



Happy St. Patrick's Day!



PIC QUESTION OF THE WEEK: 3/14/11

Q: What are some of the more recent concerns regarding administration of proton pump inhibitors?

A: Proton pump inhibitors (PPIs) are some of the most commonly prescribed drugs in this country. They are routinely used in the prevention and treatment of peptic ulcer disease, gastro-esophageal reflux, stress-related ulceration and hemorrhage, etc. This group of compounds is generally well-tolerated and, with the exception of combined use with clopidogrel and some antifungal compounds, has not been implicated in many significant drug interactions. Long-term use of PPIs may decrease absorption of non-heme iron ([PIC Question of the Week - 7/04/06](#)) due to increased gastric pH, but this rarely results in iron deficiency. There are, however, a few issues involving use of PPIs that remain to be resolved. Although a direct link has not been established, some clinical studies have suggested a possible association between the use of PPIs in an institutional setting and an increased incidence of aspiration pneumonia and *Clostridium difficile* (*C.diff*) infection. There has also been additional discussion regarding a tentative relationship between the use of PPIs and electrolyte disorders as well as an increased risk of fractures. The FDA recently released a preliminary notice addressing the possible association between use of PPIs and hypomagnesemia (*see reference link below*). The resultant increase in gastric pH upon use of PPIs seems responsible for this affect as well as the reduction in calcium absorption associated with their administration. A prospective analysis of outcomes based on the *Women's Health Initiative* revealed a statistically significant risk of spinal, forearm, wrist, and total fractures in post-menopausal women receiving PPIs. There was no increase in hip fractures in these women. A decrease in calcium absorption may not be the only mechanism by which PPIs increase risk for fracture. It appears that PPIs may also decrease osteoclastic and osteoblastic activity, thus reducing bone density. Further investigation is required to confirm this possible adverse effect of PPIs. Considering these potential risks of PPIs, some authors now recommend they be used at the lowest effective dose for the shortest period of time. If possible, the suggested duration is two weeks of continuous therapy no more than three times per year. Individuals considered at risk for fractures should take a calcium supplement to ensure optimal levels of calcium. Although PPIs are generally well-tolerated, the possible adverse consequences of prolonged use described above indicate a need to evaluate risk on an individualized basis.

References:

- Food and Drug Administration. MedWatch. FDA drug safety communication: low magnesium levels can be associated with long-term use of proton pump inhibitor drugs (PPIs). <http://www.fda.gov/Drugs/DrugSafety/ucm245011.htm>. Accessed March 8, 2011.
- Gray SL, LaCroix AZ, Larson J, et al. Proton pump inhibitor use, hip fracture, and change in bone mineral density in postmenopausal women. *Arch Intern Med* 2010;170:765-71
- McCarthy DM. Adverse effects of proton pump inhibitor drugs: clues and conclusions. *Curr Opin Gastroenterol* 2010;26:624-31

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