Is There Any Association of Osteoporosis With Proton Pump Inhibitor Use?

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Summary

Osteoporosis is a very common medical condition while osteoporosis related fractures could lead to significant disability and poor quality of life. There are several medications which are classified as the causes for osteoporosis, such as corticosteroids or antiepileptic drugs.^{1,2} Recently, an association between proton pump inhibitors (PPIs) and hip fracture was suggested.^{3,4} This is primarily based on evidence from epidemiologic analyses showing a significant association between chronic PPI use and the risk of hip fracture.

The present study was conducted to determine whether chronic PPI use is associated with an increased risk of osteoporosis based on bone mineral densitometry in cross sectional study and whether continued use of a PPI leads to an increased rate of bone mineral density (BMD) decline in longitudinal study setting.⁵

Two separate analyses were performed. In the cross-sectional study, authors compared subjects with established osteoporosis, as determined by BMD testing, to controls with normal BMD. In the longitudinal study, they analyzed the change in BMD on serial assessments between PPI users and non-PPI users. The

Manitoba Centre for Health Policy maintains the Population Health Research Data Repository. It includes a comprehensive collection of population-based health utilization data sets and the Drug Programs Information Network data set, giving researchers the ability to construct a longitudinal medical history for any person registered with the Manitoba Health Services Insurance Plan.⁶ Osteoporosis was defined by dual-energy X-ray absorptiometry, or DXA scanning in the Provincial Bone Mineral Density Database.

In the cross-sectional study, 2,193 subjects had evidence of osteoporosis at the hip and were matched to 5,527 controls with normal hip measurements. A total of 3,596 subjects had BMD measurements consistent with osteoporosis at the lumbar spine and were in turn matched to 10,257 normal controls. In univariate analyses, PPI use was associated with a lower risk of osteoporosis at the lumbar spine for all levels of PPI use, however, after adjusting for potential confounders through conditional multivariable logistic regression, no association was observed between PPI use and osteoporosis at either the hip or the lumbar spine.

In the longitudinal study, they identified 2,549 subjects who underwent 2 separate BMD assessments with mean follow-up period of 2.31 ± 0.5 years.

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The use of standard dose of PPIs over the time between BMD assessments did not have a statistically significant effect on the rate of BMD decline, either at the lumbar spine (change in BMD, $0.03\% \pm 0.22\%$; $p > 0.2$) or the total hip (change in BMD, $-0.17\% \pm 0.18\%$; $p > 0.2$). The use of bisphosphonates, systemic estrogens and estrogen receptor modulators was associated with a significant annual increase in BMD at both sites (adjusted $p < 0.0001$), whereas the use of corticosteroids was associated with a significantly greater decline in BMD at both the lumbar spine and hip in the adjusted analyses.

Comment

PPIs are widely used in clinical practice and physicians generally consider this drug as one of the safest to prescribe. The previous nested case-control study in the General Practice Research Database showed a significant association between chronic PPIs use and hip fracture in a dose dependent manner.³ Acid suppressive therapy might impair calcium absorption and therefore increase the risk of silent osteoporosis. PPI use in juvenile rats has been shown to decrease both bone density and peak bone mineral mass.⁷ However, there is little direct evidence that links the use of PPIs to the development of osteoporosis. Gastrectomy has been associated with decrease in BMD.⁸ Gastrectomy induces hypergastrinemia which may induce parathyroid hyperplasia and promote bone calcium loss.⁹ However, vagotomy without gastrectomy does not induce bone density loss and altogether these findings support the limited role of acid suppression in the development of osteoporosis.¹⁰

The present study postulates that chronic PPI use not to be associated with an increased risk of osteoporosis as determined by BMD testing, despite evidences linking their use to an increased risk of fractures. However, the absolute risk of hip fracture secondary to PPI therapy was very small. Notably, the crude incidence rate of hip fracture was nearly 2 per 1,000 person among non-PPI users, and this only increased to 4 per 1,000 person with more than 1 year of PPI use.^{3,11}

PPIs are safe medicines, however, PPIs are often chronically used in situation in which patients are at high risk for declined bone density, such as chronic corticosteroid user, chronic debilitating conditions or old ages. At this time, there is no definitive evidence to discontinue the long-term PPI use, however, we need further prospective studies on the effect of PPI use on the bone mineral metabolism and bone health.

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