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Epilepsia™

LETTER

Effect of antiseizure medications on bone health

It is with great interest that we read the article by Shi et al. in *Epilepsia*, in which the authors analyzed biochemical markers of bone metabolism in young patients receiving chronic anti-epileptic drug therapy.[1] Commendably they had a large number of children, 1487, with self-limited epilepsy with centrotemporal spikes, and they concluded correctly that both epilepsy and anti-seizure medications may affect bone metabolism. We would like to point out certain caveats that need to be considered while interpreting their data, particularly in relation to their conclusion that "oxcarbazepine, levetiracetam, and topiramate had no significant effect on bone metabolism."

1. Whereas bone markers reflect bone remodeling and are accepted surrogate markers of bone metabolism, they are, however, profoundly affected by gender, diurnal rhythms, growth, pubertal stages, and food intake.[2] Therefore, growth and puberty are both likely to have introduced a large variability in the bone-remodeling markers. That may have made detection of abnormalities due the intake of drugs quite challenging. Indeed, although the authors withdrew blood in the fasting state, they did not seem to have adjusted for the other powerful modulators of bone metabolism mentioned above. It is important to note that the age range of study subjects overlaps with the usual timing of the pubertal growth spurt. Therefore, if the children are not matched for pubertal stages, comparisons between groups may not be as meaningful. In addition, the authors did not include bone density assessments, which would have provided a complete picture of bone health, given that children and adults with epilepsy have such abnormalities.[3]
2. Related to the above, we note that there is evidence in the literature from convincing studies that is not consistent with the authors' above finding of lack of effect of oxcarbazepine, levetiracetam, and topiramate.[4–6] This suggests that the findings of Shih et al. may apply only to the patient population they studied or that they are limited by the factors described above.
3. The mean serum 25(OH) vitamin D in all three groups was on average 15 ng/mL. This level is below the desirable level as defined by the National Academy of Medicine, and depending on oral calcium intake of the children, could have contributed to secondary hyperparathyroidism and to high bone remodeling, thus masking drug-induced changes in bone remodeling. The authors did not indicate whether their patients received vitamin D supplementation, a clearly potential confounding variable. Given the evidence from other studies of vitamin D deficiency with oxcarbazepine therapy,[5] findings from the study of Shih et al. should not lead practitioners to ignore the possibility of vitamin D deficiency caused by oxcarbazepine. This is important because supplementation with vitamin D has been shown to be useful in patients with epilepsy who have low vitamin D levels.[7]
4. The authors should have provided information on whether all markers were measured in a central laboratory. It would have been preferable if they provided information regarding the intra- and inter-assay variability of all hormone tests in general, and of the bone markers in particular, including implemented quality assurance protocols, if any.

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CONFLICT OF INTEREST STATEMENT

Neither of the authors has any conflict of interest to disclose.

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