Epilepsy Costs Kids Bone Density Over Time

BY TIMOTHY F. KIRN
Sacramento Bureau

A new study of children with epilepsy has found that their bone mineral density declines steadily relative to controls, starting perhaps even in the first year of treatment.

The study compared 82 children with epilepsy with 32 age- and sex-matched, first-degree cousins, measuring their bone mineral density (BMD) with dual- energy x-ray absorptiometry. The 82 patients were all ambulatory and without any other conditions that might affect bone density, investigators reported in Neurology. Their ages ranged from 6 to 18 years, with a mean age of 12 years.

The investigators found that the 18 subjects who had had epilepsy less than 1 year had a mean BMD *z* score of 0.23. The 37 subjects who had epilepsy for 1-5 years had a mean BMD *z* score of 0.13. And the 27 subjects who had epilepsy for 6 years or longer had a mean BMD *z* score of 0.06, reported Dr. Raj D. Sheth, director of the Comprehensive Epilepsy Program at the University of Wisconsin, Madison, and colleagues.

By comparison, the control subjects had a mean BMD *z* score of 0.57.

The difference between the mean score of the control group and the mean score of the subjects who had had epilepsy for less than a year did not reach statistical significance; however, the difference between the controls and the other subjects did.

"These findings suggest that as little as 2 years of treatment could result in significant reductions in BMD," Dr. Sheth wrote (Neurology 2008;70:170-6).

The study was not able to investigate the role of specific medications in the bone density loss observed, in part because many of the patients had been on more than one drug at some time in their treatment.

Information from adults suggests medication plays a role in bone density loss, but the cause is probably multifactorial, Dr. Sheth said.

The study was able to compare subjects with partial epilepsy with those with generalized epilepsy, however. The investigators found that while those with generalized epilepsy for longer than 1 year had a significantly lower mean *z* score than controls, those with partial epilepsy had a mean score that was only slightly lower and the difference was not statistically significant.

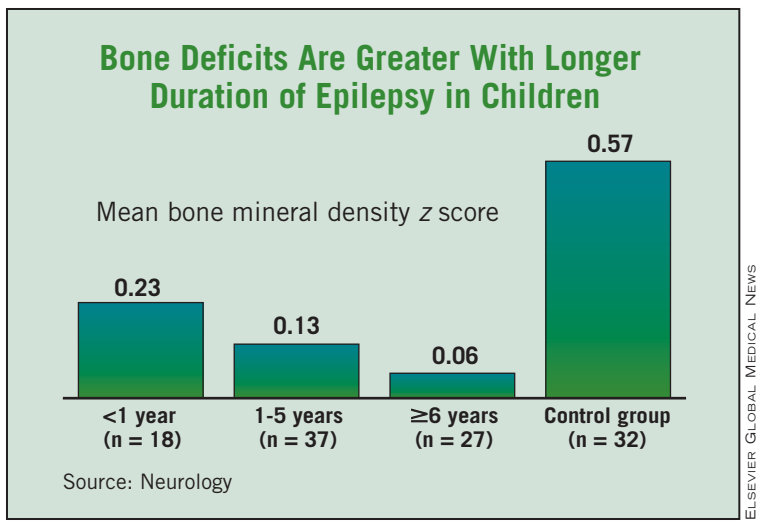
Interestingly, the study found that calcium intake for the study subjects was somewhat higher than national averages.

Two patients actually experienced a pathologic fracture while the study was underway. The evidence suggests that 40% of fractures that occur in individuals with epilepsy are pathologic; among children with epilepsy, it's 20%, Dr. Sheth said.

One of the fracture patients was a 17-year-old female who fractured her clavicle during a seizure and fractured her leg while walking. She had experienced epilepsy for 15 years and her *z* score was –3.5. The other patient had had epilepsy for 12 years and had a *z* score of –2.5. She fractured her arm during a fall.

In an editorial accompanying the study report, Dr. Edwin Trevathan noted that most physicians consider osteopenia and BMD loss to be a problem only for white, postmenopausal women, and patients who smoke, have renal disease, or take corticosteroids (Neurology 2008;70:166-7).

But a previous study found that young adults who have epilepsy have a risk of BMD loss or fracture that is 2-6 times greater than the general population.



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"We can probably prevent epilepsy-associated [BMD] loss, and the published data now demand that we make this a priority in epilepsy research and clinical practice," wrote Dr. Trevathan, who is the director of the National Center on Birth Defects and Developmental Disabilities, at the Centers for Disease Control and Prevention, Atlanta.

"Early intervention shortly after starting treatment for epilepsy among children, adolescents, and young adults should probably be a focus of screening and prevention efforts. Among the elderly with new-onset epilepsy, screening and prevention efforts may need to be started as soon as antiseizure medications are initiated," he added.

Prophylactic treatment of children with epilepsy with calcium and vitamin D may be useful, but the correct dosage has not yet been determined, Dr. Sheth said.

The study was funded in part by an investigator-initiated grant from GlaxoSmithKline, which makes treatments for epilepsy and osteoporosis.

Dr. Trevathan previously served as an investigator for a Glaxo epilepsy treatment. ■

Daily Colchicine Decreased PFAPA Attack Frequency

BY BRUCE JANCIN
Denver Bureau

ASPEN, COLO. — Daily colchicine may have a role as early therapy in children with PFAPA syndrome, Dr. Eli Somekh reported at a conference on pediatric infectious diseases sponsored by the Children's Hospital, Denver, and the University of Colorado.

Eight of 10 children with severe PFAPA (periodic fever, aphthous stomatitis, pharyngitis, adenitis) syndrome demonstrated a marked decrease in frequency of episodes in response to colchicine at 0.5-1.0 mg/day. Indeed, the average interval between episodes expanded from roughly 1.5 weeks before colchicine to 7.5 weeks afterwards. In one case, the attack frequency stretched to one episode every 18 weeks after placement on the drug, said Dr. Somekh, chairman of the department of pediatrics at the Edith Wolfson Medical Center, Holon, Israel.

The pediatrician also noted that prednisone appears to be effective in aborting episodes at much lower doses than typically employed.

PFAPA is the most common cause of periodic fever in children. Because the disorder hasn't been fully described, Dr. Somekh and his coworkers reviewed in detail the records of 54 consecutive children who had well-documented PFAPA and were seen at the center beginning in 1999.

The following clinical diagnostic criteria were employed:

- Fevers recurring with clockwork regularity and early age of onset.
- One or more of the following: pharyngitis, aphthous stomatitis, and/or cervical lymphadenitis.
- Normal growth and development.
- Complete lack of symptoms between episodes.
- Exclusion of cyclic neutropenia.

Of the 54 PFAPA patients, 33 were boys. The mean age of onset was 1.9 years. Episodes lasted an average of 5.3 days with a peak temperature of 40.1degrees C. Episodes occurred on average once every 3.7 weeks with no seasonality.

In all, 52 children presented with pharyngitis, 35 with abdominal pain, 33 with cervical lymphadenopathy, and 21 with aphthous stomatitis. Of note, only 15 children displayed the classic cluster of symptoms comprising pharyngitis, stomatitis, and lymphadenitis.

"We saw more abdominal pain and less aphthous stomatitis than reported in the original published series of PFAPA," Dr. Somekh observed.

The investigators identified four patterns of disease over time. In 23 patients, the frequency of episodes gradually decreased over the years. In two patients, the frequency gradually increased. In 15 patients, there was no change in frequency. And 14 patients displayed a previously undescribed pattern of alternating remissions and relapses; that is, after regularly experiencing episodes every few weeks, they stopped having them altogether for months or even years before the episodes returned.

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DR. SOMEKH

Forty-eight patients were treated with corticosteroids, typically a single dose of prednisone at 0.6 mg/kg, resulting in termination of attacks in a mean of 10 hours. This dose is lower than what others have reported using, and because low-dose therapy results in fewer side effects, it is the best way to go, the pediatrician said.

Half of patients experienced no change in frequency of episodes after steroid therapy. In 9 children the frequency increased, whereas in 15 it decreased.

Forty-one patients were placed on antibiotics, deemed to be without any benefit in all but one.

Other investigators have reported cimetidine to be beneficial in patients with PFAPA, but Dr. Somekh said his own experience has been that the drug has only a slight effect.

The pathogenesis of PFAPA remains unclear. "Patients are usually healthier than their siblings—less flu, less asthma and bronchitis," he noted. "So probably their immune system is just fine, even perhaps working too hard. And as far as we know, their prognosis is excellent. We don't see an increase in neoplastic or neurologic disorders."

Dr. Gerard Rabalais commented that he and his colleagues at the University of Louisville (Ky.) see many PFAPA patients, probably in part because Dr. Gary Marshall, professor of pediatrics there, is credited with the first description of the syndrome back in 1987.

Of late, they have been treating episodes with 2-3 days of prednisone, a practice to reconsider in light of the impressive Israeli experience with single low-dose therapy, said Dr. Rabalais, professor and chairman of the department of pediatrics at the university.

He added that Dr. Marshall recommends tonsillectomy for the most severely affected patients. It is curative in roughly two-thirds of cases.

Dr. Somekh noted that others have also reported tonsillectomy to be of great benefit in 60%-80% of treated PFAPA patients. In his series of 54 patients, all six children who underwent tonsillectomy were cured. ■