Clinical Practice Assessment

Effect of PPI’s on Fracture Risk

Clinical Question:

Do patients who use proton pump inhibitor’s (PPI's) for more than a year have an increased fragility fracture risk?

Bottom Line:

Yes, multiple large case control studies show a weak association with prolonged PPI use (more than 1 year) and an increased rate of fragility fractures (SORT Level 2 quality studies with grade B strength of recommendation) warranting the judicious administration of long term PPIs.

When prescribing PPI’s to manage symptoms, intermittent PPI use or use of H2 blockers with less profound acid suppression may be both effective and of less potential long term fracture risk.

Synopsis:

Multiple retrospective observational studies have compared acid suppressive therapy by class (PPI vs. H2 blocker), dose and duration of use with fracture risk. Most of the studies looked at very large groups of patients from the United Kingdom General Practice Database (Yang), the Danish population (Vestergaard), Women’s Health Initiative, Nurses’ Health study (Khalili) or Kaiser Permanente (Corley, Yu). The studies consistently show an association but do not prove causation.

The increased risk of fractures was low (adjusted relative risk (ARR) of 1.08-1.40, 95% CI 1.01-1.8) depending on the subgroups evaluated (class of acid suppression and location of the fracture). Past PPI use of more than a year was less or not associated with increased fracture risk. Kaye in a 2 phase matched nested case-control analysis identified major medical risk factors for hip fracture. Phase 2 then compared the groups with and without fractures. This study did not find an association between PPI use and hip fracture risk. This technique may have better excluded residual confounding factors. Studies that evaluated the used of H2 receptor blockers suggested less or no association with fracture risk (Vestergaard, Corley, and de Vries)
Gray et al. reported from the Women’s Health Initiative (WHI) database an increase in fractures other than hip. However the marginal effect on 3-year BMD changes at the hip but not other sites raises questions about the etiology of the noted association (Targownik).

Finally, PPI use in patients on concurrent bisphosphonates had an inconsistent effect on fracture reduction effectiveness of bisphosphonates (Roux, Abrahamsen).

Many of the common indications for PPI’s are for limited term use (4-8 weeks). These include treatment of duodenal and gastric ulcers, stress ulcer prophylaxis and erosive esophagitis. Many patients do have GERD with a need for longer term treatment to maintain symptom control or healing of erosive esophagitis. Long term PPI therapy is also indicated in rare hypersecretry conditions and for preventing ulcers in high risk patients on necessary NSAID or antiplatelet therapy.

Long term use of PPI’s is associated with a number of potential safety concerns including: increased fragility fracture risk, hypomagnesemia, atrophic gastritis, gastric polyps, enteric infections, pneumonia, interstitial nephritis and a risk of drug-drug interactions. It appears prudent to limit PPI use to intermittent use to manage symptoms or long term use of an alternative H2 blocker when appropriate.

References:


Corley DA. PPI and H2 antagonist are associated with hip fractures among at-risk patients. Gastro 2010; 139:93.


Targownik LE. PPI use is not associated with osteoporosis or accelerated bone mineral density loss. Gastro 2010; 138:896.

Vestergaard P. PPI, H2 antagonists, and other antacid medications and the risk of fracture. Calcif Tissue Int 2006; 79:76.


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