Guidelines Suggest Doubling Kids' Daily Vitamin D Dosage

BY DIANA MAHONEY
New England Bureau

BOSTON — All children should get at least 400 IU of vitamin D daily, either through dietary intake or supplementation, beginning within days of birth and continuing through adolescence.

New guidelines from the American Academy of Pediatrics double its 2003 vitamin D intake recommendation in an effort to prevent the development of rickets in specific pediatric populations and take advantage of the potential long-term health benefits associated with adequate intake of the fat-soluble nutrient, Dr. Frank Greer, chairman of the academy's National Committee on Nutrition and coauthor of the report, said at the AAP's annual meeting.

The higher daily supplementation should begin soon after birth and is aimed at preventing rickets and capitalizing on the vitamin's possible long-term benefits.

The new guidelines are "logical" amid continued reports of rickets in infants and adolescents in the United States and mounting clinical evidence that 200 IU a day may not sufficiently prevent deficiency-related conditions, said Dr. Greer, professor of pediatrics at the University of Wisconsin, Madison.

Increasing evidence in the adult literature has also implicated vitamin D in the prevention of infection; autoimmune diseases; some forms of cancer; osteoporosis; and type 2 diabetes.

The 2003 guidelines suggested vitamin D supplementation primarily for babies who were breastfed exclusively, with the belief that most other children would be able to meet the 200-IU/day recommendation through normal diet and milk consumption. But, Dr. Greer said, "now that we're at 400 IU, we are strongly recommending supplementation across the board because the presence of vitamin D as a natural ingredient in food in most diets is limited."

Specific points in the guidelines include:

▶ Breastfed and partially breastfed babies should be supplemented with 400 IU of vitamin D daily beginning in the first few days of life.

▶ Infants and children who consume less than one quart of vitamin D–fortified formula or milk daily should receive a 400-IU supplement.

▶ Adolescents who do not get 400 IU of vitamin D through diet should take a daily supplement of that amount.

▶ Children at increased risk of vitamin D deficiency, such as those with chronic fat malabsorption and those taking certain antiseizure medications, may require higher doses of vitamin D.

African American babies are at particularly increased risk for vitamin D deficiency because dark skin pigmentation interferes with the penetration of ultraviolet light and with vitamin D production.

Adolescents, whose intake of vitamin D–fortified milk and vitamin D–rich foods such as fatty fish is generally insufficient, are also at risk. "It's not clear, especially in adolescents, whether 400 IU of vitamin D is enough … but we're concerned about recommending more than 400 IU because of the likelihood that vitamin D is going to start showing up in all sorts of foods, thanks to the [Food and Drug Administration's] allowance of qualified health care claims on food packaging," Dr. Greer said, "Vitamin D is a prohormone that acts directly on cells to promote gene transcription. It's a powerful nutrient, so we have to be careful."

The guidelines will be published in the November issue of Pediatrics (2008;122:1142-52).

Dr. Greer reported no conflicts of interest with respect to his presentation. ■

Greater Loss of Bone Density Seen in Men With Diabetes

BY JEFF EVANS
Senior Writer

MONTREAL — Loss of bone mineral density over time appears to be more severe in older men with type 2 diabetes than in older men without diabetes, even though men with diabetes have higher average bone mineral density at baseline.

Data from 4 years of follow-up from a prospective study showed that fractures are more likely to occur in older adults with type 2 diabetes than in euglycemic older adults, even though studies have reported that those with type 2 diabetes have 4%-5% higher bone mineral density (BMD) after adjustment for total lean and fat mass. Higher bone loss has been especially noted in older white women with diabetes, especially in those using thiazolidinediones (TZDs), Elsa S. Strotmeyer, Ph.D., said at the annual meeting of the American Society for Bone and Mineral Research.

Dr. Strotmeyer and her associates based their investigation on men in the Osteoporotic Fractures in Men (MrOS) study, which involved osteoporosis screening initially in 2000-2002 and a follow-up exam 4 years later of 5,995 ambulatory, community-dwelling men older than 65 years. The researchers examined dual x-ray absorptiometry exams from 4,094 of these men, who had a mean age of 73 years. Most of them were white (91%), and some had type 2 diabetes (14%) or impaired fasting glucose (IFG, 37%).

Men with diabetes had higher mean BMD at baseline (0.986 g/cm^2) than did men with IFG (0.963 g/cm^2) or normal fasting glucose (0.947 g/cm^2). At the end of the follow-up period, men with diabetes still had a greater mean level of BMD at the femoral neck than did the other men. But during the study period, men with diabetes lost a significantly greater mean amount of lean mass (2.8 kg) than did men with either IFG (1 kg) or normoglycemia (gain of 1.5 kg). At follow-up, there were no differences in fat mass between the groups, said Dr. Strotmeyer of the center for aging and population health in the department of epidemiology at the University of Pittsburgh.

Despite their greater overall mean BMD, men with diabetes experienced a significantly greater annual decline in BMD at the femoral neck than did the other men. This yearly decrease (–0.562%) occurred at nearly twice the rate seen in men with IFG (–0.313%) or normal fasting glucose (–0.325%).

At the end of follow-up, the bone area of men with diabetes had increased significantly more than in the other men. The men with diabetes also showed a greater loss of bone mineral content, although there was not a statistically significant difference among the groups. This meant that men with diabetes with the lowest bone area at baseline actually had the greatest gain in bone area during the study.

The study received funding from several institutes in the National Institutes of Health. ■

Benefits Outweigh Lasofoxifene's Risks in Select Women

BY ELIZABETH MECHCATIE
Senior Writer

ROCKVILLE, MD. — The majority of a federal advisory panel agreed that the benefits of treatment with lasofoxifene, a selective estrogen receptor modulator, would likely outweigh the risks in some postmenopausal women with osteoporosis.

The Food and Drug Administration's Advisory Committee for Reproductive Health Drugs voted 9-3 (with 1 abstention) that there was a population of postmenopausal women with osteoporosis for whom the benefit of treatment would likely outweigh the risks. Most panelists supported limiting the drug's use to women who are at high risk for fractures but cannot tolerate bisphosphonates.

Dr. Diane Merritt, professor of obstetrics and gynecology at Washington University, St. Louis, said she believed there was a use for lasofoxifene, but that it would be important for physicians who prescribe the drug to appropriately counsel the patient about the associated risks.

Voting no on the risk-benefit question, Dr. Lawrence Nelson, head of the Unit on Integrative Reproductive Medicine at the National Institute of Child Health and Human Development, said that because there was still an open question about greater all-cause mortality in women on the lower dose of lasofoxifene, he found it difficult to identify a group of women to whom he would prescribe this drug. In studies, all-cause mortality was greater in women on the lower dose of lasofoxifene studied, compared with those on the higher dose and those on placebo.

Pfizer Inc. has proposed that lasofoxifene, at a dosage of 0.5 mg per day, be approved for treating osteoporosis in postmenopausal women who are at increased risk of fracture.

In a prospective, double-blind, randomized study of 8,556 postmenopausal women at increased risk of fracture, two doses (0.25 mg per day or 0.5 mg per day) of lasofoxifene were compared with placebo.

The risk of developing a new or worsening radiographic vertebral fracture within 3 years—the study's primary end point—was significantly reduced in the women who were treated with both doses of lasofoxifene, compared with those on placebo. The cumulative relative risk of developing a new or worsening radiographic vertebral fracture through the third year of treatment was reduced by 27% in those on the 0.25-mg dose and by 41% in those on the 0.5-mg dose, compared with placebo.

Within the 3 years of starting treatment, nearly 5% of those on the 0.25-mg dose and nearly 4% of those on the 0.5-mg dose developed a new or worsening radiographic vertebral fracture, compared with 6.4% of those on placebo.

The FDA asked the panel to consider several safety issues associated with the drug that were raised in the study: a numerical increase in all-cause mortality in those treated with 0.25 mg; an increase in venous thromboembolic events (VTEs), particularly pulmonary emboli (PEs); and a significant increase in gynecologic adverse events, including increased endometrial thickness, increased vaginal bleeding, and increased uterine-related procedures.

The majority of the panel (seven panelists) said that they could not determine whether the data regarding all-cause mortality reflected a real increase in mortality in those treated with lasofoxifene; four said they did not believe this was a real increase. The study was extended to 5 years, at which time the all-cause mortality rate was 3.2% (90 women) among those on the 0.25-mg dose, compared with 2.6% (73 women) among those on the 0.5-mg dose (the proposed dose) and 2.3% (65 women) among those on placebo. The causes of death that were more common among those on lasofoxifene were cancer (cancers of the brain, lung, and GI tract) and stroke. (At 5 years, the rate of fatal stroke was 0.4% among those on the 0.25-mg dose and 0.2% among those on the higher dose and those on placebo.)

The all-cause mortality rate was also higher among the women on 0.25 mg in the overall phase II/III program for the drug.

The FDA usually follows the recommendations of its advisory panels. If approved, Pfizer will market lasofoxifene under the trade name Fablyn. Raloxifene, another FDA-approved SERM, is approved for osteoporosis indications. ■