

Don't Miss Vitamin D Deficiency in Osteoporotics

More than 50% of women being treated for the bone disorder had serum D levels lower than 30 ng/mL.

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — A majority of 1,536 elderly women taking medication to prevent or treat osteoporosis were deficient in vitamin D, a study of community-dwelling patients found.

The findings echo a previous study that found 56% of medical inpatients had vitamin D deficiency. "This is a very common problem" that deserves more attention, Dolores M. Shoback, M.D., said at a meeting on osteoporosis sponsored by the University of California, San Francisco.

Physicians should look more carefully for vitamin D deficiency in inpatients and outpatients, even those who are ambulatory, on prescription therapy for osteoporosis, and lacking risk factors for vitamin D deficiency—"many of the patients, probably, in our own practices," said Dr. Shoback, professor of medicine at the university.

The recent outpatient study included postmenopausal women at 61 locations in North

America who had been taking bisphosphonates, calcitonin, or a selective estrogen receptor modulator for at least 3 months under a physician's care to prevent or treat osteoporosis. They averaged 71 years in age, and were 92% white. Investigators administered a questionnaire to assess risk factors for vitamin D deficiency and measured the women's serum concentrations of parathyroid hormone (PTH) and 25-hydroxyvitamin D—known as 25(OH)D—the form of vitamin D stored in the body.

They found that 52% of the 1,536 women had levels of 25(OH)D lower than 30 ng/mL. Of these, 36% had levels below 25 ng/mL, and 18% were below 20 ng/mL, showing that most of the women with inadequate vitamin D were severely deficient (*J. Clin. Endocrinol. Metab.* 2005;90:3215-24).

"We aren't doing a good job with the people we're actively treating for osteoporosis," said Dr. Shoback. Vitamin D deficiency is one of the most common causes of secondary osteoporosis.

Although there's no consensus on how much vitamin D the human body needs, the idea that 15-25 ng/mL is adequate has been replaced in the last few years by general cutoffs closer to 30 ng/mL or higher, she said. Some experts say people need at least 20 ng/mL 25(OH)D or else PTH levels rise and frank hyperparathyroidism develops. Others say that elderly people need 32-36 ng/mL to maximize intestinal calcium transport.

In the study patients tended to develop secondary hyperparathyroidism at 25(OH)D levels of 25 ng/mL and lower. Many physicians use PTH levels to help diagnose vitamin D deficiency, but the study found that high PTH is not 100% sensitive for low vitamin D. Only 75% of women with 25(OH)D levels of 0-9 ng/mL had secondary hyperparathyroidism. "This surprised me," Dr. Shoback said.

Women who had not discussed vitamin D and bone health with their doctors were more likely to have 25(OH)D levels below 30 ng/mL. "Sometimes we think we're talking to the wall or ourselves, but these discussions actually may be having some kind of an impact," Dr. Shoback said.

Other risk factors for vitamin D defi-

ciency included age older than 80, a body mass index over 30 kg/m², taking medications that affect metabolism of vitamin D, and taking less than 400 IU per day of vitamin D supplements. Women also were more likely to be deficient in vitamin D if they rated themselves as having "poor general health," if they exercised less than six times per week, if they ate fewer servings of foods containing vitamin D, and if they completed less than 12 years in school.

Among patients with none of these risk factors, 32% had inadequate levels of 25(OH)D. "There just seem to be people out there who have vitamin D deficiency," she said.

The 1998 inpatient study that detected vitamin D deficiency in 56% of 290 patients consecutively admitted to a hospital medical service also found that risk factors predicted the deficiency only about 60% of the time. The investigators recommended that medical inpatients be screened for vitamin D deficiency, she noted. Taking multivitamins did not prevent vitamin D deficiency in that study.

Dr. Shoback has no affiliation with companies that make vitamin D supplements. ■

Strontium Ranelate Prevents Fractures in Highest-Risk Women

BY BRUCE JANCIN
Denver Bureau

VIENNA — Strontium ranelate reduced the risk of new vertebral fractures by 41% over 3 years in a very-high-risk population of osteoporotic women with at least two prevalent vertebral fractures at baseline, Sergio Ortolani, M.D., reported at the annual European congress of rheumatology.

That's roughly as robust a relative risk reduction as seen in much lower-risk postmenopausal osteoporotic women with no previous vertebral fractures, noted Dr. Ortolani of the Center for Metabolic Bone Disease, Milan.

"It appears we have a new first-line treatment for postmenopausal osteoporosis," he declared.

Dr. Ortolani presented a prespecified subgroup analysis drawn from two large phase-III multinational placebo-controlled randomized trials of strontium ranelate for the reduction of fracture risk in osteoporotic postmenopausal women. The Spinal Osteoporosis Therapeutic Intervention (SOTI) involved 1,649 women randomized to 2 g/day of oral strontium ranelate or placebo, while the Treatment of Peripheral Osteoporosis Study (TROPOS) included 5,091 women. Both Servier Laboratories-sponsored trials will run for 5 years, although the 3-year primary outcome data have been published.

Among 2,605 combined study participants without prior vertebral fractures at baseline, the 3-year incidence of new vertebral fractures was

14.4% with placebo and 7.5% with strontium ranelate, for a 48% relative risk reduction. Among the 734 participants with two or more prevalent vertebral fractures at enrollment, the absolute 3-year new vertebral fracture rates were far higher—42.7% in the placebo group, compared with 28.5% in those taking strontium ranelate—but the relative risk reduction conferred by strontium ranelate remained highly robust at 41%.

Strontium ranelate has a unique mode of action. It simultaneously increases bone formation and reduces bone resorption. The antiresorptive effect is less potent than with bisphosphonates; however, in combination with the simultaneous

bone-forming effect, strontium ranelate becomes a highly effective antiosteoporosis medication, Dr. Ortolani said at the meeting sponsored by the European League Against Rheumatism.

The drug's chief adverse effect is diarrhea, which was limited to the first few

months of therapy in the clinical trials. When the data from TROPOS and SOTI were pooled, there was a small but statistically significant increase in deep venous thrombosis in strontium ranelate-treated patients, but no increase in strokes or cardiovascular events. "The absolute incidence of DVT is much less than with raloxifene or estrogen replacement therapy," Dr. Ortolani added.

Strontium ranelate is approved in several European countries and soon will be marketed throughout Europe. The Food and Drug Administration has requested that Servier conduct a U.S. clinical trial before filing for marketing approval in the United States, Dr. Ortolani said. ■

In Paget's Disease Patients, Zoledronic Acid Packs a Bigger Punch Than Oral Risedronate

BY BRUCE JANCIN
Denver Bureau

VIENNA — A single 5-mg IV infusion of zoledronic acid produces significantly greater therapeutic efficacy and a longer-lasting biochemical remission than 2 full months of oral risedronate at 30 mg/day in patients with Paget's disease of bone, Jacques P. Brown, M.D., reported at the annual European congress of rheumatology.

Zoledronic acid (Zometa) is clearly the clinically advantageous drug, both in bisphosphonate-naïve patients and in those previously on risedronate (Actonel) or other oral bisphosphonates, added Dr. Brown of the Centre Hospitalier Universitaire de Québec, Sainte-Foy.

At the meeting, sponsored by the European League Against Rheumatism, he presented a pooled analysis combining the data from two randomized, double-blind, multicenter trials of 349 patients with Paget's disease of bone. Participants received a single 15-minute 5-mg infusion of zoledronic acid or 30 mg/day of oral risedronate for 2 months.

The primary end point was a reduction of 75% or more in excess serum alkaline phosphatase (SAP) at 6 months. Ninety-six percent of patients in the zoledronic acid group achieved it vs. 74% in the risedronate arm. Eighty-nine percent of zoledronic acid-treated pa-

tients achieved normalization of SAP at the 6-month mark, compared with 58% on risedronate.

The therapeutic response to zoledronic acid was significantly swifter and longer lasting than the response to risedronate. At the 1-month mark, 20% of the zoledronic acid group had achieved at least a 75% reduction in excess SAP, while just 1% of the risedronate group did. At 2 months, 90% of zoledronic acid-treated patients showed a therapeutic response vs. 47% on risedronate. Moreover, only 2 patients in the zoledronic acid group lost their therapeutic response between months 6 and 18, while 36 in the risedronate group did.

One hundred percent of patients randomized to zoledronic acid after having previously been on an oral bisphosphonate had a therapeutic response to the intravenous third-generation bisphosphonate. In contrast, only 30% of patients previously on risedronate or another oral bisphosphonate achieved a therapeutic response when randomized to risedronate in the study.

Side effects of zoledronic acid include myalgia, fatigue, headache, rigors, nausea, and bone pain. In these studies, the effects were mild to moderate in nature, often began within 3 days after the first dose, and typically lasted less than 4 days.

The studies were funded by Novartis Pharmaceuticals. ■



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DR. ORTOLANI