International Journal of Medical and Health Research
ISSN: 2454-9142
www.medicalsciencejournal.com
Volume 4; Issue 3; March 2018; Page No. 13-14

Osteoporosis and its association with proton pump inhibitors

[*] Sarah I Al-Essa, Alanoud M Alyousef, Ghadah A Alharbi, Lama A Alhomayin, Rahaf E Salem, Reem N Alrakaf
Medical Intern, King Saud University, Riyadh, Saudi Arabia

Abstract
Osteoporosis is considered to be one of the most prevalent skeletal disorders worldwide, caused by an imbalance in the body's calcium leading to decreased bone density. It is diagnosed by dual energy x-ray absorptiometry. It usually occurs in the elderly population, especially postmenopausal women. The Management focuses on lifestyle modification and decreasing the risk of falls and thereby the risk of fractures. The first line of medical treatment is Bisphosphonate. Osteoporosis is a multifactorial disorder that has genetic, hormonal and environmental factors. There are many drugs that contribute to the development of osteoporosis. Researches reviewed in this article on proton pump inhibitors were found to have different results on their effect in bone mass density. To this day, there is no strong definitive evidence attributing osteoporosis to proton pump inhibitors.

Keywords: osteoporosis, BMD, proton pump inhibitor, calcium, DXA

1. Introduction

1.1 General characteristics and epidemiology

Osteoporosis is a systemic skeletal disorder characterized by low bone density making it easily susceptible to fractures. It is caused by a disturbance in the balance between osteoclast and osteoblast activity leading to bone degeneration [1].

It is considered to be a worldwide health issue, affecting approximately 200 million individuals, with the highest prevalence being amongst the elderly in both sexes but mostly postmenopausal women [2].

The prevalence of osteoporosis differs between countries suggesting environmental influencers at play [3], as well as genetic factors [4].

1.2 Pathogenesis

There are two different mechanisms in which osteoporosis occur. First is the failure of production of proper bone mass, this is maintained by adequate osteoblast activity. Second is increased bone resorption leading to decreased bone mass; which is controlled by osteoclast activity. Any imbalance between osteoclast and osteoblast activity would result in osteoporosis [5].

As mentioned above, osteoporosis is a multifactorial disorder with contributions of multiple genetic, hormonal and environmental factors [6].

Estrogen, vitamin D, calcium, parathyroid hormone and gonadotropins are all associated with decreased bone density. Studies have found that physical activity and good health during growth plays a role in preserving bone density [7].

Many researches tied to find a link between medication and the development of low bone density. Anticonvulsants, glucocorticoids, proton pump inhibitors (PPI) and selective serotonin reuptake inhibitors are part of the long list of medications that have been found to cause secondary osteoporosis [5-8].

1.3 Diagnosis

Osteoporosis is diagnosed by measuring bone mineral density (BMD). The golden standard radiological method of measuring BMD is by using dual energy x-ray absorptiometry (DXA) to assess the spine or hip [8].

To diagnose osteoporosis in men older than 50 years of age and postmenopausal women, spinal or hip BMD should be equal to or more than 2.5 standard deviations below the young adult female reference mean. This is known as a T-score less than or equal to –2.5. If the DXA scan is performed on a male or female younger than 50 years of age, Z-score is used. Z-score compares the BMD of individual tested to those of the same age and gender. A Z-score of −2.0 or less are below the expected range for age, which is diagnostic for osteoporosis [8].

Other than basic laboratory testing, evaluating the following would help reach a diagnosis of secondary osteoporosis: vitamin D levels, calcium, urea, creatinine parathyroid stimulating hormone and thyroid stimulating hormone [1].

Risk assessment is important when it comes to this disorder, especially in postmenopausal women. The Fractures Risk Assessment tool (FRAX) is also assessed; it is used to help determine the risk of fracture occurring because of osteoporosis in 10 years [9].

1.4 Management

After establishing a diagnosis, risk fall assessment must be measured. Physical exercise especially those against gravity are recommended along with muscle strengthening activities would reduce the risk of fractures.

Pharmacological management includes the following: Bisphosphonates, Raloxifene may be used for both treatment and prevention, whereas Teriparatide, and Denosumab are only used for treatment. All of the above mentioned drugs improve BMD and reduce risk of fractures.

Bisphosphonate is considered to be the first line of treatment. Calcitonin is used when other therapies are contraindicated or not tolerated. Hormonal therapy has been proven to enhance

BMD, but has no effect on fracture risk reduction. Vitamin D and calcium are either given exogenously or are obtained from the diet and sun exposure to help decrease bone loss and increase bone mass.

2. Proton pump inhibitors and osteoporosis

PPIs are used in the management of diseases in which gastric acid production is high, like gastro-esophageal reflux disease (GERD).

Physiologically, acidic juices of the stomach are produced by parietal cells through H+, K+-ATPase, these are known as the proton pump. PPIs are weak basis that inhibit the proton pump and thus decrease gastric acid production. By doing so, PPI inhibits osteoclastic proton pumps leading to decreased bone resorption and reduces calcium absorption from the small intestines, which results in an imbalance between osteoclast/osteoblast activity [11].

In a cohort study done by Fraser *et al*, an association between PPI ingestion and osteoporosis was found [12]. A study by Targownik *et al* found that subjects who were on PPIs had lower BMD, but no BMD loss acceleration over a period of 10 years. The reason for that is not yet clear [13]. In another study, it was noticed that there was no significant BMD decline in those taking PPIs when compared to those taking corticosteroids [14].

On the other hand it is believed that the decreased BMD in those on PPI is attributed to other factors and not because of osteoporosis [15].

Reimer *et al.* suggests that not all those who are taking PPIs are at risk of osteoporosis. Focus should mainly be on the elderly, malnourished and those with comorbidities. As they have higher chances of developing gastric tract infections, fractures and nutritional deficiencies [16]. As there is no strong direct evidence on their effect on BMD, Anderson *et al* recommends that PPIs should only be prescribed to those who truly need it and should also be at the lowest dose possible [17].

Surprisingly, another researcher proved that using bisphosphonate, especially Risedronate, alongside PPIs increases its effectiveness as a drug [18].

3. Conclusion

In general PPIs are considered safe medication with no obvious long-term complication. However, as suggested by some articles, the use of PPIs could have altered the body's calcium balance, which may lead to a lower BMD. While others disagree and attribute this finding to other causes. To this day, there is no strong definitive evidence attributing osteoporosis or low BMD to proton pump inhibitors. This is why doctors should be cautious when prescribing PPI.

4. Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

5. Author's contribution

All authors participated in the conception and design of this review article. They all read and approved of the final paper.

6. References

1. Sandhu SK, Hampson G. The pathogenesis, diagnosis, investigation and management of osteoporosis. Journal of Clinical Pathology. 2011; 64:1042-1050.
2. Reginster Jean-Yves, Burlet, Nansa. Osteoporosis: A still increasing prevalence. J Bone. 2006, 38(2).
3. Kanis JA, Odén A, McCloskey EV. *et al*. A systematic review of hip fracture incidence and probability of fracture worldwide. Osteoporos Int. 2012; 23:2239-2256.
4. Stewart TL, Ralston SH. Role of genetic factors in the pathogenesis of osteoporosis. Journal of Endocrinology. 2000; 166:235-245.
5. Raisz LG. Pathogenesis of osteoporosis: concepts, conflicts, and prospects J Clin Invest. 2005; 115(12):3318-3325.
6. Rosen CJ. The Epidemiology and Pathogenesis of Osteoporosis South Dartmouth. 2000.
7. Khosla S, Riggs BL. Pathophysiology of age-related bone loss and osteoporosis. Endocrinology and Metabolism Clinics of North America. 2005; 34(4):1015-1030.
8. Jeremiah MP, Unwin BK, Greenawald MH, Casiano VE. Diagnosis and Management of Osteoporosis. Am Fam Physician. 2015; 92(4):261-8.
9. Cosman F, De Beur SJ, LeBoff MS. *et al* Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014; 25(10):2359-2381.
10. Mora S, Gilsanz V. Establishment of peak bone mass. Endocrinol Metab Clin North Am. 2003; 32(1):39-63.
11. Yang Y. Proton Pump Inhibitor Therapy and Osteoporosis, Current Drug Safety. 2008; 3(3):204-209.
12. Fraser LA, Leslie WD. *et al*. The effect of proton pump inhibitors on fracture risk: report from the Canadian Multicenter Osteoporosis Study Osteoporosis International. 2013; 24(4):1161.
13. Targownik LE, Leslie WD, Davison KS, Goltzman D, Jamal SA, Kreiger N. *et al*. The Relationship Between Proton Pump Inhibitor Use and Longitudinal Change in Bone Mineral Density: A Population-Based From the Canadian Multicentre Osteoporosis Study (CaMos). Am J Gastroenterol American College of Gastroenterology. 2012; 107:1361-1369.
14. Jung H-K. Is There Any Association of Osteoporosis With Proton Pump Inhibitor Use? (Gastroenterology. 2010; 138:896-904. Journal of Neurogastroenterology and Motility. 2010; 16(3):335-336.
15. Targownik Laura E. *et al*. Proton-Pump Inhibitor Use Is Not Associated With Osteoporosis or Accelerated Bone Mineral Density Loss Gastroenterology. 2009; 138(3):896-904.