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4/21/11

Critically Appraised Topic: Osteoporosis risk with Omeprazole

Question: Is omeprazole use associated with an increased risk of osteoporosis?

Article: Roux, *et al.* (2009). Increase in vertebral fracture risk in postmenopausal women using omeprazole. *Calcif Tissue Int 84*: 13-19.

Study Description: Multicenter prospective cohort study to assess association between exposure to Omeprazole and risk of vertebral fractures in postmenopausal European women

Relevance: Two prior case-controlled studies have suggested increased risk of hip fractures with PPI therapy. Because of their widespread use, potentially increased risk of fractures related to PPIs needs to be confirmed.

Research Question: Did omeprazole use increase the incidence of vertebral fractures in postmenopausal women?

Population: Ambulatory postmenopausal European women from 5 European centers
- Substudy of 2,389 women, age 55-79, recruited for Osteoporosis and Ultrasound Study
- Random population samples between 1999-2001 and followed until March 2007

Excluded women without baseline data on omeprazole use, users of bisphosphonates or raloxifen, and those without x-ray follow-up

Intervention: Omeprazole use at baseline or during the year prior to enrollment (*n*=61)
- Assessed via questionnaire

Comparison: No omeprazole use (*n*=1,150*)*

Outcome: Vertebral fracture determined by lumbar and thoracic spine x-rays after mean follow-up of 6.1 yrs

Validity:

Were patients similar for prognostic factors that are known to be associated with the outcome (or did statistical adjustment level the playing field)?

No. Omeprazole users had higher BMI, lower alcohol intake, higher thiazide use, more prevalent history of fracture, and lower spine bone mineral density (Table 1). Study authors also suggested differences in diet and inflammatory states (H.pylori infection). Data on diet and H.pylori status was not available.
Channeling bias--Omeprazole users are at higher risk for fractures because of existing comorbidities

Were circumstances and methods for detecting the outcome similar?

- Yes. X-rays at baseline and follow-up using same procedure and read by two radiologists.

Was the follow-up sufficiently complete?

- No. Did not obtain information regarding duration of Omeprazole exposure, changes in dose, or changes in confounding conditions over time.

Summary of Results:

Age-adjusted rates for vertebral fractures were 1.89 per 100 person-years for omeprazole users and 0.60 per 100 person-years for non-users (P=0.009)
Relative risk of vertebral fractures for omeprazole users = 3.10 (95% CI 1.14-8.44, P=0.027)
Prevalent vertebral fractures and lumbar spine BMD score -2.5 were also significant predictors of vertebral fracture (statistically different characteristics between omeprazole users and non-users)

Application:

Were the study patients similar to the patient in my practice? Postmenopausal women only

Was follow-up sufficiently long? With ages ranging from 55-79, follow-up may have been relatively short for the younger patients, although no significant age difference between groups, plus, duration of use may also determine risk of fracture

Is the exposure similar to what might occur in my patient? Yes

What is the magnitude of risk? Morbidity related to fracture

Are there any benefits associated with exposure? Therapeutic effects, GI protection

Conclusion: Omeprazole may contribute to increased vertebral fracture in postmenopausal women, especially those who have other conditions that also predispose to fractures. Omeprazole should be used judiciously based on each patient's risk profile pending further evidence.