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Proton Pump Inhibitors and Hip Fracture Risk

THE ISSUE

A matched case-control study published in the December 27, 2006 issue of the *Journal of the American Medical Association* indicates that patients over fifty years old who take proton pump inhibitors (PPIs) for greater than one year are at increased risk for hip fracture. This risk further increases when patients use more than 1.75 doses per day.

THE STUDY

The General Practice Research Database (GPRD), a medical record system of patients in the UK, was used to construct a nested, matched, case-control population. Patients selected for inclusion were fifty or older, did not have a history of hip fracture, did not have a history of PPI or histamine-2 receptor antagonist (H2RA) use, and were followed in the database for at least one year. Since the populations differed in associated factors (BMI, smoking history, use of certain medications, etc.) that may predispose to hip fracture, a conditional logistic regression was applied to adjust for these differences. One hundred ninety-two thousand twenty-eight patients received PPIs, and 1.4 million patients made up the acid suppression non-users arm. Ten controls were matched to each case. Individuals receiving or not receiving a PPI were compared in the primary analysis; patients receiving both a PPI and H2RA were designated for the PPI arm. Additional comparisons were made based on length of therapy, dose of therapy, and between patients receiving an H2RA only versus those not taking acid-suppressive therapy. Results were presented as odds ratios adjusted for differences between the two populations under investigation.

RESOURCES

JAMA article (subscription required): <http://jama.ama-assn.org.ezproxy.library.wisc.edu/cgi/content/full/296/24/2947>

DISCLAIMER

This publication is intended to provide key practical information regarding this drug product in a brief format. It does not contain sufficient information upon which to base formulary or other medication use policy decisions.

WHAT YOU NEED TO KNOW

Crude outcomes show hip fracture rate with PPIs to be 4/1,000 person-years and 1.9/1,000 person years for non-acid suppression users. The average adjusted odds ratio (AOR) for hip fracture increased over time with PPI use: 1.22, 1.41, 1.54, and 1.59 for 1, 2, 3, and ≥ 4 years, respectively. Patients using >1.75 doses/day had an average AOR for hip fracture of 2.65. The association between long-term PPI use was stronger in men than in women, with an average OR 1.78 for males and 1.36 for females; this association may be related to females being more likely to use calcium supplementation. The average AOR for patients taking only H2RA for more than one year was 1.23, indicating greater risk with PPIs. The study did not explain why PPIs increased hip fracture risk, although the authors theorized that reduced absorption of insoluble calcium from dietary sources or calcium carbonate supplements due to increased gastric pH might be a cause.

WHAT TO TELL YOUR PATIENTS

Long-term use of PPIs may increase the risk for hip fracture, particularly for patients taking more than one dose per day. Using soluble calcium salts, such as calcium gluconate or citrate, may allow more calcium to be absorbed when acid-suppression therapies are being used. Both men and women taking PPIs should be taking some form of calcium supplementation since dietary calcium absorption may be decreased. Taking calcium supplements with a meal may also increase absorption.