

## Epilepsy Drugs Increased Fracture Risk in Elderly

BY SUSAN LONDON

SEATTLE — Older adults in the general population have an elevated risk of fractures related to osteoporosis if they take certain antiepileptic drugs, according to a population-based analysis.

"Prior studies have shown that antiepileptic drugs [AEDs] are associated with an increased risk of bone loss and fractures," presenting author Jane McChesney said at the annual meeting of the American Academy of Neurology. "However, population-based data assessing the association between AEDs and osteoporotic-related fractures are scarce."

"This study found that AEDs, except for fatty acid derivatives, are associated with an increased risk of osteoporotic-related fractures in men and women over age 50," Ms. McChesney said.

"This is concerning as many of these AEDs are not only used to manage epilepsy, but are also widely used in older adults for the treatment of neuropathic pain, headaches, and psychiatric conditions, to name a few," she added.

In the study, Ms. McChesney, a nursing student at the University of Calgary, Alta., and her colleagues analyzed population-based data from the province of Manitoba for the years 1996-2004.

Individuals were included if they were at least 50 years of age and had continuous health care coverage during the study period. They were excluded if they had taken osteoprotective medications in the year before a fracture or were residents of long-term care facilities.

Fractures were ascertained from diagnostic codes and were limited to vertebral, wrist, and hip fractures that were

not related to severe trauma, according to Ms. McChesney.

Using the fracture date as the index date, each older adult with a fracture was matched with three fracture-free older adults by age, sex, ethnicity, and number of comorbidities.

Use of AEDs, defined as dispensation of a prescription to the individual in the past 4 months, was assessed from a drug database containing virtually all pharmacy dispensations for the province.

Analyses were based on 15,792 older adults who had experienced a fracture and 47,289 older adults who had not, Ms. McChesney reported. Overall, 70% were female, 62% were aged 70 years or older, and 67% had three or more comorbidities.

Fractures most commonly occurred in the wrist (52%), followed by the hip (26%) and vertebrae (22%).

After adjustment for social and demographic characteristics, home care, and comorbidities known to affect fracture risk, older adults had elevated odds of fracture if they used carbamazepine (odds ratio, 1.9), clonazepam (1.3), gabapentin (1.6), phenobarbital (2.2), and phenytoin (2.1). In contrast, their odds were not elevated if they used valproic acid.

It remains unknown if osteoprotective agents are beneficial in this context, she acknowledged, and that would be an important focus of additional research.

"Future studies are needed to determine the individual effects of the newer AEDs on bone health in this age group and to elucidate the mechanism of this association," she concluded.

Ms. McChesney reported that she had no disclosures to make in relation to the study. ■

## Bisphosphonates Curbed Valve Calcification in Older Women

BY MITCHEL L. ZOLER

ORLANDO — Bisphosphonate use was linked with an unexpected, increased risk for aortic valve calcification in women aged 55-64 years in an analysis of about 3,700 women.

The analysis also showed the more expected finding that among older women, aged at least 75, bisphosphonate treatment was linked to a significantly reduced risk for aortic valve calcification. This effect probably occurs because bisphosphonate treatment slows calcium loss from bone, thereby preventing the lost calcium from winding up deposited on valves, Dr. Sammy Elmariah said while presenting a poster at the annual meeting of the American College of Cardiology.

The significantly increased risk for aortic valve calcification among younger women treated with a nitrogen-containing bisphosphonate has no clear explanation. "In my opinion it's due to confounding," Dr. Elmariah said in an interview. Women younger than 65 who go on bisphosphonate treatment often have a special risk for osteoporosis that may somehow relate to a high level of valve calcification.

He and his associates used data collected in the Multi-Ethnic Study of Atherosclerosis (MESA), a longitudinal cohort study of about 6,800 men and women aged 45-85 recruited from six U.S. communities and sponsored by the National Heart, Lung, and Blood Institute. Among the 3,710 women in MESA, 214 were treated with a nitrogen-containing bisphosphonate, either an oral or intravenous formulation, and the other 3,496 were not receiving a bisphosphonate. The bisphosphonate

group included 100 women aged younger than 65.

Cardiovascular calcification was evaluated by electron-beam CT (in three communities) or multidetector row helical CT (at three communities). Aortic valve calcification was defined as any calcified lesion on an aortic-valve leaflet.

Among women younger than 65, imaging showed aortic valve calcification in 18% of those on a bisphosphonate and in 4% of those not on the drug. In women aged 65 or older, imaging showed a rate of 13% with calcification in the bisphosphonate group and 20% in those not on the drug, reported Dr. Elmariah, a cardiologist at Mount Sinai Medical Center in New York.

In a model that adjusted for age, body mass index, ethnicity, study site, education, income, health insurance, treatment for hypertension or lipid lowering, diabetes, smoking, blood pressure, and cholesterol level, bisphosphonate use was linked with a 3.9-fold increased risk for aortic valve calcification in women younger than 65, a statistically significant association. The vast majority of these women were aged 55-64.

In contrast, among women aged 65 or older, bisphosphonate use was associated with a nonsignificant, 30% reduction in valve calcification. In the subgroup of women aged 75 or older, bisphosphonate use was linked with a significant reduction in the prevalence of valve calcification, a roughly 50% relative risk reduction compared with women not on a bisphosphonate.

The finding warrants further investigation in other groups of women taking bisphosphonates, Dr. Elmariah said. He reported no financial relationships for this study. ■

## After Hip Fracture, Only 25% Get Osteoporosis Diagnosis

BY MICHELE G. SULLIVAN

WASHINGTON — Three-fourths of patients hospitalized for a hip fracture do not receive an osteoporosis diagnosis before discharge, and the majority are not taking a bisphosphonate at discharge or 6 months after the injury, a small study has shown.

The findings are dismaying, said Dr. Pardeep Bansal, because 24% of patients older than 50 years who sustain an osteoporotic hip fracture die within a year. "The 1-year mortality rate is higher than it is in some cancers, and even higher than it is after a heart attack," said Dr. Bansal, chief resident at the Scranton-Temple Residency Program, Scranton, Pa. "But if you have a heart attack, no physician is going to let you leave the hos-

pital without aspirin, a beta-blocker, and a statin. If you have a hip fracture, you're likely to be discharged without even the underlying diagnosis, much less the appropriate treatment."

The two-part study began with a chart review of 191 patients who were admitted to a hospital with a hip fracture. Most (80%) were white females older than 70 years. At the time of discharge, 25% had been assigned a diagnosis of osteoporosis. Only 30% were taking calcium; patients who had been diagnosed with osteoporosis were significantly more likely to be taking both calcium and vitamin D than were patients without a diagnosis.

Furthermore, only 15% were

taking a bisphosphonate at discharge, Dr. Bansal said. Clinical contraindications did not appear to play a significant role in the lack of treatment: Only 2% of patients had a glomerular fil-



**Discharged hip fracture patients are unlikely to be diagnosed, much less get the appropriate treatment.**

DR. BANSAL

tration rate of less than 30 mL/min per 1.73 m<sup>2</sup>, which could be a contraindication for bisphosphonate therapy.

Dr. Bansal then performed a telephone survey of the 105 patients who could be contacted; 33% of the original cohort had

died since their fractures, and another 12% could not be found. All of the patients interviewed reported having seen their primary care physicians within 6 months of the fracture. Yet still, only 50% had received a diagnosis of osteoporosis, 50% were taking calcium, 40% were taking vitamin D, and only 28% were taking a bisphosphonate.

"Another painful finding was that 14% of the group had experienced a subsequent fragility fracture," Dr. Bansal said.

To help improve the rate of osteoporosis diagnosis at his hospital, Dr. Bansal and his colleagues have instituted a standardized protocol. "It's very simple," he said. "Any patient who comes in with a fracture suggestive of osteoporosis is started on calcium, vitamin D,

and a bisphosphonate before discharge. If they have a contraindication to a bisphosphonate, such as an allergy or a low GFR, then we call the family physician and discuss an alternative treatment."

Although a dual-energy x-ray absorptiometry scan is a helpful diagnostic tool, Dr. Bansal said treatment should not be delayed until a scan can be obtained. "You have to wait for the fracture to heal and then schedule that as an outpatient, and during that time the patient can be lost to follow-up. It's a good idea to get it, but don't delay the treatment while waiting for the scan."

Dr. Bansal presented the study in a poster session at an international symposium sponsored by the National Osteoporosis Foundation. He had no conflicts of interest to declare. ■