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Gratis

Letter to Editor

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Treatment of Osteoporosis with Bisphosphonates: Is Vitamin D Necessary?

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Bisphosphonates (BP) are the most commonly used medications for the treatment of osteoporosis. Of them, the most frequently prescribed worldwide is alendronate. Of the various compounds available, those that are ingested are usually indicated, but they are also available for intravenous use at different intervals, depending on their potency [1].

BP have good anti-fracture efficacy, especially at the level of the spine and the peripheral skeleton, and most are also effective for the prevention of hip fractures [2].

These drugs are currently recommended for a limited time of approximately 5 years, although in high-risk patients this period may be prolonged. The reason for this limitation is the risk of complications due to chronic use, such as osteonecrosis of the jaw and atypical fractures [3]. Due to fear of these complications, many indicate a "medication holiday", taking advantage of the prolonged stay of BP in bone, which is shorter for risedronate, longer for alendronate, and even longer for ibandronate and zoledronate. However, when the "vacation" lasts more than 4-5 years, the fracture risk seems to increase, so the following strategy is proposed:

If the patient has a very low bone mineral density (BMD), or BMD is lost during the annual controls, or the resorption markers are elevated, it is necessary to consider either the reinitiation of the BP or the beginning of another anti-osteoporotic medication [4,5]. Likewise, if high risk indicators (such as falls, new fractures, diagnosis of diabetes, or indication of glucocorticoid therapy) appear in the course of follow-up, BP must be reindicated, or another treatment must be started [6].

The deficiency of vitamin D is highly prevalent in the world. Among the groups at risk of having hypovitaminosis D are precisely patients with osteopenia/osteoporosis [7].

There is a general consensus on the reduction of risk of non-vertebral fractures in groups of patients with vitamin D deficiency who receive supplements, provided that the indicated doses are sufficient and that the adherence is adequate [8].

However, there are some doubts about the advisability of adding calcium and vitamin D supplements in patients treated with BP. In general, combined calcium + D supplements are tablets that must be taken daily; when tolerance is not good, they are discontinued, with the consequence that calcium is not received but neither is vitamin supplementation [9]. Whenever possible, enough calcium intakes should be encouraged with dietary modifications, especially adding dairy products. The supplements of vitamin D are usually well tolerated, with recommended doses of 1,000-4,000 IU

per day, which can then be indicated on a daily, weekly or monthly basis [7].

We must emphasize that all clinical trials published on the efficacy of BP for the treatment of osteoporosis have incorporated calcium and vitamin D supplements for the participating subjects.

Some pharmaceutical companies, especially in the Far East, have combined BP with cholecalciferol, calcitriol or alphacalcidol (the last two are active forms of vitamin D) in the same tablet, which improves the effectiveness of the medication and facilitates adherence [10].

A Japanese study determined that the minimum required serum level of 25-hydroxyvitamin D (25OHD) to obtain significant increases in BMD after treatment with alendronate is 25 ng/ml [11].

An Italian study found that the baseline 25OHD level (generally deficient in patients) did not influence the densitometric response to alendronate, although all participants received a daily supplement of calcium (500 mg) and vitamin D (250 IU) [12].

An expert opinion, based on personal experience, found that osteoporotic patients lacking vitamin D have secondary hyperparathyroidism, and that only those with a sufficient level of 25OHD and normal serum PTH levels benefit from good densitometric response to BP [13]. Two recent Japanese studies in more than 1,200 osteoporotic patients treated with risedronate confirm that the densitometric response is better in subjects with vitamin D sufficiency [14,15].

Adami et al. found that the densitometric response to anti-resorptive drugs (BP, raloxifene) is greater in patients with good levels of vitamin D, but they also saw that patients with initial vitamin deficiency are significantly more likely to fracture one year after starting treatment [16].

To conclude this letter, I would like to recall the high prevalence of hypovitaminosis D among osteoporotic patients, especially those recently fractured. When studying a large group of patients with wrist, humeral or femoral fractures, the prevalence of vitamin D insufficiency (25OHD < 30 ng/ml) was 70%, and that of deficiency (25OHD < 20 ng/ml) was 40% [17]. In addition, I think it is important to note that an adequate intake of calcium, and vitamin D supplementation at appropriate doses, are an integral and necessary part of any treatment with anti-osteoporotic drugs [18].

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