High Vitamin D Intake May Prevent Fractures

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FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR BONE AND MINERAL RESEARCH

VITALS

Major Finding: People taking 792-2,000 IU/day of vitamin D had a statistically significant, 14% reduced rate of any nonvertebral fracture and a significant, 30% reduced rate of hip fractures compared with control subjects who did not receive a vitamin D supplement.

Data Source: Meta-analysis of 11 double-blind, randomized, controlled trials with individual participant data available for 31,022 subjects with an average age of 76.

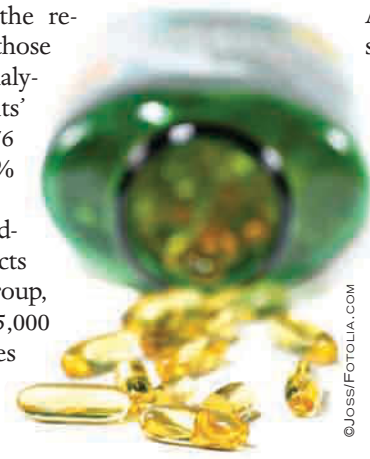
Disclosures: Dr. Bischoff-Ferrari said that she had no disclosures.

TORONTO – A daily vitamin D dose of at least 792 IU was linked with significantly reduced rates of nonvertebral fractures and hip fractures in a meta-analysis of data from 11 randomized, controlled trials.

But the benefit from vitamin D appeared blunted when combined with a higher calcium dose, or when patients received vitamin D once yearly, Dr. Heike A. Bischoff-Ferrari reported.

In the meta-analysis, patients in the highest quartile for daily vitamin D intake, 792-2000 IU, had a statistically significant 14% reduced rate of any nonvertebral fracture and a significant 30% reduced rate of hip fractures after adjusting for age, gender, and type of dwelling, said Dr. Bischoff-Ferrari, a rheumatologist at the University of Zurich.

Her meta-analysis pooled individual participant data from 12 double-blind, randomized, controlled trials that examined the impact of vitamin D supplements on fracture rate in people aged 65 years or older published through June 2010, and for which she could obtain individual participant data. The primary analysis focused on the 11 studies of the 12 in which participants received the supplement at least monthly, with 31,022 people enrolled. The twelfth study tested once annual dosing, and the researchers included those data in a separate analysis. The participants' average age was 76 years, and about 90% were women.



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The analysis divided the study subjects into the control group, with more than 15,000 people, and then into quartiles of their received amount of vitamin D, including both their study-treatment dose and any additional vitamin D intake. The analysis also took into account adherence to treatment. Each vitamin D quartile contained nearly 4,000 people, with a daily dose range of 792-2,000 IU forming the top quartile. Only the top quartile of vitamin intake linked with statistically significant differences, compared with the controls, for any nonvertebral fracture and for hip fracture.

An additional analysis that looked at the interaction of calcium supplements along with vitamin D showed that, with a daily calcium dose below 1,000 mg/day, a high-dose vitamin D supplement (792-2,000 IU/day) linked with a statistically significant reduction in nonvertebral fractures, but when the daily calcium supplement delivered 1,000 mg or more, this amount of vitamin D did not associate with any significant change in fracture rate, suggesting an adverse effect from higher calcium intake. ■

Six-Year Zoledronic Acid Regimen Maintains BMD

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR BONE AND MINERAL RESEARCH

TORONTO – Patients who continued annual treatment with zoledronic acid for 6 years had significantly better bone mineral density and fewer morphometric vertebral fractures than did patients who received 3 years of treatment and then stopped, in a controlled study with more than 1,200 patients.

Six continuous years of annual zoledronic acid treatment also proved safe, making continued treatment with this bisphosphonate formulation an option for patients who might benefit, said Dennis M. Black, Ph.D., professor of epidemiology and biostatistics at the University of California, San Francisco.

"After 3 years, it might be beneficial for some women, particularly those at high vertebral fracture risk, to continue zoledronic acid for an additional 3 years," he said.

"These new findings show that continued treatment with zoledronic acid for 6 years continues to maintain bone mass and reduced vertebral fracture risk with no change to its favorable safety profile compared with discontinuation of treatment after 3 years," Dr. Black said in a written statement.

On the other hand, the decision to continue bisphosphonate treatment long term must be individualized, he said. It may be possible to identify women who would benefit from a drug holiday.

The new zoledronic acid findings came from an extension of the Health Outcomes and Reduced Incidence With Zoledronic Acid Once Yearly (HORIZON) Pivotal Fracture Trial, which compared a single, annual infusion of zoledronic acid with placebo in postmenopausal women with osteoporosis during 3 years of treatment (N. Engl. J. Med. 2007;356:1809-22).

Dr. Black and his associates randomized 1,233 women who completed the zoledronic acid arm of the study to either continue with another 3 years of annual infusions of 5 mg zoledronic acid or switch to placebo.

Their average age was 76, and about 55% had a femoral neck T score of less than –2.5.

At the end of the study, the percent change in femoral neck bone mineral density, compared with the level at entry into the study, averaged 1% higher in patients treated with zoledronic acid, a statistically significant difference in the study's primary end point.

Femoral neck bone mineral density in the zoledronic acid–treated patients increased by an average of 1.4% over their baseline 6 years earlier (when they started on the drug), compared with those who switched off the bisphosphonate after 3 years, also a statistically significant difference.

The rate of morphometric vertebral fractures during the 3 years of the new study totaled 6% in the patients on placebo and 3% in those on zoledronic acid, a statistically significant difference.

The HORIZON trial was funded by Novartis, which markets zoledronic acid (Aclasta).

Dr. Black said that he has served as a consultant and done teaching for Amgen Inc. and Nycomed, and that he has received research contracts from Amgen, Merck & Co., Novartis, and Roche/Genentech. ■

T Score at Bisphosphonate's End May Predict Risk of Fractures

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VITALS

Major Finding: Patients withdrawn from bisphosphonate treatment after 5 years on the drug with a total hip T score of more than –1.5 had a 9% risk for any clinical fracture during the following 5 years. Patients with a T score of –1.5 to –2.1 at the time bisphosphonate treatment stopped had a 23% fracture rate during the next 5 years. Patients with a total hip T score of less than –2.1 had a 33% fracture rate during the 5 years after bisphosphonate withdrawal.

Data Source: Review of 437 postmenopausal women enrolled in the FLEX study who were randomized to placebo following 5 years of continuous alendronate treatment.

Disclosures: Dr. Bauer said he received research funding from Amgen, Merck, and Novartis. The FLEX study was sponsored by Merck.

TORONTO – The stronger a patient's bones are when bisphosphonate treatment is stopped, the less likely the bones are to fracture later, based on an analysis of 437 patients.

In contrast, changes in bone mineral density following the end of bisphosphonate therapy had no significant link with subsequent fracture risk, said Dr. Douglas C. Bauer of the University of California, San Francisco

The finding calls into doubt the common practice of running annual dual-energy x-ray absorptiometry examinations on patients who have withdrawn from bisphosphonate treatment.

Routine BMD measurement "1-2 years after stopping prolonged alendronate therapy may not be useful for predicting the patient's fracture risk," Dr. Bauer said. The BMD at the time of alendronate discontinuation "was highly predictive of who was going to fracture."

Patients who stopped alendronate therapy with a total hip BMD T score of –1.4 or greater had a 9% rate of clinical fracture during 5 years of follow-up.

Patients with a T score of –2.1 to –1.5 when they stopped bisphosphonate treatment had a 23% fracture rate during 5 years of follow-up, and those who stopped with a T score lower than –2.1 had a 33% fracture rate over the next 5 years. The between-group differences were statistically significant.

Dr. Bauer and his associates used data collected in the FLEX (Fracture Intervention Trial Long-Term Extension) study, which randomized 1,099 postmenopausal women who had completed 5 years of treatment with alendronate to either continue on alendronate for another 5 years or switch to placebo (JAMA 2006;296:2927-38). They focused on the 437 patients who switched to placebo.

Even among patients who had relatively substantial bone loss during 1 year of follow-up, the amount of lost BMD did not significantly correlate with their follow-up fracture rate.

The researchers saw no significant link to fracture rate among the 21% of patients who lost at least 3% of their BMD during the first year of follow-up, or among the 8% of patients who lost at least 5% of their BMD during 1 year of follow-up. ■