



Do Proton Pump Inhibitors (PPIs) Increase the Risk of Hip Fracture?

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Question – I suffered for years from pain and heartburn until I was diagnosed with GERD two years ago. The problem was finally brought under control when my doctor prescribed a proton pump inhibitor. Now I just read an article on the Internet about a report in a medical journal (JAMA, December 27, 2006) saying that people who take this medicine for over a year have a high risk of hip fracture. My mother had osteoporosis. How concerned should I be about this?

Answer –Many patients were alarmed recently by news reports of a 44% increase in the risk of a hip fracture if they are taking a proton pump inhibitor (PPI). The currently available PPIs include omeprazole (Prilosec, Prilosec OTC, Zegerid), lansoprazole (Prevacid), pantoprazole (Protonix), rabeprazole (Aciphex) and esomeprazole (Nexium). This is the latest in a series of articles that have questioned the safety of these powerful, widely used medications. Worldwide, PPIs have been available for over 20 years. In the 1980's there were concerns that, by profoundly decreasing stomach acid production, they might lead to other health problems such as serious infections, poor absorption of vitamins and minerals, even gastrointestinal cancers. However, by the mid-1990s, based largely on anecdotal experience, it was becoming clear that PPIs were remarkably safe. Formal studies looking at the use of PPIs in hundreds of patients showed virtually no long term side effects. As a result, new PPIs were developed, PPIs became generic and ultimately available over the counter without a prescription. This was a

great advance in our ability to treat the millions of patients worldwide that have acid-peptic diseases.

In the last few years, researchers have been able to evaluate the side effects and complications of medications by using large databases of millions of patients. A recent report in the Journal of the American Medical Association looked at the medical records of over 9 million people in the United Kingdom. They were able to identify over 13,000 people with a hip fracture and compare them to over 135,000 people who did not have a hip fracture. They found that using a PPI for over 1 year increased the risk of a hip fracture by 44%. They also found that the risk increased further if the patients were taking the PPI a longer period of time, or at higher doses. This is probably due to impaired calcium absorption when there is less acid in the stomach. Now, it must be mentioned that the patients with hip fractures in this study were much more likely to be a cigarette smoker, be thin, be a diabetic, be alcoholic, have had a stroke, had dementia or had previous bone fractures. Studies like this talk about the risk per patient-year of follow up. For example if one follows 100 patients for 10 years, that is 1,000 patient-years of follow-up. This study suggests that the risk of a hip fracture that is specifically related to PPI use is about 2 per 1,000 patient-years.

There have been other reports over the past couple of years about the possible risk of pneumonia and infections of the colon with a bacterium called clostridium difficile in patients taking PPIs. Again, these articles looked at the medical records of hundreds of thousands of patients and found a small increased risk in patients using PPIs. Additionally, like the hip fracture study, other medical illness such as diabetes, heart and lung disease were also important risk factors.

The Canadian Task Force for Preventative Health Care recently published recommendations for the prevention of osteoporosis in women. It mentioned major risk factors such as advanced age, family history of osteoporosis, early menopause, propensity to fall and minor risk factors such as being thin, smoking, excess alcohol or caffeine intake. We may learn that long term PPI use will be considered a minor risk factor. If you need to take a PPI, you should talk with your doctor about your risk of osteoporosis. If you have other risk factors, you may need a bone density test. You may simply need to take exercise more or take calcium supplements. You may need to take one of the many excellent medicines for osteoporosis.

It has probably been wishful thinking that the long-term use of PPIs was perfectly safe. Like most medications, there are side-effects and complications. Fortunately the overall risk of long-term PPI use still seems to be relatively small. Common sense tells that if you don't need to take a PPI, you should stop it. There are many people taking PPIs that could get away with using a less powerful medication. However, most people who need to take a PPI should be able to safely continue to take it without the fear of serious complications.

Suggested IFFGD Reading

Waring JP. *Long-term use of proton pump inhibitor medication and GERD*. IFFGD Fact sheet No. 531. 2007.

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