Consider T Score as Just One Factor in Osteoporosis Treatment Decisionmaking

BY NANCY WALSH
New York Bureau

NEW YORK — While bone mineral density T scores clearly are predictive of a postmenopausal woman's osteoporotic fracture risk, treatment decisions should take into account other factors, including her overall health and history of previous fractures, Stephen Honig, M.D., said at a rheumatology meeting sponsored by New York University.

"We have to do better than the T score in deciding who needs treatment for osteoporosis, because the long-term use of bisphosphonates has not been determined to be safe," said Dr. Honig, director of the osteoporosis center at the Hospital for Joint Diseases Spine Center in New York.

Very long-term bisphosphonate therapy may lead to oversuppression of bone turnover, he said. This superhardening can hinder subsequent fracture healing, as was seen in a recent report of nine patients who sustained spontaneous, nonhealing fractures while on alendronate therapy (J. Clin. Endocrinol. Metab. 2005;90:1294-301).

These patients showed histomorphometric evidence of markedly suppressed bone formation, Dr. Honig said.

This new finding has heightened interest in targeting osteoporosis treatment. Research findings have begun to provide guidance on which patients can most benefit from treatment.

Most notable was the National Osteoporosis Risk Assessment (NORA) study, which enrolled 200,160 postmenopausal women aged 50 and older. In that study, bone mineral density (BMD) measurements were obtained at baseline, and the participants were followed for 1 year.

At follow up, one-third of all fractures and one-fifth of all hip fractures in particular occurred in women aged 50-64. Although the majority of fractures did occur in women 65 and older, the high number in the younger cohort "was a little surprising," said Dr. Honig.

Another finding that emerged from NORA was that 80% of the women who had fractures during the yearlong study had T scores that were higher than –2.5 and therefore did not meet the World Health Organization definition of osteoporosis. Most fell between –1 and –2.5, the osteopenic range, he said.

"We want to identify patients at risk in this middle range and not wait until they have obvious fractures," he said.

The NORA investigators subsequently followed 57,421 osteopenic women and developed an algorithm for determining risk. As it turns out, identifying patients with a previous fracture, a T score below –1.8, a self-reported health status of fair or poor, and poor mobility were all factors significantly predictive of fracture risk (Arch. Intern. Med. 2004;164:1113-20).

Another prospective study conducted in France followed 672 healthy postmenopausal women for more than 5 years, and found an annual incidence of osteoporotic fractures of 21 per 1,000 women per year (Bone 2003;32:78-85). The French investigators identified the key risk factors (in order of importance) to be: a past fracture, hip BMD, low physical activity, low grip strength, age over 65, maternal fracture history, and past falls.

Other studies have also suggested additional risk factors, including smoking, low body mass index, and increased markers of bone absorption.

Based on the available data and tools at hand, Dr. Honig recommends that clinicians now consider treatment for the following patients:

- Women 65 and older, with or without a history of fracture, who have low BMD or other risk factors, such as low BMI and family history.
- Women 50 and older with a previous fracture and a T score of –1.8 or less.
- Women in poor overall health with mobility problems and low BMD.
- Women with low BMD and increased markers of bone resorption.

But questions remain, he said. How long can a bisphosphonate be used? When should teriparatide or a selective estrogen receptor modulator be used? What place does hormone replacement therapy have in treatment strategies? "There is some new evidence that postmenopausal women with certain levels of endogenous estradiol have a lower incidence of fractures. This may translate into using very low-dose [hormone therapy], which conceivably could be safer than what was seen in the Women's Health Initiative," he said.

Dr. Honig disclosed that he receives support from Eli Lilly & Co. and is on the speakers' bureau of Sanofi-Aventis. ■

Past Vertebral Fractures Predict Future Risk

WASHINGTON — The risk of vertebral fragility fractures is threefold higher among postmenopausal women with at least one prevalent radiographic fracture, compared with those without such a history, Ethel S. Siris, M.D., said at an international symposium sponsored by the National Osteoporosis Foundation.

Awareness of previous vertebral fractures can help physicians evaluate vertebral fragility and target osteoporosis therapy appropriately, Dr. Siris, a professor of clinical medicine at Columbia University, New York and her colleagues, said in a poster presented at the meeting.

Their review of data on 2,651 postmenopausal women, mean age 67 years, included 1,181 women with prevalent vertebral fractures and assessed fracture risk independent of lumbar spine bone mineral density. Overall, the greater the number of prevalent vertebral fractures, the greater the risk of sustaining subsequent fractures.

Patients with three or more fractures had as much as an eightfold increased risk. Greater severity scores on the semi-quantitative deformity scale were associated with as much as an 11-fold increase in the risk of fracture.

Dr. Siris is a consultant for and has received honoraria from Eli Lilly & Co., Merck & Co., Sanofi-Aventis, Procter & Gamble Pharmaceuticals, and Novartis.

—Heidi Splete

Intravenous Ibandronate Every Few Months More Effective Than Oral Daily Dosing

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Postmenopausal women with osteoporosis who can't tolerate oral ibandronate may welcome an intravenous option, Michael Bolognese, M.D., reported at an international symposium sponsored by the National Osteoporosis Foundation.

One-year results from the Dosing Intravenous Administration (DIVA) study, an ongoing randomized, double-blind, phase III trial, showed that rapid injections of ibandronate (Boniva) in amounts of 2 mg every 2 months or 3 mg every 3 months were more effective than the standard oral daily dose of 2.5 mg at increasing bone mineral density (BMD), Dr. Bolognese of Bethesda (Md.) Health Research and his colleagues wrote in a poster presentation of their findings.

The increases in the BMD at the lumbar spine were significantly greater for women on both the 2-mg/2 mo (5.1%) and 3-mg/3 mo (4.8%) regimens compared with the 2.5-mg daily oral dosage (3.8%). In addition, significantly more patients demonstrated increased BMD from baseline in both the lumbar spine and total hip in the 2-mg/mo and 3-mg/mo groups compared with the daily oral 2.5-mg group.

Significantly more patients on intravenous drug had increased BMD from baseline in both the lumbar spine and total hip in the 2-mg/mo and 3-mg/mo groups.

The study included 1,395 women aged 55-80 years with postmenopausal osteoporosis. In addition to their ibandronate regimens, women in all treatment groups received 500 mg of calcium and 400 IU of vitamin D daily. The incidence of renal adverse events such as urinary incontinence, renal impairment, or nephrolithiasis, was 3% or less across all treatment arms, and there were no significant changes in serum creatinine levels in any of the patients compared with baseline. The incidence of flu-like illness was low as well—3.3%, 3.2%, and 0.6% in the 2-mg/2 mo, 3-mg/3 mo, and 2.5-mg oral groups, respectively.

In addition, the overall incidence of clinical fractures, including vertebral fractures, was 3.1%, and did not differ significantly among the three groups, although it was slightly higher in the oral group (3.7%) compared with the 2-mg/2 mo group (2.9%) and the 3-mg/3 mo group (2.8%).

Dr. Bolognese is a consultant for Eli Lilly & Co. and Procter & Gamble Co., and has received grants or research support from Aventis Pharmaceuticals Inc., Pfizer Inc., Lilly, and Wyeth. ■

Vitamin D Deficiency Rampant

WASHINGTON — Vitamin D levels are inadequate in up to half of postmenopausal women who receive treatment for osteoporosis, Ethel S. Siris, M.D., reported at an international symposium sponsored by the National Osteoporosis Foundation.

Vitamin D inadequacy was significantly worse among women who took less than 400 IU of vitamin D supplementation daily, compared with women who took at least 400 IU of vitamin D daily (63% vs. 45%).

Previous study findings suggest that serum 25-hydroxyvitamin D concentrations of at least 30 ng/mL are needed to stabilize serum parathyroid hormone levels, Dr. Siris, director of the metabolic bone diseases program at Columbia University, New York, and her colleagues, wrote in a poster presentation.

In a cross-sectional, observational study conducted between November 2003 and March 2004, the investigators collected blood samples from 1,536 postmenopausal women, mean age 71 years, at 61 sites throughout North America. They used several cut points of serum 25-hydroxyvitamin D to define inadequacy—less than 9 ng/mL, less than 20 ng/mL, less than 25 ng/mL, and less than 30 ng/mL.

Parathyroid hormone values stabilized among patients with serum 25-hydroxyvitamin D concentrations of at least 29.8 ng/mL, which suggests that concentrations of approximately 30 ng/mL are important for healthy parathyroid levels.

Additional factors significantly related to vitamin D inadequacy in a multivariate analysis included age older than 80 years, BMI greater than 30, lack of exercise, and lack of physician counseling about the importance of vitamin D. More than half (59%) of the women reported that they had not discussed vitamin D with a doctor.

Dr. Siris is a paid consultant for Eli Lilly & Co., Merck & Co., Sanofi Aventis, Procter & Gamble Pharmaceuticals, and Novartis.

—Heidi Splete

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