Newer Antiepileptics May Worsen Osteoporosis

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BOSTON — Keep the risk of osteoporosis and osteopenia in mind when elderly patients are being treated even with the newer antiepileptic drugs, Georgia D. Montouris, M.D., said at a meeting on epilepsy in the elderly sponsored by Boston University.

While drug-to-drug interactions are less common with newer antiepileptic drugs (AEDs), there are no data suggesting they pose less of an osteoporosis risk than the earlier P450 enzyme-inducing versions do.

The diagnosis of new-onset seizures is made in an estimated 68,000 patients over age 60 every year in the United States, said Dr. Montouris, a neurologist at Boston University. All of these patients are at risk for osteoporosis.

"The fastest-growing population with new-onset seizures is over the age of 60, a large population that is in the prime years to develop osteoporosis," she said.

There is no evidence to support withdrawal of the enzyme-inducing antiepileptic medication to reverse the osteoporotic condition.

Dr. Montouris reported that she usually starts elderly patients with new-onset seizures on one of the newer AEDs that don't induce enzymes, to avoid drug-to-drug interactions and liver metabolism.

All of the older P450 enzyme-inducing drugs—carbamazepine, phenytoin, primidone, and phenobarbital—metabolize through the cytochrome P450 system. Phenobarbital, primidone, and phenytoin are most commonly associated with altered bone disease and decreased bone density, said Dr. Montouris. There are conflicting results for carbamazepine.

Lacking data on the effect of newer drugs on bone health, Dr. Montouris said she prefers not to switch older patients with epilepsy to newer AEDs when the older drugs have controlled their seizures for many years. In addition, there is no evidence to support withdrawal of the enzyme-inducing antiepileptic medication to reverse the osteoporotic condition.

The newer drugs, indicated as add-on agents for refractory seizures, include gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine hydrochloride, topiramate, and zonisamide. Oxcarbazepine is approved for monotherapy, lamtorigine is approved for conversion to monotherapy, and topiramate is under Food and Drug Administration evaluation for use in monotherapy. No information is available yet on the effect of these agents on bone health, she added.

"I feel it is more appropriate to keep them on a regimen that works and treat the bone health issues, than risk exacerbating the epilepsy and not improving bone health."

Seizures in this age group present most often as confusion and mental status changes, putting the patients at risk for falls.

Dr. Montouris said she tries to correct a patient's vitamin D deficiency or insufficiency. She usually prescribes, as preventatives, supplementation with 200 IU of vitamin D twice a day, along with at least 500-600 mg (or more depending on age) of calcium twice per day. If signs of osteoporosis or osteopenia are present, she refers the patient to either an endocrinologist or a rheumatologist for assessment and treatment. She prescribes a calcium-containing diet, weight-bearing exercise, and exposure to sunlight.

A vitamin D deficiency can lead to defects in calcium absorption and sometimes secondary hyperparathyroidism. "It's reported that carbamazepine and phenytoin can affect osteoblast formation," she said. "Phenytoin can actually reduce the intestinal calcium absorption as well." In epileptic patients taking AEDs, osteoporosis may occur as a result of the medication and can lead to fractures of the hip and spine. "A tonic-clonic seizure is known to cause thoracic spine fractures," Dr. Montouris said.

She sends epileptic patients taking AEDs to be tested for baseline levels of 25-hydroxyvitamin D and parathyroid hormone and for a dual-photon absorptiometry scan.

The tests can be repeated 1-2 years later if normal or, if not, the patient should be treated or referred. ■