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Bone health in young women with epilepsy after one year of antiepileptic drug monotherapy

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Objective: Antiepileptic drugs (AEDs) may have adverse effects on bone mineral density (BMD) and metabolism. We previously reported biochemical evidence of increased bone turnover in premenopausal women with epilepsy on phenytoin monotherapy compared with those on carbamazepine, lamotrigine, and valproate. We therefore hypothesized that rates of bone loss would be higher in young women treated with phenytoin.

Methods: Ninety-three premenopausal women with epilepsy receiving a single AED (carbamazepine, lamotrigine, phenytoin, or valproate) participated. Subjects completed nutritional and physical activity questionnaires. Biochemical indices of bone and mineral metabolism and BMD of the proximal femur and lumbar spine were measured at baseline and 1 year.

Results: Participants reported high calcium intake (>1,000 mg/day) and were physically active. Significant loss (2.6%) was seen at the femoral neck in the phenytoin group. BMD remained stable in the other AED groups. Bone turnover markers and calciotropic hormones were unchanged after 1 year in all groups except for a significant decline in urine N-telopeptide in the phenytoin group. In women receiving phenytoin, lower serum 25-hydroxyvitamin D concentrations were associated with higher parathyroid hormone, bone alkaline phosphatase, and urine N-telopeptide levels, a biochemical pattern consistent with secondary hyperparathyroidism and increased remodeling.

Conclusion: In this study, young women treated with phenytoin had significant femoral neck bone loss over 1 year. In contrast, those treated with carbamazepine, lamotrigine, and valproate did not have detectable adverse effects on bone turnover or bone mineral density. These results raise concerns about the long-term effects of phenytoin monotherapy on bone in young women with epilepsy.

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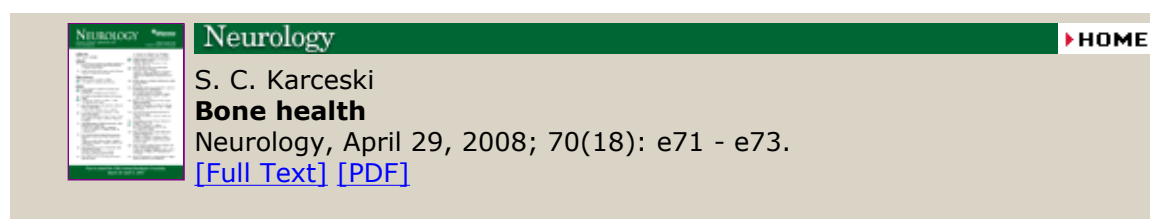
GLOSSARY: **1,25(OH)₂D** = 1,25-dihydroxyvitamin D; **AED** = antiepileptic drug; **ANOVA** = analysis of variance; **BCE** = bone collagen equivalent; **BMD** = bone mineral density; **BMI** = body mass index; **BSAP** = bone-specific alkaline phosphatase; **CBZ** = carbamazepine; **FN** = femoral neck; **LS** = lumbar spine; **LTG** = lamotrigine; **NTx** = cross-linked N-telopeptide of type I bone collagen; **OHD** = 25-hydroxyvitamin D; **PHT** = phenytoin; **PTH** = parathyroid hormone; **TH** = total hip; **VPA** = valproate.

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