Alter Bone Care in Patients on Glucocorticoids

BY KERRI WACHTER

DENVER — People on long-term glucocorticoids have a significant risk for fracture at relatively high bone mineral density T scores, a finding that may lead to changes in the management of such patients.

"In glucocorticoid osteoporosis, the fracture risk seems to take off quite dramatically somewhere around T scores of –1.5," Dr. Philip Sambrook said at the annual meeting of the American Society for Bone and Mineral Research. "Most of the guidelines around the world are now suggesting that the intervention threshold [for those on glucocorticoids] should be [a T score of] about –1.5."

Patients on glucocorticoids typically have midline fractures of the vertebrae, where the bone just collapses in the middle of the vertebra. "This is different from the anterior wedge fracture that occurs most commonly in postmenopausal women with osteoporosis," noted Dr. Nancy Lane, director of the center for healthy aging at the University of California, Davis. This is because there are some differences in how bones become fragile in the presence of glucocorticoids, she said.

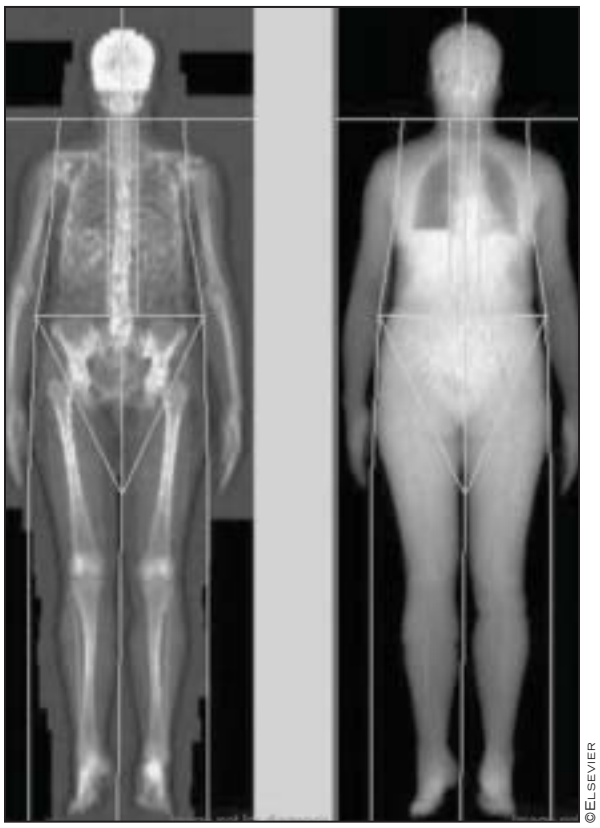
Dr. Sambrook, of Royal North Shore Hospital in Sydney and head of the bone and joint group at the Kolling Institute of Medical Research, presented cases that "really illustrate the type of patients that we often struggle with."

Patient No. 1

A 66-year-old woman was recently diagnosed with polymyalgia rheumatica. She had been started on 25 mg/day prednisone and the disease activity lessened in response. Her history included chronic atopic dermatitis and hypothyroidism. She had no other medical problems. There was no family history of hip fracture. She did not smoke or drink. She had a slightly early menopause but had not used hormone therapy. She reported eating one or two servings of dairy products daily. She also considered herself to be physically active, although she had no formal exercise program.

In her work-up, a spine x-ray showed a vertebral compression. Bone mineral density (BMD) measurements showed modest osteopenia (T scores of –1.5 at the spine and –1.6 at the hip). She had normal levels of calcium and parathyroid hormone (PTH). Her vitamin D level was equivocal, however. Her thyroid function was normal.

This patient had modest osteopenia at the time of her diagnosis. Once she was started on glucocorticoids, her T scores could have fallen rapidly and then stabilized over time, without treatment for bone loss, Dr. Sambrook said. "As she becomes established on glucocorticoids, she will perhaps not lose that much bone," but she's at risk of fracture.



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A whole-body dual-energy x-ray absorptiometry scan can provide information on total and regional BMD (left) and body composition (fat, muscle mass).

When clinical trial data are interpreted, it's important to keep two clinical scenarios in mind: prevention (when initial rapid loss of bone is to be avoided) and treatment (when the patient is on chronic glucocorticoids and may not be losing a lot of bone but is still at risk for fracture).

"Most of us would believe that vitamin D [plus] calcium is an adjunctive therapy," Dr. Sambrook said. The data appear to back that up. In a 1996 trial, patients with glucocorticoid osteoporosis were randomized to 50,000 U/week of vitamin D plus 1,000 mg/day of calcium, or placebo. Both groups lost bone at the spine quite rapidly, although there was a trend for patients on vitamin D and calcium to do slightly better (J. Rheumatol. 1996;23:995-1000).

In another study, researchers demonstrated that daily alendronate increases bone density in patients who receive glucocorticoids, compared with those on placebo (N. Engl. J. Med. 1998;339:292-9). Similar results have been demonstrated with etidronate, risedronate, and zoledronic acid.

Dr. Sambrook recommended that the patient receive calcium and vitamin D supplementation. Also, "we would primarily give her bisphosphonates until prednisone is discontinued" and possibly beyond, depending on her overall fracture risk after prednisone treatment.

Patient No. 2

A 24-year-old woman has had systemic lupus erythematosus for 3 years, which is now severe. Her SLE complications have included encephalitis, vasculitis, renal involvement, and deep vein thrombosis. She had no family history of osteoporosis. She did not consume much dietary calcium, but claimed to get adequate sun exposure. She had been on an oral contraceptive since the age of 17. Her appetite and weight were average and stable.

At the time of her presentation, she had been on prednisone for 6 months, with dosages averaging 25-50 mg daily. However, the recent onset of renal complications required increasing the dose to 75 mg daily. She was also taking an antimalaria drug. Her vitamin D level was equivocal and needed to be addressed. She had normal calcium and PTH levels and normal thyroid function. However, her spine T score was –1.4 and her hip T score was –1.0.

Dr. Sambrook's concern was the effect of bisphosphonates on fetal development. The patient was not pregnant, but might have become so intentionally or unintentionally. Bisphosphonates are classified as pregnancy category C drugs by the Food and Drug Administration, meaning that they are contraindicated in pregnancy.

One approach to managing this patient is to simply watch her and measure BMD in 12 months. Another is to use a bisphosphonate in conjunction with vitamin D and calcium supplementation. Risedronate might be the better choice, given its quicker onset and offset of action, he said.

"As long as she stayed on prednisone, I might not be as aggressive as with postmenopausal women," Dr. Sambrook noted. If the prednisone dose was decreased, he said that he might consider stopping bisphosphonate treatment.

Dr. Lane and Dr. Sambrook both reported financial relationships with several pharmaceutical companies. ■

FRAX 10-Year Hip Fracture Predictions Match Incidence

BY KERRI WACHTER

DENVER — The FRAX 10-year fracture risk tool was fairly accurate in predicting the observed number of hip fractures that occurred among more than 5,000 participants of the Framingham Heart Study, according to data presented as a poster at the annual meeting of the American Society for Bone and Mineral Research.

The 10-year observed incidence of hip fracture for women was 117 cases, which did not differ significantly from the FRAX predicted number of 113. For men, the observed incidence was 29 cases, also not significantly different from the FRAX predicted number of 38, reported Elizabeth J. Samelson, Ph.D., of the Institute for Aging Research in Boston, and her coinvestigators.

FRAX is an online tool that was developed by the World Health Organization to calculate the 10-year probability of hip fracture and major osteoporotic fracture in women and men, aged 40-90 years, on the basis of bone mineral density (BMD), sex, age, smoking status, glucocorticoid use, height and weight, diagnosis of rheumatoid arthritis or secondary osteoporosis, history of fracture, and parental history of fracture. FRAX was developed using several population-based cohorts.

This study included 5,204 Framingham cohort members (2,917 women and 2,287 men) who had a baseline examination in 1987-2001 and were followed for hip fracture over 10 years. All were white. At baseline, patients were assessed for age, body mass index, current smoking status, alcohol consumption, glucocorticoid use, diagnosis of rheumatoid arthritis, prior fragility fracture, parental history of fracture, and T score. History of parental hip fracture was not available for members of the original cohort (1,456); these participants were classified as having no parental history of hip fracture. Femoral neck BMD was available for 4,224 participants.

The researchers used FRAX version 3.0 to calculate the 10-year probability of hip fracture and compared the expected number with the number observed in the cohort. A hip fracture was defined as a proximal femur fracture and was confirmed by review of medical records (including radiographic and surgical reports). Data were further analyzed by age and sex.

Among women aged 40-75 years, the incidence was 52 cases, compared with 57 expected by FRAX; among men aged 40-75 years, the incidence was 12 cases, compared with 23 expected by FRAX. Notably, the observed probability of hip fracture in the oldest adults (aged 76-90 years) exceeded the number predicted by FRAX, while the opposite was true for those aged 40-75. However, these differences were not significant, the authors noted. Among women aged 76-90 years, the incidence was 65 cases, compared with 55 expected by FRAX; among men aged 76-90 years, the incidence was 17 cases, compared with 14 expected by FRAX.

FRAX can be useful to communicate osteoporosis risk in white U.S. adults in the clinical or public health setting; "however, the tool may overestimate hip fracture risk in persons aged 40-75 years," the researchers wrote.

The latest version of FRAX can be accessed at www.shef.ac.uk/FRAX. The study was supported by the National Institutes of Health. The researchers reported that they have no relevant financial relationships. ■

A related video is at www.youtube.com/InternalMedicineNews (search for 69343).