Calcium, Vitamin D Link to Fractures Questioned

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Recent data challenge the assumption that sufficient levels of calcium and vitamin D are fundamental in preventing and treating osteoporotic fracture, Eric S. Orwoll, M.D., said at a meeting on osteoporosis sponsored by the University of California, San Francisco.

Calcium absorption and vitamin D levels decline with age. A number of studies over the years have solidified the idea that calcium and vitamin D supplements are effective and important in preventing osteoporosis and fractures, said Dr. Orwoll, professor of medicine at Oregon Health and Science University, Portland.

A large, well-designed study stirred up controversy when results indicated that there were no differences in the rates of repeat fractures among 5,292 patients with a previous fracture who took either calcium, vitamin D (800 IU per day), or calcium and vitamin D for nearly 5 years. By 2 years into the Randomized Evaluation of Calcium or Vitamin D (RECORD) trial, only 55% of patients were still taking the calcium and vitamin D tablets, he noted.

"This is more a compliance issue than an efficacy trial, but it's in the real world," he said. Analysis of various subgroups could find no effects on fracture rates from the supplements.

The results contradict earlier findings. A 2003 study of 2,686 people aged 65-85 years who were vitamin D deficient found a 22% lower rate of fractures after 5 years in those who took oral vitamin D (100,000 IU every 4 months), compared with those who took placebo. A 2004 metaanalysis of five randomized, controlled trials of vitamin D for people older than 60 years found a 30% lower risk of falls in those taking vitamin D.

A 2005 metaanalysis of seven randomized trials of vitamin D supplementation containing 9,820 participants each showed that people taking higher doses (700-800 IU/day) of vitamin D had lower rates of hip fractures or any nonvertebral fractures, compared with participants who took 400 IU/day. Nearly all studies included calcium supplements (JAMA 2005;293:2257-64).

Differences between the RECORD trial and earlier trials may account in part for the conflicting findings, Dr. Orwoll said. In an earlier trial in France, 800 IU/day of vitamin D significantly reduced fracture risk, compared with placebo, in frail, elderly patients with a mean age of 85 years all of whom resided in group housing and had very low baseline levels of calcium and vitamin D (Osteoporosis Int. 2002;13:257-64).

Patients in the RECORD trial were a bit younger (mean age 77 years), had somewhat higher baseline levels of calcium and vitamin D, and were home-dwelling instead of institutionalized. "So calcium and vitamin D might show the most robust effect in the frailest patients," he suggested.

Whether or not calcium and vitamin D supplements reduce fracture risk, and in which patients, remains to be seen, but they are necessary for maintaining bone mass and muscle function, Dr. Orwoll said. Most adults don't get enough calcium and vitamin D, and current recommendations on adequate vitamin D levels are too low, he added.

The Institute of Medicine in 1997 recommended vitamin D doses of 200 IU/day for adults aged 31-50 years, 400 IU/day for ages 51-70, and 600 IU/day for older people.

A serum level of 30-35 ng/mL of 25-hydroxyvitamin D (25[OH]D) is possibly ideal for maximizing GI absorption of calcium and to avoid elevated parathyroid levels, Dr. Orwoll noted. A recent poll of six experts suggested that much higher doses of vitamin D supplements are needed. The experts said that 1,000-1,600 IU/day vitamin D would be needed to reach serum levels of 30-32 ng/mL 25(OH)D.

"We've all had this mind-set that vitamin D is this toxic compound," Dr. Orwoll said. "The point is to liberalize your idea of how much to recommend." Some physicians are even suggesting that 3,000-4,000 IU/day might be appropriate, he added.

Vitamin D and calcium supplements are inexpensive and safe, so there's little reason not to use them, he said. Recommended daily calcium requirements are scientifically reasonable, even though they're based more on physiologic data than on clinical outcome studies.

Institute of Medicine guidelines in 1997 recommended calcium doses of 1,000 mg/day for adults aged 25-50, 1,200 mg/day for older adults, and 1,000-1,300 mg/day for pregnant or lactating women.

Vitamin D supplementation should be at least 800-1,000 IU/day, Dr. Orwoll said. For pure nutritional inadequacy, it may be appropriate to treat with a loading dose of 50,000 IU per week for 2 months followed by 1,000 IU/day, depending on baseline vitamin D levels, he suggested. Vitamin D deficiency due to malabsorption or increased catabolism may require doses as high as 100,000 IU/day.

Lab analyses of vitamin D in serum samples can vary widely, he cautioned. "I would tend to use a well-established reference lab rather than, say, a local lab that doesn't have as much experience with it," he said. ■

Dietary Supplements Had No Impact on Preventing Second Fractures, Study Shows

BY DOUG BRUNK
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Routine dietary supplementation with oral calcium and vitamin D3, either alone or in combination, had no impact on reducing the incidence of low-trauma secondary fractures in patients aged 70 years and older, a large randomized trial demonstrated.

The findings run counter to the conclusions of at least four published prevention trials, but "our study population was younger and less frail [than theirs] … and most were mobile and living in the community," wrote the investigators, whose primary author was Adrian M. Grant, M.D., of the University of Aberdeen (Scotland). "Therefore, the participants in our trial might have been less likely to have vitamin D insufficiency and secondary hyperparathyroidism than those in the [other] trials."

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The investigators enrolled 5,292 patients aged 70 and older who were mobile before developing a low trauma fracture. They randomized the patients to one of four groups—800 IU daily oral vitamin D, 1,000 mg calcium, oral vitamin D combined with calcium, or placebo—and followed them for a median of 45 months (Lancet 2005;365:1621-8).

Every 4 months, study participants were asked via mailed questionnaire how many times in the last 7 days they had taken their tablets. They were also asked about general health status, hospital admission, falls, and possible adverse events. The investigators obtained information on further fractures and death from the questionnaires, from hospital staff, family and friends of study participants, and from national health statistics. Additional confirmation of radiologically confirmed fractures was sought from a second source.

The mean age of patients was 77, and most (85%) were women.

Of the 5,292 patients, 698 (13%) sustained a new low-trauma fracture. Of these, 183 (26%) were hip fractures.

Investigators observed no significant differences in the incidence of new, low-trauma fractures between patients who received calcium vs. those who did not (12.6% vs. 13.7%, respectively); between those who received vitamin D3 vs. those who did not (13.3% vs. 13.1%, respectively) or between patients who received combination treatment and those who received placebo (12.6% vs. 13.4%).

There were also no differences between the groups in terms of the incidence of all new fractures, fractures confirmed by radiography, hip fractures, death, number of falls, or quality of life.

The investigators concluded that the best pharmaceutical intervention to prevent secondary low-trauma fractures in the elderly is with "antiresorptive drugs, such as bisphosphonates, which have rarely been assessed in patients who have not been taking calcium or vitamin D," they wrote. "This trial was not designed to directly address whether supplementation should be used as a primary-prevention measure or in those who live in a care-home environment. Clarification of the role of supplementation in these settings awaits the results of other trials." ■

Osteoporosis Specialists Vary in Diagnosis, Tx

WASHINGTON — Endocrinologists and rheumatologists are the most aggressive specialists when it comes to the screening, diagnosis, and treatment of osteoporosis, Tiffany Karas, M.D., and her associates reported in a poster at the annual meeting of the American Association of Clinical Endocrinologists.

Of 122 physicians who responded to an electronic survey, there were 27 geriatricians, 25 endocrinologists, 23 obstetrician/gynecologists, 20 rheumatologists, 19 primary care physicians, and 8 orthopedic surgeons. In screening for osteoporosis, 94% of the entire group said they would order a dual-energy x-ray absorptiometry (DXA) scan for a patient with two or more risk factors, said Dr. Karas and her associates, of Loyola University Medical Center, Maywood, Ill.

The risk factors most likely to prompt DXA scanning were height loss (93%), chronic prednisone use (89%), and menopause (86.6%). Among the risk factors least likely to prompt DXA were low testosterone (60%) and vertebral deformities (74%) in an elderly male patient. In general, all physicians surveyed were much less likely to order DXA for men with indications than for women. "This is one area where continuing education about osteoporosis may improve patient care," the investigators noted.

Endocrinologists and rheumatologists were more likely to order DXA given any risk factor or patient scenario than were other specialties, while orthopedic surgeons were least likely. Rheumatologists were the most likely to initiate treatment in patients, followed by endocrinologists, geriatricians, primary care physicians, and ob.gyns.

Alendronate and risedronate were deemed the most efficacious treatments by more than 98% of all physicians, while calcium/vitamin D and calcitonin were thought to be the least efficacious. Overall, patients were more likely to be screened, diagnosed, and treated for osteoporosis by female physicians who had been in practice more than 6 years and who practice in urban, academic settings, Dr. Karas and her associates reported.

—Miriam E. Tucker