Low Vitamin D and Breast Cancer: Is There a Link?

Consider vitamin D supplements in postmenopausal women being treated with aromatase inhibitors.

BY JANE SALODOF MACNEIL
Southwest Bureau

ATLANTA — Vitamin D supplementation should be considered for postmenopausal breast cancer patients treated with aromatase inhibitors, Dr. Per E. Lønning reported at the annual meeting of the American Society of Clinical Oncology.

"Low vitamin D status could be one of the factors predisposing patients to breast cancer," said Dr. Lønning, a professor at Haukeland University in Bergen, Norway.

Postmenopausal breast cancer patients who were treated with exemestane and had vitamin D deficiency lost bone mineral density (BMD) at a higher rate than all other patients in a Norwegian trial, according to Dr. Lønning, who presented the trial's results.

The double-blind study enrolled early breast cancer patients at six sites between January 1999 and October 2001. Participants were postmenopausal with estrogen receptor–negative or progesterone receptor–positive breast cancer. Median patient age was 59.5 years, and all had a low risk of breast cancer recurrence after surgery.

Of the patients enrolled in the randomized, controlled trial, 128 of 147 (87%) had low levels of vitamin D, defined as 30 ng/mL or less.

Investigators randomized 73 women to 25 mg of oral exemestane daily and 74 women to a daily placebo for 2 years. Local guidelines did not routinely offer adjuvant endocrine therapy at the time of the study, the investigators noted. Mean vitamin D levels were reported as 21.6 ng/mL for the exemestane arm and 22.6 ng/mL for the control group.

Average patient change in femoral neck BMD was –4.7% after 2 years of treatment with exemestane, an aromatase inhibitor. Placebo patients with low vitamin D also had bone loss in the femoral neck, but the reduction was –3.0%.

Women with normal vitamin D levels had similar outcomes whether they were treated with exemestane or placebo: reductions of –3.7% and –3.3%, respectively.

"It has not fully been examined that breast cancer patients on average have a poorer vitamin D status in comparison to the normal population in general," he added, calling for further investigation of the relationship between vitamin D and breast cancer.

An annual BMD loss of 0.5% is normal for postmenopausal women, according to Dr. Lønning and his fellow investigators from the Norwegian Breast Cancer Screening Program. Interviewed during the poster session where he presented trial data, he said low vitamin D levels could be expected in about 50% of postmenopausal women in Norway.

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DR. LØNNING

However, he warned against assuming that low vitamin D levels are entirely explained by reduced sun exposure in northern latitudes, because people in other climates are spending more time indoors and out of the sun.

"You should not think of this as a preventive problem only in the far north," he said. "This could be a problem to populations all over the world."

While the investigators reported some significant differences in subgroups and "a trend toward higher loss of BMD in the femoral neck" among women with low vitamin D during the 2 years of exemestane treatment, low vitamin D did not appear to make as much of a difference in lumbar spine BMD.

The reductions were –3.4% for 52 vitamin D–deficient women who completed the study on exemestane and –2.5% for 59 women who stayed on placebo.

"Vitamin D has influence on compact bone, not trabecular bone," Dr. Lønning said. "When you look at the low toxicity of vitamin D, you are not running much risk with supplementation," he said. "However, I have to say for research purposes, we need more data." ■

Single, IV-Dose Zoledronic Acid Bests Alendronate on Resorption Markers

BY NANCY WALSH
New York Bureau

TORONTO — A single intravenous dose of zoledronic acid reduced markers of bone resorption in postmenopausal women more rapidly and to a greater extent than did weekly oral alendronate, Dr. Kenneth Saag reported in a poster session at a world congress on osteoporosis.

Zoledronic acid is the most powerful of the available bisphosphonates, and its long duration of effect now has been demonstrated in a multicenter double-blind trial that randomized 118 women aged 45-79 years to a single infusion of 5 mg zoledronic acid or 70 mg weekly oral alendronate for 24 weeks. Patients receiving intravenous zoledronic acid also received oral placebo, and those receiving oral alendronate also received intravenous placebo.

Early on, zoledronic group patients were more likely to have adverse events associated with flulike symptoms.

DR. SAAG

In the zoledronic acid group, mean urine cross-linked N-telopeptide of type I collagen (NTx) fell from 46.1 to 15.2 nmol/bone collagen equivalent (BCE)/mmol creatinine at 1 week, while the level of this marker of bone turnover decreased from 45.8 to 35.5 nmol BCE/mmol creatinine in the alendronate group at 1 week. This relative change from baseline in NTx was significantly different between the two groups, and the greater reduction in urine NTx with zoledronic acid persisted throughout the 24 weeks of the study, according to Dr. Saag of the division of rheumatology, University of Alabama, Birmingham.

Levels of bone-specific alkaline phosphatase (BSAP) also decreased from baseline through week 24 in both groups. While reductions in BASP levels were significantly greater in the zoledronic acid group at week 12, levels in both groups were within the premenopausal range of 6.2 to 12.8 ng/mL.

Overall, a comparable proportion of patients in each treatment arm reported adverse events, with 91% of those in the zoledronic acid group and 86% of those in the alendronate group experiencing any adverse event. During the first 3 days after drug initiation, flulike symptoms led to a greater frequency of adverse events in the zoledronic acid group compared with the alendronate group (64% versus 37%), but after 3 days the adverse event rates were similar in the two groups, Dr. Saag reported.

Serious adverse events were reported by two patients in the zoledronic acid group (one report of osteoarthritis and one of chest pain) and by three in the alendronate group (one patella fracture and two reports of osteoarthritis). None were considered to be treatment related.

Patient preferences for the treatments also were analyzed, with study participants expressing a "strong preference" for the single infusion compared with the weekly regimen (66% versus 20%), Dr. Robert Lindsay noted in another poster session at the meeting, which was sponsored by the International Osteoporosis Foundation.

Even among patients who experienced adverse events during the 3 days following the infusion, 74% expressed an overall preference for the single-dose treatment, according to Dr. Lindsay of the clinical research center, Helen Hayes Hospital, West Haverstraw, N.Y.

The study was funded by Novartis Pharma AG, Basel, Switzerland. ■

Lymphoma Chemotherapy Raises Risk for Osteoporosis

BY NANCY WALSH
New York Bureau

GLASGOW, SCOTLAND — Chemotherapy for lymphoma should be recognized as a risk factor for the development of osteoporosis, Dr. Bhaskar Dasgupta reported in a poster session at the annual meeting of the British Society for Rheumatology.

Patients with lymphoma have greatly improved survival rates because of advances in treatment, but their quality of life may be compromised by long-term complications of chemotherapy, reported Dr. Dasgupta, director of rheumatology, Southend Hospital NHS Trust, Westcliff on Sea, England. Osteoporosis is one such potential complication that can result from treatment with alkylating agents and the steroids that are often given with chemotherapy.

Height loss as a surrogate marker for vertebral osteoporosis was evaluated in a study of patients attending a lymphoma clinic. A total of 25 patients, 8 with Hodgkin's and 17 with non-Hodgkin's lymphoma, were enrolled. Mean age was 57.6 years, and 13 of the patients were female, reported Dr. Dasgupta.

Exclusion criteria included a previous osteoporosis diagnosis, lymphoma with spinal involvement, and previous corticosteroid treatment.

When baseline height was compared with height 24 months or more after chemotherapy, the mean loss was found to be 22.8 mm, according to Dr. Dasgupta.

The degree of height loss increased with age—every 10-year increase in age was associated with a 5.2-mm decrease in height, he reported. No association was seen between height loss and gender, and none of the patients had other risk factors for osteoporosis, according to questionnaires they had filled out.

Case notes were examined for cumulative steroid dose and the type of chemotherapy received, with no height loss association found. Patients whose height loss exceeded 40 mm were more likely to be symptomatic. Two patients whose height loss was 50 mm or more reported disabling back pain and poor quality of life.

Despite the fact that significant height loss was seen in this group of patients, none had received bisphosphonates or vitamin D, and only one patient was taking a calcium supplement, Dr. Dasgupta noted. Also, none of the patients had had a bone mineral density determination.

"Our findings suggest that larger studies of osteoporosis and its complications following chemotherapy are needed, and that appropriate investigations and prophylactic management are indicated, especially in the elderly," Dr. Dasgupta concluded. ■