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News on current events in osteoporosis and rheumatology

Long-term proton pump inhibitor therapy and risk of hip fracture

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Hip fracture is the main manifestation of senile osteoporosis, which results from secondary hyperparathyroidism associated with calcium malabsorption, low calcium intake, and other factors. Among the various forms of low-trauma fractures, hip fracture leads to the most devastating consequences.

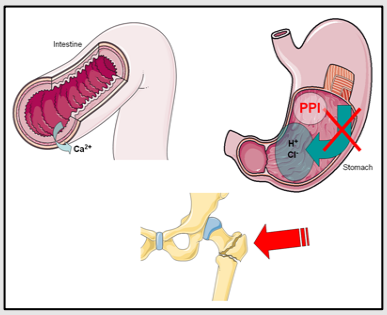
The advent of potent acid-suppressive medications such as proton pump inhibitors (PPIs) has revolutionized the management of acid-related diseases such as gastroesophageal reflux disease (GERD). Significant hypochlorhydria, particularly among the elderly population who may have decreased PPI clearance and may be more likely to have hypochlorhydria at baseline due to higher prevalence of *Helicobacter pylori* infection, could theoretically result in calcium malabsorption.

Yang et al. conducted this study [1] to determine whether these opposing effects of PPI therapy on bone metabolism translate into clinically important alterations in hip fracture risk in a large cohort representative of the general population. A nested case-control study was conducted using the General Practice Research Database (1987-2003), which contains information on patients in the United Kingdom. The study cohort consisted of users of PPI therapy and nonusers of acid suppression drugs who were older than 50 years. Cases included all patients with an incident hip fracture. Controls were selected using incidence density sampling, matched for sex, index date, year of birth, and both calendar period and duration of up-to-standard follow-up before the index date. The main outcome measure was the risk of hip fractures associated with PPI use. There were 13 556 hip fracture cases and 135 386 controls. The adjusted odds ratio for hip fracture associated with more than 1 year of PPI therapy was 1.44. The risk of hip fracture was significantly increased among patients prescribed long-term high-dose PPIs. The strength of the association increased with increasing duration of PPI therapy.

This study indicates that long-term PPI therapy, particularly at high doses, is associated with an increased risk of hip fracture.

1. Yang YX et al. *JAMA.* 2006; 296: 2947-2953.
2. Talley NJ et al. *Nature Clin Practice.* 2007; 4(8): 420-421.

Proton pump inhibitor (PPI) therapy increases risk of hip fracture



Reduction of gastric proton and chloride secretion are the expected effects of PPIs. Reduced chloride secretion results in hypochlorhydria which impairs downstream intestinal calcium absorption. This mechanism may underlie the increased occurrence of hip fractures observed in patients treated with long term high-dose PPIs.

However, this mechanism remain uncertain and further investigation is needed. [2] For example, another possible mechanism by which long-term PPIs might induce osteoporosis could be through acid suppression precipitating small-bowel bacterial overgrowth and inducing malabsorption. In this instance, calcium malabsorption might not reduce the risk. Therefore, the mechanism of action requires further research.