Antiepileptic drugs and bone loss: A twin/sibling study

Petty et al. used an exposure-discordant twin and sibling pair approach in 70 subjects to quantify antiepileptic drug-associated loss of bone mineral density and determine other risk factors for bone loss. Patients using antiepileptic drugs (AEDs) for more than 2 years—particularly those taking enzyme-inducing AEDs and age > =40 years—had lower bone mineral density at fracture risk sites.

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Antiepileptic drugs enhance age-related osteoporosis

Commentary by Raj Sheth

Suspicion that bones are weakened in patients with epilepsy dates back to the 1960s when institutionalized patients with severe symptomatic epilepsy were found to have rickets. However, over the last 15 years, reports have documented reduced bone mineralization in ambulatory patients, even those with the idiopathic epilepsies. Lowered bone mineralization correlates with an increased risk of fractures: 40% of women and 13% of men over the age of 50 years will sustain an osteoporotic fracture of the hip, spine, or forearm. Osteoporotic fractures lower quality of life and create an additional societal burden; further, 30% of patients with a hip fracture die within 1 year of the injury.

Factors that predispose to bone loss in those with epilepsy include seizure-related injuries, osteopenia associated with symptomatic epilepsy such as cerebral palsy, AED-induced osteopenia, AED-associated loss of balance, and inactivity associated with epilepsy.

Inherited risk factors play an important role, as these contribute to bone mineralization. Separating the relative contributions of genetic and environmental factors including AED usage to osteopenia has been difficult. Petty et al. studied twins discordant for epilepsy providing valuable insights. The authors found that exposures as brief as 2 years, particularly in women over age 40 years receiving an enzyme-inducing AED, resulted in a 17% reduction in bone mineralization at the lumbar spine as compared to the untreated twin. Thus AEDs enhance age-related reductions in bone mineralization. While this article is authoritative, questions remain. Can osteopenia resulting from an enzyme-inducing AED be reversed by changing to a non-enzyme-inducing AED? Valproate, a non-enzyme-inducing AED, is also reported to be associated with osteopenia. Twin studies provide a powerful tool to understand small differences in bone mineralization, although the use in this study of both monozygotic and dizygotic twins as well as sisters is a limitation. Preventing the devastating effect of fractures requires an awareness of the importance of bone health in epilepsy and measurement of bone density and vitamin D levels in at risk patients. Because AED therapy is usually long-term and often lifelong, it is also essential to investigate therapeutic strategies to maintain bone health in the young and in this way prevent bone loss in the elderly. Finding AEDs that do not have an osteopenic effect is also essential.

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