Fracture Risk Sees an Uptick With Use of PPIs

BY MARY ANN MOON

FROM THE ARCHIVES OF INTERNAL MEDICINE

The use of proton pump inhibitors doesn't appear to raise the risk of hip fracture in postmenopausal women but may raise the risk of spine, forearm, wrist, and total fractures modestly.

Several large epidemiologic studies have suggested that PPI use may be associated with an increased risk for osteoporotic fractures, but other studies have found no such link. Shelly L. Gray, Pharm.D., and her associates examined the issue using data from the Women's Health Initiative, a large study of an ethnically diverse cohort of postmenopausal women followed at 40 U.S. medical centers for a mean of 7.8 years.

For this analysis, data on 161,806 women aged 50-79 years were included. A total of 3,396 (2%) of these study subjects were taking omeprazole or lansoprazole at baseline.

Women who took PPIs were more likely than those who didn't to have osteoporosis or a history of fractures, obesity, treated diabetes, or a history of several health conditions; to take other medications chronically; and to have poorer self-reported health and physical function. "We did our best to adjust for these baseline differences, but, like all observational studies, residual or unmeasured confounding could explain increased associations for some fracture types," said Dr. Gray of the University of Washington School of Pharmacy, Seattle, and her colleagues.

During more than a million person-years of follow-up, there were 1,500 hip fractures, 4,881 forearm or wrist fractures, 2,315 clinical spine fractures, and 21,247 total fractures.

After the data were adjusted to account for possible confounding factors, PPI use was not related to hip fracture risk. There also was no association between hip fracture risk and longer duration of PPI use, Dr. Gray and her associates reported (Arch. Intern. Med. 2010;170:765-71).

'Once our patients fully appreciate the adverse effects of PPIs, they themselves may prefer other treatments, including tincture of time' or eating smaller meals.

In addition, there were no differences between women who used PPIs and women who didn't in the change in bone mineral density over time. Similarly, there was no consistent relationship between duration of PPI use and risk of any fracture. However, the drugs raised the relative risk of clinical spine fracture by 47% (hazard ratio, 1.47); the relative risk of forearm or wrist fracture by 26% (HR, 1.26); and the relative risk of total fractures by 25% (HR, 1.25).

For older patients who do require the treatment, "it is reasonable to focus on using the lowest effective dose, ensuring adequate dietary calcium intake, and adding calcium supplements when necessary," the investigators said.

In an editorial comment accompanying this report, Dr. Mitchell H. Katz of the San Francisco Department of Public Health characterized the increases in nonhip fractures as "modest" but said that PPIs are so widely used that those modest increases "add up to a lot of morbidity on a population level" (Arch. Intern. Med. 2010;170:747-8).

"Once our patients fully appreciate the adverse effects of PPIs, they themselves may prefer other treatments, including tincture of time"; behavioral changes such as smaller meals, losing weight, quitting smoking, and reducing stress; and nonmedical interventions such as raising the head of the bed, he said. ■

Disclosures: *The WHI Program was funded by the National Heart, Lung, and Blood Institute. Dr. Gray reported no financial conflicts. Her associate, Andrea Z. LaCroix, Ph.D., reported ties to Pfizer Inc., Procter & Gamble Co., and Sanofi-Aventis. Dr. Katz is an independent consultant for Health Management Associates.*