

Proton Pump Inhibitors and Dementia

Cumulative use increases risk

Stomach acid blockers, known as Proton pump inhibitors (PPI), are available both as prescription and over-the-counter medications. Popular brands like Prilosec and Nexium are commonly used. However, there are rising concerns about their potential links to various diseases such as cardiovascular disease, kidney disease, and stroke. This study aimed to investigate the connection between long-term use of PPI medication and the risk of dementia. Specifically, the study sought to determine the duration of PPI medication use that could lead to an increased risk of dementia.



Abstract

- **Background.** Studies on the association between proton pump inhibitor (PPI) use and dementia report mixed results and do not examine the impact of cumulative PPI use. We evaluated the associations between current and cumulative PPI use and risk of incident dementia in the Atherosclerosis Risk in Communities (ARIC) Study.
- **Methods.** These analyses used participants from a community-based cohort (ARIC) from the time of enrollment (1987-89) through 2017. PPI use was assessed via visual medication inventory at clinic Visits 1 (1987-89) to 5 (2011-13) and reported annually in study phone calls (2006-2011). The present study uses ARIC Visit 5 as baseline, since this was the first visit in which PPI use was common. PPI use was examined two ways: current use at Visit 5 and duration of use prior to Visit 5 (Visit 1 to 2011, exposure categories: 0 days, 1 day – 2.8yrs, 2.8-4.4yrs, >4.4yrs). The outcome was incident dementia after visit 5. Cox Proportional Hazard models were used, adjusted for demographics, co-morbid conditions, and other medication use.
- **Results.** A total of 5,712 dementia-free participants at visit 5 (mean age 75.4±5.1 years; 22% Black race; 58% female) were included in our analysis. The median follow-up was 5.5 years. Minimum cumulative PPI use was 112 days and maximum use was 20.3 years. There were 585 cases of incident dementia over median follow up time. Participants using PPIs at Visit 5 were not at a significantly higher risk of developing dementia during subsequent follow-up than those not using PPIs (Hazard Ratio (HR): 1.1 [95% Confidence Interval (CI): 0.9-1.3]). Those who used PPIs for >4.4 cumulative years prior to Visit 5 were at 33% higher risk of developing dementia during follow-up (HR: 1.3 [95%CI: 1.0-1.8]) than those reporting no use. Associations were not significant for lesser amounts of PPI use.
- **Discussion.** Future studies are needed to understand possible pathways between cumulative PPI use and the development of dementia.

During this study spanning 5.5 years and involving 5712 participants, researchers investigated whether the use of proton pump inhibitor (PPI) medications was linked to a higher risk of dementia. While previous research has yielded mixed results, there have been growing concerns regarding other health issues. The study found that those who used PPIs for over 4.4 years had a 33% higher risk of developing dementia. However, no association was observed for those who used PPIs for less than this duration. It's worth noting that PPIs fully inhibit the acid pump in the stomach, whereas H2 blockers (such as Pepcid and Axid) only partially block acid. Dementia was not found to be related to H2 blockers. The exact mechanism behind these findings is unknown, but it could be linked to reduced absorption of B vitamins, which is associated with dementia, or the reduction in diversity in the GI biome. These medications are highly effective for healing ulcers and are commonly used. However, those taking PPIs long-term should be aware of the risks and benefits.

Cumulative Use of Proton Pump Inhibitors and Risk of Dementia: The Atherosclerosis Risk in Communities Study
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