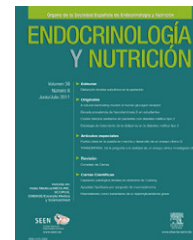




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EDITORIAL

Treatment holidays in patients with postmenopausal osteoporosis: Whom and when?☆

Vacaciones terapéuticas en pacientes con osteoporosis postmenopáusica: ¿a quién y cuándo?

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The controversy about the ideal duration of treatment with bisphosphonates is not new. As early as in 2005, some experts suggested that treatment with alendronate for patients with postmenopausal osteoporosis could be discontinued after five years, provided no fractures had occurred during this period and bone mass had improved as compared to baseline. This recommendation was based on the lack of data showing an additional fracture rate reduction when treatment was continued beyond five years, and on the fact that remodeling markers continued to be suppressed despite treatment discontinuation, which suggested a residual effect.¹

The final data of the FLEX study² were reported in 2006. In this study, 1099 women from the Fracture Intervention Trial (conducted to assess the anti-fracture efficacy of alendronate) were randomized again to three treatment arms: placebo, alendronate 5 mg/day, and alendronate 10 mg/day, for five years. In the placebo group, a decrease in bone mineral density (BMD) associated with increased remodeling was seen, but values prior to the start of treatment were not reached. The patients who continued to receive alendronate had a lower risk of clinical vertebral fractures as compared to the placebo patients, but no differences

were seen in nonvertebral fractures. Based on these findings, the authors concluded that although treatment with alendronate for 10 years was safe, the drug could be discontinued at five years in most women with no resultant increase in fracture risk. By contrast, in patients with high fracture risk, such as those with prior vertebral fracture or low bone mass, they considered that continued treatment beyond five years might provide an additional benefit.

In our view, insufficient attention was paid to these recommendations, and it is only in the past year that there has been a renewed interest in this issue at meetings, in publications, and at scientific forums. One of the reasons for this renewed interest may be the issues related to the potential complications of long-term treatment with bisphosphonates, such as atypical femoral fractures, although it should be noted that the etiopathogenesis of these fractures is complex and their relationship with bisphosphonates, and especially with treatment duration, has not been fully proven.³

In this regard, the *New England Journal of Medicine* has recently published two editorials on the subject.^{4,5} Both editorials recommended regular re-assessment of the need to continue treatment with bisphosphonates in postmenopausal osteoporosis. In the first editorial,⁴ the authors proposed treatment discontinuation after three to five years in patients with low fracture risk, such as young patients with no history of fracture and normal BMD. In the second editorial,⁵ Black et al.² proposed objective criteria, based on data from the FLEX study of alendronate and from the HORIZON study⁶ of zoledronate, to help decision-making in clinical practice. Thus, in patients who have been treated

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with zoledronate for three years or with alendronate for five years, treatment should be continued if BMD in the femoral neck continues to be below -2.5 DS (T -score less than -2.5) or if there is a history of vertebral fracture and a T -score less than -2 , as these are situations with an increased risk of fracture.

This is an attractive approach with which we are in complete accord. However, there are some practical problems which need to be resolved. As recognized by the authors, these recommendations are not applicable to other widely used anticatabolic drugs such as risedronate and ibandronate. Moreover, they are only valid for women with postmenopausal osteoporosis, as they are based on data from studies conducted on this patient group. Finally, the monitoring to be performed following treatment discontinuation needs to be established. Thus, although the regular monitoring of BMD using DXA and the measurement of bone remodeling markers are recommended, we do not know what the ideal intervals for performing such tests are and what criteria should be used for restarting treatment. In conclusion, and as occurs with other diseases, the treatment of osteoporosis should be individualized by taking into account the characteristics and preferences of each patient. Evaluation of the risk/benefit ratio and patient participation in decision-making should also be parts of standard clinical practice.

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