

Proper compliance of treatment for osteoporosis: we still have much to do

Sosa Henríquez M^{1,2}, Gómez de Tejada Romero MJ^{1,3}

1 Instituto Universitario de Investigaciones Biomédicas y Sanitarias - Universidad de Las Palmas de Gran Canaria - Las Palmas de Gran Canaria (España)

2 Unidad Metabólica Ósea - Hospital Universitario Insular - Las Palmas de Gran Canaria (España)

3 Departamento de Medicina - Universidad de Sevilla - Sevilla (España)

e-mail: msosah@hotmail.com

Osteoporosis is a common disease, its main clinical complication being bone fragility¹. This chronic, generally asymptomatic process deteriorates the bone, exposing it to fracture risk. Current treatment techniques aim to minimize the possibility of new fractures¹⁻⁴ but there is no medication to eliminate such risk. Most drugs currently available for treating osteoporosis achieve reductions of between 40 and 65%²⁻⁴, if the medication is taken continuously over a period ranging from 3 to 5 years. This would be mere utopian, as, in fact, the patients frequently abandon their osteoporosis treatment, once they have begun.

Numerous studies have shown that adherence to osteoporosis treatment is generally low, and that in the first year the dropout rate is between 30-50% in most cases⁵. One reason may be their asymptomatic condition, which does not provide the patient with a sense of improvement. Perhaps, if all goes well, the patient does not suffer fracture, but subjectively does not perceive anything. In this respect, osteoporosis differs from other chronic diseases in which symptoms return as soon as the patient discontinues treatment, such as migraines, ischemic heart disease or diabetes mellitus. The treatment procedure could be another factor related to the patient's carrying on correctly with their prescribed medication. Several studies have shown that compliance with bisphosphonate was better when the doses were spaced. Thus, Penning-van Beest et al observed that after one year, 51.9% of patients continued treatment with weekly administration, whereas only 30-42% of those with daily doses, regardless of the type of bisphosphonate administered (etidronate, alendronate or risedronate)⁶. In another study, Cramer et al assessed the compliance of 2,741 women treated with bisphosphonates and found that, after one year, adherence was 44.2% in those taking it on a weekly basis, compared to 31.7% among those on a daily regime⁷.

In the US, Ettinger et al analyzed sales of alendronate and risedronate prescriptions in more than 211,000 women and found that after one year, 56.7% of patients taking weekly bisphosphonate continued taking the drug, compared with 39% of those who took the medication daily. These

authors pointed out, however, that over 40% of patients continued weekly treatment with bisphosphonates⁸. In a study of 15,640 women in the UK, France and US, Cramer et al found that after one year, patients' adherence with bisphosphonates was higher in those receiving medication weekly, compared to daily (44% vs 32%, respectively, in the United States; 52% vs 40% in the UK, and 51% vs 44% in France), where in all cases the value of $p < 0.001$ ⁹.

There have been other studies comparing monthly and weekly administration of bisphosphonates. In the PERSIST study, adherence to treatment was compared for six months in a group of women receiving monthly ibandronate versus another taking alendronate weekly. It was found that of those taking medication monthly 56.6% kept up the treatment, compared to 38.6% of those taking alendronate weekly¹⁰.

The introduction of zoledronate and denosumab, drugs with a longer half-life that allows an annual and biannual administration respectively, has significantly changed the scenario of therapeutic failure and patient preferences. A multi-center, randomized, double-blind study conducted by McClung et al. to assess the safety and efficacy of a single intravenous dose of 5 mg zoledronic acid vs 70 mg weekly oral alendronate, and performed in 225 women with postmenopausal osteoporosis who had previously been treated with weekly alendronate result showed that 78.7% of patients expressed a preference for intravenous versus oral treatment on a weekly basis¹¹, as most participants expressed in a similar study by Saag et al.¹².

Clearly, patients regularly taking medication for osteoporosis have better results, both in terms of changes in bone mineral density¹³ and, more importantly, the reduced rate of fracture and lower mortality^{14,15}. A study by Siris et al in a large population of postmenopausal women over 45 years, treated with bisphosphonate for osteoporosis, showed that after two years of follow-up, those women taking the treatment properly (43%) reduced the risk of fracture, both vertebral and non-vertebral, 21% higher than patients who did not follow the treatment correctly¹⁶. Previously, Caro et al had obtained similar results, finding a reduction in the appearance of new superior fractures (16%) among those patients who complied

compared to those who did not. In this follow-up study period of 2 years, and the treatments evaluated were calcitonin, hormone replacement therapy and bisphosphonates¹⁷. The same authors repeated the study using a broader base of data, with a cohort of more than 38,000 women suffering from osteoporosis, and obtained similar figures: poor adherence to treatment was associated with an increased risk of fracture of 17% after 1.7 years¹⁸. These results are corroborated by those obtained in other studies¹⁹⁻²¹.

In this issue Blanch et al complete the perspective of non-compliance and poor adherence to treatment of osteoporosis from the physicians' point of view²². So far, most studies have analyzed the views of patients, that the degree of abandonment existed, the reasons and consequences, but the doctors' opinion regarding this matter had been rarely considered and is now published here. The authors interviewed 235 doctors throughout Spain and among other findings obtained responses that, so far, had not been collected in other studies, which gives it an additional value for its originality. Thus, among the reasons that cause nonadherence, lack of coordination between levels of care, polypharmacy and side effects are suggested.

Understanding these facts can help us gain better adherence and compliance by patients, in addition to improved levels of communication between doctors and patients. Knowledge of the expected side effects (frequency) and, when indicated, the introduction of drugs with a longer life and a semiannual or annual administration, could be useful.

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