12 levels will be ordered in the months and years to come.”



Acid suppressants are used to treat gastroesophageal reflux disease, or GERD, and ulcers in the stomach or duodenum. The authors of the new research do not recommend stopping P.P.I.'s or H2RA's in people with clear indications for treatment. But studies have found the drugs are often overused or used for longer than

necessary.

“It’s very common for people to start these drugs and stay on for long periods,” Dr. Valuck said.

He and other experts noted the benefits of P.P.I.’s must be weighed against their risks, including increasing the likelihood of bone fractures, pneumonia, *C. difficile* infection, and now, vitamin B12 deficiency.

Although the authors accounted for a number of potential variables, factors other than P.P.I. use might explain the link to vitamin B12 deficiency. One is diet: vitamin B12 is found in meat, seafood and dairy products, so it matters whether patients taking a P.P.I. might also be vegetarian or vegan, Dr. Dharmarajan said. The new report did not address this question.

Dr. Joel J. Heidelbaugh, an associate professor of family medicine at the University of Michigan, commended the researchers for calculating how many people would need to be exposed to a potential hazard before a person is affected. “If you treat 67 people with P.P.I.’s for two years, one of them will have a vitamin B12 deficiency,” he said.

But Dr. Heidelbaugh cautioned that it’s hard to know the clinical relevance of the finding. “Just because someone is deficient in B12, you don’t know if they will develop a serious consequence,” he said.

To see whether study patients were asymptomatic or not, researchers did review the charts of 20 randomly selected P.P.I.-using patients to determine why their vitamin B12 levels had been tested. Twenty-five percent of that small sample had also been tested for anemia and 15 percent for memory loss. “Though there may be many people who have asymptomatic B12 deficiency, that did not seem to be the situation” in this study, Dr. Corley said.

In light of this new research, Dr. Dharmarajan argued that when P.P.I.’s are not indicated, “physicians need to play a greater role in their discontinuation,” including asking patients about their over-the-counter use. “It’s so much easier to allow a patient who is happy staying on the drug to do so, but you have to consider the unintended harm.”