Keeping Steroid-Induced Bone Loss in Check

BY PATRICE WENDLING

CHICAGO — Fracture risk increases in arthritis patients within about 3 months of starting corticosteroids and remains high, according to Dr. Nelson Watts.

"How much of this is steroids and how much of this is the underlying disease is unanswered," said Dr. Watts, director of the bone health and osteoporosis center at the University of Cincinnati.

Glucocorticoid-induced osteoporosis results from a variety of systemic effects of corticosteroids, but it's the combination of reduced bone formation and increased bone resorption that causes a "double whammy" for patients—a troubling aspect for rheumatologists, who regularly dispense corticosteroids for their patients, Dr. Watts said at a symposium sponsored by the American College of Rheumatology.

The exact dose at which corticosteroids increase fracture risk is also difficult to tease out because of the underlying disease. One study observed that fracture risk was dose dependent and significantly higher with 2.5 mg/day or more of oral prednisone, with increases of 61% in hip and 160% in vertebral fractures (J. Bone Miner. Res. 2000;15:993-1000).

"It may well be that people who need 2.5 [mg]/day of prednisone are at increased risk for fracture not because of prednisone, but because of their rheumatoid arthritis; … clearly, as the dose goes up, the risk increases," he said.

The American College of Rheumatology just began the process of revising its 2001 guidelines for the prevention and treatment of glucocorticoid-induced osteoporosis. The current guidelines highlight lifestyle modifications, such as calcium and vitamin D supplementation, weight-bearing exercise, and minimization of alcohol intake.

Studies show that the risk for spinal fracture drops within a year or two of stopping therapy, although hip fracture risk remains increased over baseline.

There is at least one supportive trial for virtually all therapies, but several intervention trials have produced conflicting results for some agents, according to a recent review of glucocorticoids and the risk of osteoporosis (Expert Opin. Drug Saf. 2009;8:33-47).

The value of calcium and vitamin D supplementation is unclear, Dr. Watts said. In a relatively small trial in 96 RA patients on prednisone, daily supplementation with 500 IU of vitamin D and 1,000 mg of calcium carbonate per day significantly improved bone mineral density, at a rate of 0.72% in the lumbar spine and 0.85% in the trochanter per year, compared with losses of 2% and 0.9%, respectively, among patients on placebo (Ann. Intern. Med. 1996;125:961-8).

In four prospective studies in 173 patients who recently started corticosteroid therapy, however, bone loss occurred at a rate of 3%-5% per year, despite daily supplementation with 500-800 mg of calcium.

Two other studies that Dr. Watts highlighted reported no bone loss in patients who were given up to 1,000 mg per day of calcium and up to 500 IU per day of vitamin D, although he noted that these patients had been on corticosteroid therapy for at least 1 year and in most cases almost 5 years.

"It's not clear to me how much of a role vitamin D and calcium will play in preventing bone loss," he said.

Studies show that the risk for spinal fracture falls within a year or two of stopping therapy, although hip fracture risk remains increased over baseline.

Dr. Watts disclosed that he has relationships with Amgen Inc., Eli Lilly & Co., Procter & Gamble Co., Sanofi-Aventis, Novo Nordisk Inc., and Novartis Pharmaceuticals Corp., which manufactures Reclast. ■

Osteoporosis Patients Fail to Grasp Increased Fracture Risk

BY MICHELE G. SULLIVAN

WASHINGTON — A majority of women susceptible to fragility fractures fail to appreciate those risks, even if they have been told by a physician that they have osteoporosis, a large international survey-based study has concluded.

"We found a remarkable failure of many women to perceive that these clear-cut factors are putting them at increased risk for a fracture," said Dr. Ethel Siris, an investigator for GLOW (Global Longitudinal Study of Osteoporosis in Women). "It's really a critique of the medical profession. We have not adequately educated women that osteoporosis is a common disorder that increases future fracture risk."

GLOW included more than 60,000 postmenopausal women who were recruited from 706 physician practices in 10 countries. The women completed questionnaires on demographic and medical information, risk factors for fragility fracture, any personal history of and treatment for osteoporosis, and health and functional status. Many of these questions were taken from the World Health Organization's Fracture Risk Assessment Tool (FRAX). A FRAX index score of 5 or more represents a 26% probability that a patient will experience a nonvertebral fracture within the next 5 years.

Comparing themselves with women of the same age, the majority of subjects with risk factors for fracture did not perceive themselves at increased risk, Dr. Siris said in an interview. "For example, 64% of women who had already had a fracture thought their risk of future fracture was lower than or the same as another woman of their age."

Even more surprising, she said, 55% of women who had been told by a physician that they had osteoporosis thought that they were not at increased risk. "There was an obvious disconnect between knowing that they had the disorder and recognizing that it put them at increased risk of a fracture in the future," she said. Of those with a FRAX index score of 5 or more, 75% also failed to identify themselves as being at high risk.

Women with other risk factors displayed a similar ignorance, Dr. Siris noted. Of women whose mother had experienced a hip fracture, 74% thought they were at a lower fracture risk than their peers or had a similar risk, as did 74% of those with a low body mass index, 80% of current smokers, 77% of those who frequently consumed alcohol, 61% of those taking corticosteroids, and 71% of those with rheumatoid arthritis.

The replies were consistent across countries, she said at an international symposium sponsored by the National Osteoporosis Foundation.

The failure to appreciate the implications of fracture risk may help account for the "lousy adherence" to osteoporosis therapy, said Dr. Siris, director of the osteoporosis center at Columbia University, New York. "People may simply just not comprehend the reason they are being treated."

Patients clearly need more risk counseling, she said. "Bone health has to be something we, as doctors, pay constant attention to. And certainly as part of our discussions with patients, we need to collect information on risk factors and convey to patients that these factors do put them at increased risk for a fracture." Those discussions should include information about how to mitigate risk factors.

Dr. Siris disclosed that she has received consulting fees for her time working on GLOW from Sanofi-Aventis and Procter & Gamble Co., which funded the project. ■

Bone Loss May Contribute To Benign Positional Vertigo

BY MICHELE G. SULLIVAN

Benign positional vertigo appears to strongly correlate with osteopenia and osteoporosis in both men and women, researchers in a case-control study have concluded.

Compared to controls, patients with osteopenia were twice as likely to experience positional vertigo, and those with osteoporosis were three times as likely to experience the disorder, Dr. Ji Sook Kim and colleagues wrote.

"These findings suggest a deranged calcium metabolism in idiopathic benign positional vertigo," Dr. Kim of the Seoul National University College of Medicine, Korea, said in an interview. "Restoring normal calcium metabolism may prevent recurrences" of BPV.

The study compared bone mineral density in 209 patients with a diagnosis of idiopathic benign positional vertigo (BPV) and 202 controls. Most of the patients (142) were female; their mean age was 60 years.

Among female patients, only 28% had normal bone mineral density, while 47% had osteopenia (T score greater than –2.5 and less than –1.0) and 25% had osteoporosis (T score = –2.5). Among female controls, normal bone mass was found in 57%; 33% had osteopenia and 9% had osteoporosis. (Percentages do not add up to 100% due to rounding.) The differences were significant at all points measured (Neurology 2009;72:1069-76).

In male patients, 48% had normal bone mass, while 40% had osteopenia and 12% had osteoporosis. Among male controls, 67% had normal bone mass, 27% had osteopenia, and 6% had osteoporosis. The differences were significant at the femur and first lumbar vertebra, but not at the other lumbar measurements.

Recurrent attacks of BPV (defined as at least two previous attacks at least 1 month apart) had occurred in 40% of patients. Compared to patients with new-onset BPV, patients with recurrent BPV were older (62 vs. 60 years) and more likely to be women (77% vs. 62%). A logistic regression analysis controlled for age, sex, smoking, and hyperphosphatemia; none of these variables represented a significant risk factor for BPV.

In women older than 45 years, the mean lowest T scores were lower in the recurrent group than in the new-onset group (–2.1 vs. -1.6). There were no between-group T-score differences in younger patients. This finding supports the premise that estrogen deficiency may contribute to the development of BPV by weakening the bond of otoconia to the utricle, the investigators wrote. In men, the weakening may be the result of bone loss initiated by a combination of hormone deficiency, poor nutrition, and decreased physical activity. ■