



Osteoporosis Canada

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Bisphosphonates and atypical fractures

We are aware of recent media reports that long-term use of bisphosphonates for osteoporosis (sold under the names of Fosamax [alendronate] and Actonel [risedronate]) may be associated with the occurrence of unusual fractures, most commonly reported to affect the thigh bone.

It is a fact that all medications have risks associated with them. Osteoporosis medications are no exception. Every time a medication is recommended or prescribed, a careful weighing of the risks and benefits associated with taking that medication is included.

The concern raised in some recent press reports relates, in part, to two studies presented at the annual meeting of the American Academy of Orthopaedic Surgeons in March 2010.¹ One study, from Columbia University, evaluated bone structure in 111 women, half of whom had been taking bisphosphonates for a minimum of 4 years. Using a research technique called Hip Structural Analysis, the study found that in the early treatment period bisphosphonates improved the structural integrity of bone, but that the effects were diminished with long term use. The second study examined bone biopsies from 12 patients treated with bisphosphonates for an average of 8 years and 9 without bisphosphonate therapy. They found no differences in the architecture between the groups, but the group treated with bisphosphonates had less microscopic variability in bone tissue. Other reports have not seen a definite link between prolonged bisphosphonate use and atypical femoral fractures. Using national observational register-based data from Denmark, the ratio between hip and subtrochanteric/diaphyseal femoral fractures was identical in alendronate-treated patients and the control cohort even in the limited number of patients who received long-term treatment.² The other study reviewed data from three large randomized trials and concluded that subtrochanteric/diaphyseal femoral fractures were very rare, even among women who had been treated with bisphosphonates as long as 10 years, without a significant increase in risk associated with bisphosphonate use.³

This data prompted the Food and Drug Administration (FDA) to state that they were going to undertake a thorough review of possible association between bisphosphonate use and thigh bone fractures. Specifically, the FDA worked with outside experts, including members of the recently convened American Society for Bone and Mineral Research Subtrochanteric Femoral Fracture Task Force to gather additional information that might provide more insight into this issue. It is important to note that the FDA did review the data concerning the link between oral bisphosphonates and thigh bone fractures in 2008

and concluded that there was no clear association between bisphosphonate use and these fractures.

The ASBMR Subtrochanteric Femoral Fracture Task Force report has now been published in the Journal of Bone and Mineral Research (JBMR). As mentioned in the task force report, atypical fractures are very rare, but one should be aware of warning signs and symptoms in someone on long term bisphosphonate therapy (new groin or thigh pain): “we know that bisphosphonates prevent many, many common fractures. For this reason, we want to emphasize that patients should not stop taking these drugs because they are afraid of the much more uncommon femur fractures. They should talk to their health professionals about their concerns and should let them know if they experience any new groin or thigh pain.”⁴ The exact cause for these unusual atypical fractures is still uncertain and more research is needed to identify who is at risk and why these fractures occur.

Other studies, evidence and data support the notion that **thigh fractures associated with bisphosphonate use are extremely rare with less than 1% of femur fractures being atypical. The risk of other osteoporotic fractures is significantly reduced with bisphosphonate therapy and the benefits far exceed the risks. Nonetheless, if groin or thigh pain is present, this should be further evaluated with bone scans or MRI and if necessary a change in therapy may be required.**

References:

1. <http://www6.aaos.org/news/pemr/releases/release.cfm?releasenum=877>
2. Abrahamsen B, Eiken P, Eastell R. Subtrochanteric and diaphyseal femur fractures in patients treated with alendronate: a register-based national cohort study. J Bone Miner Res. 2009;24:1095-102.
3. Black DM et al N Engl J Med 2010; 362: 1761-71
4. <http://www.asbmr.org/About/PressReleases/Detail.aspx?cid=a68f2b70-a117-4094-9f6f-b5993c6a6149>

Related Links:

1. For more information on the ASBMR task force report and to access the press release, please visit:
<http://www.asbmr.org/About/PressReleases/Detail.aspx?cid=a68f2b70-a117-4094-9f6f-b5993c6a6149>
2. Journal of Bone and Mineral Research: <http://www.jbmr.org>

3. [National Osteoporosis Foundation press release](#)

4. American Academy of Orthopaedic Surgeons :

<http://www6.aaos.org/news/pemr/releases/release.cfm?releasenum=877>