High Vitamin C Intake Lowered Hip Fracture Risk

BY JEFF EVANS
Senior Writer

MONTREAL — Consumption of vitamin C at sufficiently high levels is associated with nearly a 50% decrease in the risk of hip and nonvertebral osteoporotic fractures in elderly men and women, according to a 15- to 17-year follow-up of patients in the Framingham Osteoporosis Study.

Previous studies of menopausal and postmenopausal women have shown that dietary intake of vitamin C is associated with increased bone mineral density (BMD), and that a high vitamin C serum level is associated with a decreased prevalence of fracture. Poor dietary intake of vitamin C also has been associated with an increased risk of hip fracture, Marian T. Hannan, D.Sc., said at the annual meeting of the American Society for Bone and Mineral Research.

Vitamin C, an antioxidant, plays an important role in the formation of collagen, which is a major component of connective tissue. Published evidence suggests that oxidative stress may result in increased osteoclast formation, resulting in greater bone resorption, said Dr. Hannan, who presented the study on behalf of Shivani Sahni of Tufts University, Boston. (Ms. Sahni performed the research as a part of her thesis but could not attend the meeting.)

Of 5,209 men and women in the original Framingham Heart Study cohort, the investigators identified 958 individuals who had participated in the beginning of the osteoporosis study in 1988-1989, had answered a food-frequency questionnaire, and had no history of a hip fracture. These individuals had a mean age of 75 years and experienced 100 hip fractures and 180 nonvertebral osteoporotic fractures during the follow-up period, Dr. Hannan reported.

For the study, participants were divided into three groups based on their intake of vitamin C. The relative risk of hip fracture was significantly lower for individuals who had the highest total intake of both dietary and supplemental vitamin C (a median of 305 mg/day) than it was for people with the lowest total intake (median of 97 mg/day). This translated into a 44% decrease in relative risk of hip fracture, according to Dr. Hannan of Harvard Medical School's Institute for Aging Research, Boston.

Those with the highest total intake of vitamin C also had a 36% lower relative risk of having a nonvertebral osteoporotic fracture than did individuals with the lowest total intake.

When the investigators looked at supplemental vitamin C intake alone, the highest users (median of 260 mg/day) had a 70% lower relative risk of hip fracture than did nonusers. Supplements accounted for about 28% of the individuals' total vitamin C intake, Dr. Hannan said.

The investigators found no effect for dietary intake of vitamin C alone.

All of the comparisons were adjusted for age, sex, body mass index, height, smoking status, estrogen use in women, physical activity, alcohol use, multivitamin use, femoral neck BMD, and total intake of energy, calcium, vitamin D, and potassium.

One audience member suggested that the discrepancy between the effects of supplemental and dietary vitamin C intake could mean that there are residual confounding effects from factors that were not accounted for in the study, such that supplemental use of vitamin C may be a marker for people who care more about their health and take better care of themselves. This is a problem that can only be answered with a randomized, controlled trial, Dr. Hannan noted.

"We were intrigued by the lack of a BMD effect on [the association between] vitamin C and fracture, and we believe that it implies that vitamin C may affect a different pathway or other fracture risk factors, for example, fall risk factors or mobility risk factors," Dr. Hannan said.

Future research should investigate "alternative mechanisms for vitamin C that are independent of BMD …[and] evaluate whether an increase in the recommended dietary intake for vitamin C should take into account the preventive effects seen in this study" and in other types of studies, as well as the protective effects that vitamin C has in other chronic diseases. ■

Teriparatide Effective for Resistant Osteoporosis

BY JEFF EVANS
Senior Writer

MONTREAL — A history of unresponsiveness to bisphosphonate therapies does not appear to diminish the bone-building effects of teriparatide in women with osteoporosis, judging from the findings of a small, uncontrolled, 18-month study.

The anabolic effects of teriparatide (Forteo), an injectable form of recombinant human parathyroid hormone, on bone mineral density (BMD) were apparent by 6 months into treatment and were accompanied by significant changes in biomarkers of bone turnover and positive changes in bone structure on MicroCT imaging, Dr. Burkhard Muche said at the annual meeting of the American Society for Bone and Mineral Research.

The results suggest that patients who are resistant to oral bisphosphonate therapy could use teriparatide in treatment cycles lasting at least 6 months, followed by an antiresorptive agent such as raloxifene (Evista), strontium ranelate, or an intravenous bisphosphonate, in order to optimize the beneficial effects of the anabolic agent, said Dr. Muche of the department of metabolic diseases/osteology at Immanuel-Krankenhaus, Berlin.

Of 25 women in the study with a mean age of 69 years, 14 had a new fragility fracture and 11 had a significant decline in BMD of greater than 3.5%, despite previous treatment with oral bisphosphonates lasting at least 12 months. Half had taken risedronate (Actonel) and half had taken alendronate (Fosamax) for a mean of 3.5 years (range of 1-7 years). The women also received 500 mg of calcium and 400 IU of vitamin D_3 each day.

The investigators detected significant increases in BMD at the lumbar spine after 6, 12, and 18 months of teriparatide. By 18 months, the women had a mean 9% increase in BMD at the lumbar spine. No significant changes developed in the total BMD of the femoral neck or the hip.

Intermittent asymptomatic hypercalcemia occurred in four patients.

Levels of the bone formation marker bone alkaline phosphatase significantly increased from 15 ng/L at baseline to 28 ng/L at 6 months, but then decreased through 18 months. Concentrations of a marker of bone resorption, beta C-terminal telopeptide of type I collagen (β-CTX), followed the same trend.

Dr. Muche and his colleagues obtained paired bone biopsies from the dorsal iliac crest at baseline, from the opposite side at 6 months, and again from the original side at 18 months. Parameters of bone structure on MicroCT imaging increased early during the course of treatment.

Dr. Muche received a travel grant from Lilly Germany, which funded the study. Eli Lilly & Co. makes teriparatide. ■

Sparse Data Exist for Alternative, Efficacious Therapies for Osteoporosis

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — When it comes to alternative therapies for osteoporosis, data are sparse and most do not point to efficacy.

Speaking at the annual meeting of the International Society for Clinical Densitometry, Rogene Tesar, Ph.D., reported available data based on her review:

► **Strontium.** The form that is studied most of 20 supplement compounds is strontium ranelate, which consists of about 340 mg strontium in 1 g of compound.

The Food and Drug Administration is considering approval of strontium ranelate for the treatment of osteoporosis because in two large phase III studies it promoted bone formation, decreased resorption, and reduced fracture risk in postmenopausal women, said Dr. Tesar, who is in private practice in Austin, Texas. The Spinal Osteoporosis Therapeutic Intervention (SOTI) trial of 1,649 patients with a previous vertebral fracture found a 41% reduction in vertebral fracture risk after 3 years of taking strontium ranelate 2 g/day, compared with placebo. Bone mineral density (BMD) increased in the spine by 14% and in the hip by 8% in the strontium group, compared with placebo. The Treatment of Peripheral Osteoporosis (TROPOS) study of 5,091 patients with low hip BMD showed a 39% reduction in vertebral fractures and a 16% reduction in non–vertebral fractures, compared with placebo, over a 3-year period.

A related product, OsteoValin, has strontium carbonate as its main ingredient and is licensed in Europe as a prescription drug to treat osteoporosis. OsteoValin is available in the U.S. over the counter for around $27 for 30 capsules, Dr. Tesar said. Efficacy data, however, are based on only six patients and no control group. In addition, the product is not regulated well enough to ensure its quality and safety.

There is evidence for prevention of bone loss in animals given soy isoflavones, but human data are mixed.

DR. TESAR

► **Soy isoflavones.** Although there is solid evidence for prevention of bone loss in animals given soy isoflavones, human data are mixed, Dr. Tesar said.

A double-blind, randomized, placebo-controlled study of 203 women within a decade of menopause reported in 2005 that high-dose isoflavones (80 mg) produced a mild but significant preservation of hip BMD over 1 year. A separate randomized, placebo-controlled study found that 2 years of soy milk with isoflavones prevented spine bone loss in postmenopausal women. The study concluded that two glasses of soy milk containing 76 mg isoflavones per day prevent lumbar spine bone loss.

► **Vitamin K_2.** Positive evidence comes mainly from Japan, where a vitamin K_2 compound called menatetrenone is standard treatment for osteopenia, Dr. Tesar said. A 2-year study of 241 osteoporotic women reported in 2000 that those taking 45 mg/day of a menatetrenone product called Gla-kay, plus calcium lactate, lost 1% of lumbar spine BMD, compared with a 3% loss in patients taking calcium supplements alone. A separate 2-year study of 172 postmenopausal women found a slight (0.1%) increase in lumbar spine density with vitamin K_2 and a more marked (5%) increase with vitamin K_2 plus vitamin D_3.

► **Tai Chi.** A 1-year study of 34 postmenopausal women in 2002 found generalized bone loss in the 17 women who did 3.5 hours/week of tai chi and in the 17 who did not exercise, but the tai chi group had a lower rate of bone loss. A separate randomized study of 132 menopausal, sedentary women in 2004 also showed a lower rate of bone loss in those who practiced tai chi for 45 minutes a day, 5 days a week, compared with sedentary controls. ■