BONE

Use of antiepileptic drugs implicated in fracture risk

A significant association has been uncovered between the use of antiepileptic drugs (AEDs), falls and fractures in a group of postmenopausal women enrolled in the Women's Health Initiative (WHI). "The take-home message is clear. If you are a postmenopausal woman and use AEDs, then you should have an evaluation of your bone health and fall risk," states lead researcher Laura D. Carbone, a Professor of Rheumatology at the University of Tennessee Health Science Center in Memphis, TN.

AEDs comprise a diverse group of compounds that modify or inhibit processes involved in the development of seizures. They broadly fall into one of two groups: enzyme-inducing and nonenzyme-inducing. AEDs are increasingly used in clinical practice to treat conditions other than epilepsy; for example, diabetic neuropathy, hot flashes, and Parkinson disease. Evidence from several small studies suggests that the use of AEDs might be linked to an increased risk of fracture; however, such reports have suffered from a number of limitations, including failure to account for potential confounding variables.

Carbone and her colleagues routinely provide medical care for patients who take AEDs and so wished to clarify the potential role of these drugs in the development of osteoporosis. To achieve this goal, they decided to perform a subgroup analysis of the WHI database, which includes information on both the use of AEDs and bone health.

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The WHI enrolled a large number of healthy postmenopausal women from 40 centers in the USA with the aim of assessing the effects of hormone therapy, dietary modification and calcium and vitamin D supplementation on osteoporosis, cancer and cardiovascular disease. Carbone and coworkers analysed data from 1,385 women who used AEDs versus 137,282 women who did not use these drugs. Women who took AEDs were further subdivided into those who took enzyme-inducing AEDs versus those who took nonenzyme-inducing AEDs and those who used only one AED versus those who used more than one AED. The main outcomes assessed by the investigators were falls and fractures at 7.7 years and changes in BMD from baseline at 3 years.

Users of AEDs were more likely to be receiving hormone therapy, bisphosphonates or calcitonin than were nonusers of AEDs. Nevertheless, the use of AEDs was found to have a positive correlation with total fractures, site-specific fractures (except hip fractures) and a history of two or more falls. Women who used more than one AED were at greater risk of fracture than women who used just one type of AED; furthermore, enzyme-inducing AEDs posed a higher risk of fracture than did nonenzyme-inducing AEDs. By contrast, use of AEDs was not associated with statistically significant differences in BMD.

The precise mechanisms whereby AEDs increase fracture risk in postmenopausal women remain to be determined. Carbone and colleagues speculate that the enzyme-inducing AEDs could promote vitamin D deficiency, as induction of the cytochrome P450 system by these drugs increases catabolism of vitamin D. Future studies of serum 25-hydroxyvitamin D levels in patients who use enzyme-inducing AEDs versus those who use nonenzyme-inducing AEDs might help clarify this point.

The investigators conclude that in light of their findings, strategies to prevent falls should be considered for all postmenopausal women who take AEDs, in order to reduce their risk of future fracture.

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Original article Carbone, L. D. *et al.* Antiepileptic drug use, falls, fractures and BMD in postmenopausal women: findings from the Women's health Initiative (WHI). *J. Bone Miner. Res.* doi:10.1359/jbmr.091027