

BONE

Bisphosphonate use and atypical femur fractures

Bisphosphonate use is associated with only a very low risk of atypical fractures to the subtrochanteric or diaphyseal femur, even in women who receive the drugs for up to 10 years, data from an article published in the *New England Journal of Medicine* suggests.

Several case reports and series have suggested that bisphosphonate use may increase the risk of atypical fractures to the subtrochanteric or diaphyseal femur. Examples of atypical fractures described include those with transverse morphology, cortical thickening or fractures that result from low-level trauma. Evidence of such an association from randomized controlled trials was, however, lacking.

The investigators reviewed records of hip or femur fractures from three large, randomized controlled trials of bisphosphonate treatment (two trials of oral alendronate and one of zoledronic

acid infused annually). The three trials together included >14,000 women and >51,000 patient-years of follow-up for up to 10 years.

Overall, 283 hip or femur fractures occurred in the trials, but after exclusion of fractures that were periprosthetic, pathological, associated with high-energy trauma or in other locations, only 12 fractures of the subtrochanteric or diaphyseal femur in 10 women were of interest.

Risk of fracture to the subtrochanteric or diaphyseal femur associated with the use of bisphosphates was, therefore, very low: 2.3 per 10,000 patient-years overall in the three trials and ranged from one to six cases per 10,000 patient-years for the separate trials.

The investigators, unfortunately, could not assess atypical features of these fractures, such as cortical thickness and fracture morphology, because radiographic evidence was lacking. This information might have excluded additional events and, thus, reduced the risk further. The relative risks of subtrochanteric or diaphyseal femur fractures among treated patients compared with those



receiving placebo for the alendronate trials were 1.03 (95% CI 0.06–16.46) and 1.33 (95% CI 0.12–14.67), and for the zoledronic acid trial, relative risk was 1.5 (95% CI 0.25–9.00), but the researchers conceded that the small number of events and the associated wide CIs make it difficult to draw firm conclusions about the relative risk of treatment.

In conclusion, the researchers reflect that balanced against the established fracture-prevention risk of bisphosphonates in women with osteoporosis, the hypothetical risk of atypical fractures of the subtrochanteric or diaphyseal femur is small.

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Original article Black, D. M. *et al.* Bisphosphonates and fractures of the subtrochanteric or diaphyseal femur. *N. Engl. J. Med.* 362, 1761–1771 (2010)

