

Acid-reducing medicines may lead to dependency

1 July 2009

Treatment with proton pump inhibitors (PPIs) for eight weeks induces acid-related symptoms like heartburn, acid regurgitation and dyspepsia once treatment is withdrawn in healthy individuals, according to a new study in *Gastroenterology*, the official journal of the American Gastroenterological Association (AGA) Institute.

"The observation that more than 40 percent of healthy volunteers, who have never been bothered by heartburn, acid regurgitation or dyspepsia, develop such symptoms in the weeks after [cessation](#) of PPIs is remarkable and has potentially important clinical and economic implications," said Christina Reimer, MD, of Copenhagen University and lead author of the study. "This study indicates unrecognized aspects of PPI withdrawal and is a very strong indication of a clinically significant acid rebound phenomenon that needs to be investigated in proper patient populations."

The use of PPIs for acid-related symptoms and disorders is extensive and rapidly escalating. While the incidence of new patients being treated with PPIs remains stable, the prevalence of long-term treatment is rising, the reasons for which are not fully known. Studies have shown that up to 33 percent of patients who initiate PPI treatment continue to refill their prescriptions without an obvious indication for maintenance therapy. Rebound acid hypersecretion, defined as an increase in gastric acid secretion above pre-treatment levels following antisecretory therapy, is observed within two weeks after withdrawal of treatment and could theoretically lead to acid-related symptoms such as heartburn, acid regurgitation or dyspepsia that might result in resumption of therapy.

In a randomized double-blind placebo-controlled trial, researchers aimed to determine the clinical relevance of rebound acid hypersecretion in order to establish if long-term treatment with a PPI creates a need for continuous treatment. A total of

120 healthy participants were randomized to 12 weeks of placebo or eight weeks of esomeprazole (40 mg per day) followed by four weeks with placebo. The Gastrointestinal Symptom Rating Scale (GSRS) was filled out weekly.

The symptoms observed in this trial caused mild to moderate discomfort and appeared for the majority of subjects in the first two weeks after withdrawal of therapy. While there were no significant differences between the groups in GSRS scores at baseline, GSRS scores for acid-related symptoms were significantly higher in the PPI group in weeks 10, 11 and 12. Of those randomized to PPIs, 44 percent reported at least one relevant acid-related symptom in weeks nine through 12 compared to 15 percent in the placebo group. The proportion reporting dyspepsia, heartburn or acid regurgitation in the PPI group was 22 percent in week 10, 22 percent in week 11 and 21 percent in week 12. Corresponding figures in the placebo group were 7 percent, 5 percent and 2 percent.

"We find it highly likely that the symptoms observed in this trial are caused by rebound acid hypersecretion and that this phenomenon is equally relevant in patients treated long term with PPIs. If rebound acid hypersecretion induces acid-related symptoms, this might lead to PPI dependency. Our results justify the speculation that PPI dependency could be one of the explanations for the rapidly and continuously increasing use of PPIs," Dr. Reimer added.

[More information:](#) To learn more about heartburn and gastroesophageal reflux disease, read the AGA Institute patient brochure on this topic at www.gastro.org/patient.

Source: American Gastroenterological Association ([news](#) : [web](#))

APA citation: Acid-reducing medicines may lead to dependency (2009, July 1) retrieved 22 September 2019 from <https://medicalxpress.com/news/2009-07-acid-reducing-medicines.html>

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