Data Don't Support High-Dose Vitamin D Intake

BY SHARON WORCESTER

EXPERT ANALYSIS FROM THE CONGRESS OF CLINICAL RHEUMATOLOGY

DESTIN, FLA. – More is not necessarily better when it comes to vitamin D.

"The optimal intake and blood levels are probably much more moderate than many have led us to believe," Dr. JoAnn E. Manson said.

As a member of the 14-person Institute of Medicine Committee charged with developing a recently published report on dietary reference intakes of vitamin D and calcium, Dr. Manson assisted in a "rigorous comprehensive review" of more than 1,000 studies, and while many researchers and clinicians have argued that people need much higher levels than the 400-800 IU/day intake (depending on age) recommended by the IOM to promote optimal health, the available evidence simply has not borne that out, said Dr. Manson, professor of epidemiology at Harvard University and chief of the division of preventive medicine at Brigham and Women's Hospital, Boston.

Although some IOM report naysayers advocate for levels up to 6,000 IU/day – and the lay press is replete with stories touting vitamin D as a panacea, it is actually very difficult to find any solid data showing increased benefit with higher doses, she said.

In fact, the committee's findings indicate that adequate intake for infants through age 12 months is 400 IU/day, and that the Recommended Dietary Allowance for individuals aged 1-70 years should be at least 600 IU/day, and in those over age 70 years it should be 800 IU/day. The upper intake levels are 1,000 and 1,500 IU/day for those ages 0-6 months and 6-12 months, respectively, 2,500 IU/day for those ages 1-3 years, 3,000 IU/day for those ages 4-8 years, and 4,000 IU/day for those over age 8 years, according to the IOM report (J. Clin. Endocrinol. Metab. 2011;96:53-8).

These minimum levels represent the intake needed to meet the vitamin D requirements of 97.5% of the population, and correspond to a serum 25-hydroxyvitamin D [25(OH)D] level of 20 ng/mL, which the data indicate is the optimal level. At levels above the upper intake level, which correspond to a serum 25-OHD level of about 50 ng/mL, adverse effects have been reported, Dr. Manson said.

Emerging evidence suggests excess intake may be associated with increased all-cause mortality, cancer, cardiovascular disease, falls, and fractures, she noted.

National Health and Nutrition Examination Survey (NHANES) data from 2008 showed that age-adjusted mortality was highest among those with serum 25(OH)D levels below 19 ng/mL in African Americans and below 27.5 ng/mL in the entire cohort, and that mortality decreased with increasing levels – but only to a certain point. At levels in the 50 ng/mL range for African Americans, and above 85 ng/mL in the entire cohort, mortality increased steadily.

Data on the effects of vitamin D on skeletal health, which provided the strongest basis for the IOM committee's report as they were most plentiful and convincing in terms of showing cause and effect (although evidence regarding numerous other diseases such as cancer, diabetes, and more were also considered), also suggest that too much vitamin D can lead to adverse effects. Women's Health Initiative findings, for example, show that adjusted hip fracture rates are highest among those with serum 25(OH)D levels of 19.04 ng/mL and those greater than 28.3 ng/mL, and lowest among those between these levels (Ann. Intern. Med. 2008;149:242-50), she said.

In older men in the Osteoporotic Fractures in Men (MrOS) study, the adjusted risk of hip fractures was shown to be highest in those with serum 25(OH)D levels less than 19 ng/mL (odds ratio 2.36, compared with those with levels greater than 28 ng/mL), with risk declining steadily in those with levels up to 28 ng/mL (J. Bone Miner. Res. 2010;25:545-53).

The skeletal benefits of vitamin D are dependent on adequate calcium intake, which the committee determined is 200 and 260 mg/day for those aged 0-6 and 6-12 months, respectively; 700 mg/day for those aged 1-3 years; 1,000 mg/day for those aged 4-8 years, 19-70 years, and for women aged 19-50 years who are pregnant or lactating; 1,200 mg/day for those aged 51 years and older; and 1,300 mg/day for those aged 9-18 years, and for women aged 14-18 years who are pregnant or lactating.

An Agency for Healthcare Research and Quality report in 2009 showed that three randomized controlled trials indicated no significant effect of vitamin D alone on fracture risk, but that one randomized controlled trial showed a benefit in those who received 800 IU of vitamin D_3 plus 1,200 mg/day of calcium for 2 years (OR of fractures 0.80), she said.

Dr. Manson has funding from the National Institutes of Health to conduct a large-scale randomized trial of vitamin D and omega-3 fatty acids. ■

Vitamin D Screening Not Needed for Most Healthy Folks

BY KERRI WACHTER

FROM THE ANNUAL MEETING OF THE ENDOCRINE SOCIETY

BOSTON – Healthy individuals do not need to be screened for vitamin D deficiency, according to guidelines from the Endocrine Society.

"That's an important message. So we're recommending screening for those at risk for vitamin D deficiency – those who are obese, African Americans, pregnant and lactating women, patients with malabsorption syndromes, and a whole list that we have provided in the guidelines," lead author Dr. Michael F. Holick said at the meeting.

Dr. Holick headed a task force appointed by the clinical guidelines subcommittee of the Endocrine Society to formulate evidence-based recommendations on vitamin D deficiency. The subcommittee deemed vitamin D deficiency a priority area in need of practice guidelines.

The task force recommended that those at risk for vitamin D deficiency be screened by measuring serum 25-hydroxyvitamin D levels using a reliable assay. Causes of vitamin D deficiency include obesity, fat malabsorption syndromes, bariatric surgery, nephrotic syndrome, a wide range of medications (anticonvulsants and anti-HIV/AIDS drugs), chronic granuloma-forming disorders, some lymphomas, and primary hyperthyroidism.

The guidelines were released at the meeting and will be published in the July issue of the Journal of Clinical Endocrinology & Metabolism (doi: 10.1210/jc.2011-0385).

The guidelines provide long-awaited recommendations on vitamin D intake and the diagnosis and treatment of vitamin D deficiency.

Physicians have struggled for years to delineate how much vitamin D is necessary for different clinical groups, how to measure it, and how best to supplement deficiencies.

'In the absence of unprotected sun exposure, it is difficult if not impossible to obtain an adequate amount of vitamin D from dietary sources.'

The task force commissioned two systematic reviews of the literature to inform its key recommendations and followed the approach recommended by GRADE, an international group with expertise in development and implementation of evidence-based guidelines.

"All available evidence suggests that children and adults should maintain a blood level of 25(OH)D above 20 ng/mL to prevent rickets and osteomalacia, respectively. However, to maximize vitamin D's effect on calcium, bone, and muscle metabolism, the 25(OH)D blood level should be above 30 ng/mL," the group wrote.

In the new guidelines, vitamin D deficiency is defined as a 25(OH)D concentration less than 20 ng/mL (50 nmol/L). The task force suggests:

- Infants aged 0-1 year require at least 400 IU/day (IU = 25 ng) of vitamin D to maximize bone health.
- Children 1 year and older require at least 600 IU/day.
- Adults aged 19-50 years require at least 600 IU/day.
- Adults aged 50-70 years require at least 600 IU/day.
- Adults 70 years and older require 800 IU/day.
- Pregnant and lactating women require at least 600 IU/day.

The task force also recommends that obese children and adults and children and adults on certain medications (anticonvulsant medications, glucocorticoids, antifungals such as ketoconazole, and medications for AIDS) be given at least 2-3 times more vitamin D for their age group to satisfy their bodies' vitamin D requirements. Either vitamin D_2 or vitamin D_3 can be used for the treatment and prevention of vitamin D deficiency.

The group recommends that adults who are vitamin D deficient be treated with 50,000 IU of vitamin D_2 or vitamin D_3 once a week for 8 weeks or its equivalent of 6,000 IU of vitamin D_2 or vitamin D_3 daily to achieve a blood level of 25(OH)D greater than 30 ng/mL.

This should be followed by maintenance therapy of 1,500-2,000 IU/day.

The task force also recommends vitamin D supplementation for fall prevention. "We know that there is sufficient evidence to give vitamin D for fall prevention. It's well documented that vitamin D is very important for muscle strength," said Dr. Holick, professor of medicine, physiology and biophysics at Boston University.

However, the group does not recommend prescribing vitamin D supplementation beyond recommended daily needs for the purpose of preventing cardiovascular disease or death or improving quality of life, because there is insufficient evidence.

The task force noted that most individuals do not get adequate vitamin D for a number of reasons. In particular, "there needs to be an appreciation that unprotected sun exposure is the major source of vitamin D for both children and adults and that in the absence of sun exposure it is difficult, if not impossible, to obtain an adequate amount of vitamin D from dietary sources without supplementation to satisfy the body's requirement. Concerns about melanoma and other types of skin cancer necessitate avoidance of excessive exposure to midday sun," they wrote.

The guidelines are cosponsored by the Canadian Society of Endocrinology and Metabolism and the National Osteoporosis Foundation.

All but one of the authors reported having significant financial relationships with pharmaceutical companies, medical organizations and/or food industry groups. ■