

## Case Report

# Osteoporosis in a 61 Year-old Male with Gastroesophageal Reflux Disease

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**\*Corresponding author:** Stephanie Anderson, College of Healthcare Sciences, Nova Southeastern University, USA**Received:** August 05, 2016; **Accepted:** September 02, 2016; **Published:** September 06, 2016**Abstract**

This article describes a patient who developed osteoporosis with significant risk of fracture after chronic therapy with high dose proton pump inhibitors for the treatment of gastroesophageal reflux disease. Recent research has shown evidence of a detrimental effect of PPI therapy on bone mineral density causing osteoporosis and a subsequent increase in fracture risk. Osteoporosis affects many people in the United States and its associated hip fractures are a major cause of morbidity and mortality. While PPIs are commonly used for the effective treatment of GERD, they should be prescribed with caution and awareness of the potential for bone demineralization.

**Keywords:** Osteoporosis; Gastroesophageal reflux disease; Proton pump inhibitor; Bone density; Fracture

**Case Presentation**

A 61 year-old male presented to his family medicine physician for an annual wellness exam. The patient had a history of gastroesophageal reflux disease (GERD) treated with 40mg esomeprazole twice a day; generalized anxiety with panic disorder treated with alprazolam 0.5mg extended release twice a day; and untreated chronic Hepatitis C. During the visit, he requested a medication evaluation due to negative side effects. He denied past or current use of tobacco or ETOH and mentioned a healthy diet low in sugar and fat along with a 3-mile daily walk for exercise.

The patient reported that his GERD causes severe, constant, reflux symptoms well controlled by esomeprazole at a high dose for the past 4 years, but GERD symptoms are worsened by anxiety. Although the medication provided adequate symptom control, the patient mentioned negative side effects of frequent headaches and abdominal pain. He denied nausea, vomiting, hematemesis, melena, and any neurological deficits. He was concerned that his research of esomeprazole suggested a correlation between proton pump inhibitors and fracture risk. Subsequently, the patient requested a dual-energy x-ray absorptiometry scan (DXA) to evaluate his bone density.

On exam, the patient appeared in good health with a slender body habitus. His weight measured 137.0 pounds with a height of 66 inches. Vital signs revealed blood pressure 184/78, heart rate 87 beats per minute, respiratory rate 16 breaths per minute, temperature 98.6°F, and oxygen saturation 99% on room air. The remainder of the physical exam was normal. Routine labs were ordered including CBC, CMP, lipid panel, TSH, testosterone, PSA, uric acid, and urinalysis.

Review of labs on a subsequent visit revealed only slight elevation of ALT (52 U/L) and PSA (4.8ng/mL). A DXA scan was ordered at the patient's request, which revealed a lumbar spine (L1-L4) T score of -3.2 along with a hipbone T score of -2.6 confirming a diagnosis of osteoporosis with significant increase in fracture risk.

Additional labs were ordered including PTH, calcitonin, and vitamin D which all returned within normal limits. Treatment with a high dose PPI for 4 years was presumed to be the cause of this patient's osteoporosis. Esomeprazole was stopped immediately and the patient started GERD treatment with famotidine 20mg four times a day. He started daily doses of 1000mg calcium carbonate and 2000 IU cholecalciferol. Bisphosphonate medications were avoided in this case due to risk of pill-induced esophagitis in a patient with symptomatic GERD. The patient was advised to start a receptor activator of nuclear factor kappa-b ligand (RANKL) inhibitor to help increase bone mass, undergo a DXA scan every 2 years, and increase weight-bearing exercise.

**Discussion/Conclusion**

Proton pump inhibitors are widely used for the treatment of gastroesophageal reflux disease in both the acute phase and chronic maintenance phase. While the drug class is considered highly effective in the treatment of GERD, recent studies have demonstrated an increased risk of adverse effects when used for long term treatment outside of their various indications and in at risk populations including the elderly, postmenopausal women, and smokers [1]. One study mentioned that approximately 50-80% of geriatric and internal medicine patients admitted to acute wards have an inappropriate PPI prescription [2].

Although an exact mechanism is unclear, there are several hypotheses to account for the mechanism of action. One theory mentions the necessity of an acidic gastric pH for effective calcium absorption into the serum, which is inhibited by PPIs as they raise the gastric pH [3]. While cortical bone confers overall strength, trabecular bone is considered most metabolically active and is more likely to be affected by metabolic and pharmacologic changes in the body including mineral metabolism. Osteoporosis is associated with early changes in the trabecular bone and PPIs may exacerbate these changes through their effects on mineral metabolism [2].

There is evidence that PPIs cause decreased bone mineral

density and increased fracture risk. A prospective study that sought to discover the effect of PPIs on bone density evaluated a group of patients aged 18 to 58 with symptomatic and endoscopic findings of GERD treated with PPIs for a period of 6 months [4]. Bone mineral density was measured with a DXA scan prior to treatment and repeated after the 6-month PPI trial, and all confounding factors were adjusted for. Results in the PPI treatment group revealed significant mean reductions of L3 T scores, L4 T scores, total lumbar vertebra T scores and femur neck T scores and concluded that bone mineral density in both the vertebra and femur were reduced in patients receiving long-term treatment with PPIs [4].

Hip fracture stands as the most dangerous adverse outcome of osteoporosis. Another study was conducted to determine whether a correlation exists between the effects of PPIs on bone mineral metabolism and hip fracture risk [5]. The study evaluated a cohort of 1.8 million patients representative of the general population and included users and non-users of PPIs age 50 and up who experienced a hip fracture [5]. Confounding diagnoses, medications, and sex of the patient were adjusted for. Results showed a significantly increased risk of hip fracture among people who used PPIs for more than one year at a high dose compared to acid suppressor non-users [5]. Of importance to the patient presented, this study revealed an increased strength of association with duration of PPI therapy at 4 years and a stronger risk in men than in women [5]. The study concluded chronic, high-dose, PPI therapy is associated with a significantly increased risk of hip fracture [5]. Subsequently, the FDA revised all PPI prescription labels to include safety information regarding the possible increased risk of fractures with their use [6].

Current statistics by the National Osteoporosis Foundation state that 54 million Americans are affected by osteoporosis or low bone mass placing them at risk for osteoporosis [7]. Osteoporosis should be taken seriously as complications of hip fractures are responsible for the death of 25% of seniors within one year of hip fracture [7]. It is also taxing to our healthcare system financially, with predictions of \$25.3 billion in costs annually and 3 million fractures due to osteoporosis by the year 2025 [7]. According to the United States Preventive Services Task Force, osteoporosis screening with DXA should begin at age 65 for all women [8]. USPTF guidelines do not currently recommend screening for men due to lack evidence for benefit or harm with screening [8]. However, the National Osteoporosis Foundation recommends DXA for all men age 70 and up and men age 50-69 at increased risk of developing osteoporosis [8]. In the case presented, DXA screening was performed to fulfill the patient's request under the assumption of increased risk due to chronic PPI therapy. Results

revealed a unique diagnosis of osteoporosis, which would not have been discovered without the requested DXA. Therefore, it may be beneficial to offer DXA screening in both male and female patients who have undergone chronic treatment with PPIs.

Though research reveals evidence of an association between use of PPIs, osteoporosis, and increased fracture risk, the association is likely multifactorial and more research is necessary. Regardless of the commonality and effectiveness of PPIs for the treatment of GERD, they should always be managed with caution. When prescribing PPIs, ensure that the benefits outweigh the risks, use the lowest effective dose, frequently reassess the need for treatment, and avoid chronic therapy at high doses when possible. If a calcium supplement is used prophylactically in patients taking PPIs, calcium citrate is recommended because it does not require an acidic gastric pH for absorption [9]. Osteoporosis is a serious, but often-silent disease that requires careful monitoring. Awareness, appropriate use, and safe management of proton pump inhibitors may prevent the development of osteoporosis and its associated increase in fracture risk.

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