An Update on Vitamin D From ANA

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"D" is for Dilemma: Two Vitamin Guidelines, Two Recommendations

Abstract

Also, as a key part of this review, we have included the following: Dietary Reference Intakes for Calcium and Vitamin D, Institute of Medicine of the National Academies. National Academic Press. Washington, DC. Available at: http://books.nap.edu/openbook.php?record_id=13050

Background

Many adults are deficient in vitamin D, placing them at elevated risk for fracture. But what is the ideal way to prevent this deficiency? And does the method used matter in terms of health outcomes? Osteoporosis Canada recently reviewed these issues and offers bold new recommendations for vitamin D supplementation. But their recommendations are quite different from those by the Institute of Medicine.

Vitamin D is important in the prevention of disease, but the degree of benefit associated with vitamin D is a matter of debate. Although the most obvious role of vitamin D is maintenance of bone health, research has suggested that it may also be important as a means to prevent cancer and falls among older adults. Moreover, many adults lack adequate levels of vitamin D. Recognizing this significant public health issue, Osteoporosis Canada recently released its recommendations for the assessment and management of vitamin D deficiency.

Vitamin D deficiency is more common than many physicians might believe. In a clinically relevant population of postmenopausal women, the prevalence of vitamin D deficiency was as low as 1.6% among

community-dwelling women to as high as 86% among institutionalized women.[1] Significant vitamin D deficiency was present in up to 76% of women with osteoporosis and 50%-70% of women with a history of fracture.

One of the challenges of reducing vitamin D deficiency across populations is determining the most appropriate source of the hormone. Most adults get the majority of their vitamin D stores from exposure to ultraviolet B radiation from the sun. This results in considerable variability in serum vitamin D levels among adults based on climate, latitude, and skin pigmentation. As a rough guide, the authors note that a young white person needs approximately 4 minutes of direct exposure to sunlight on the arms and legs to generate approximately 1000 IU of vitamin D3.

The fact that sunlight is the principal source of vitamin D creates a conflict for patients, particularly those with light skin: How to get enough sunlight to promote higher levels of vitamin D without increasing the risk for skin cancer? No clear consensus exists on this issue. One means to mitigate the potentially harmful effects of sunlight is the use of sunscreen. Although some research has suggested that sunscreen reduces the synthesis of vitamin D, a randomized trial of 113 Australian citizens found that serum levels of 25-hydroxyvitamin D3 (25-OH-D) increased by similar amounts over 1 summer whether sunscreen or a placebo was used.[2]

Current Trial and Other Studies on Vitamin D

The review from Osteoporosis Canada reminds physicians that measuring serum 25-OH-D is the best way to evaluate a patient's level of vitamin D. However, this measurement may not be appropriate for patients with abnormalities of calcitriol synthesis, such as sarcoidosis. Moreover, the assays that measure 25-OH-D vary among laboratories, and physicians should keep this in mind when evaluating readings from different laboratories.

Who should be tested for vitamin D deficiency? The current recommendations do not advocate widespread screening among patients without osteoporosis or diseases that could interfere with vitamin D metabolism. The optimal serum level of 25-OH-D is debatable, but seems to be between 75 and 80 nmol/L. Vitamin D deficiency is usually defined by levels less than 25 nmol/L.

Among patients treated with oral vitamin D supplements, serum levels can be expected to plateau after 3-4 months. Therefore, among patients with osteoporosis, it is reasonable to check 25-OH-D levels at baseline and 3 months after initiation of vitamin D supplementation.

The record of clinical efficacy of vitamin D supplements in the prevention of disease is mixed. In the Women's Health Initiative (WHI), supplementation with calcium carbonate 1000 mg plus vitamin D3 400 IU daily improved bone mineral density at the hip but did not significantly affect the risk for fracture over a

mean follow-up of 7 years.[3] However, women in the supplementation group had a 17% increase in the risk for renal calculi.

The WHI trial has been criticized for using a dose of vitamin D that was too low. Indeed, a meta-analysis demonstrated that doses of vitamin D at 700-800 IU daily reduced the risk for hip fracture by 26% and any nonvertebral fracture by 23% compared with either calcium supplements or placebo.[4] By contrast, the dose of 400 IU was not effective for fracture prevention.

Higher levels of vitamin D also seem to reduce the risk for falls, possibly by improving muscle strength. In a meta-analysis of 5 randomized trials involving a total of 1237 participants, vitamin D supplements reduced the risk for falling by 22% compared with calcium or placebo.[5] Although the dose of vitamin D did not seem to affect the main study result, the demographics of the included research meant that the conclusion was only significant for women.

Vitamin D has also received a significant amount of attention regarding its relationship to cancer. In the WHI cohort, the rate of colorectal cancer was the same whether the women were assigned to calcium and vitamin D supplements or to placebo.[6] Overall, although epidemiologic studies have suggested that lower serum markers of vitamin D are associated with a higher risk for colon cancer, intervention studies have mixed results regarding the ability of vitamin D supplements to reduce the risk for this disease.[7]

The authors from Osteoporosis Canada synthesize these themes into recommendations for vitamin D supplementation at significantly higher doses than those of previous guidelines. Overall, they believe that exposure to sunlight and dietary intake are insufficient to maintain 25-OH-D at recommended levels among most Canadians and offer the following recommendations for vitamin D supplementation:

- Low-risk individuals are adults younger than 50 years without comorbid conditions. Supplementation should consist of 400-1000 IU daily. There is no need to monitor 25-OH-D levels during treatment of these individuals.
- Moderate-risk individuals are adults older than 50 years with or without osteoporosis. These persons should take 800-2000 IU daily. Levels of 25-OH-D should be measured after 3-4 months of treatment, and the vitamin D dosage may be titrated upward if levels are insufficient.
- High-risk individuals are those who have recurrent fractures or bone loss despite treatment for osteoporosis. Levels of 25-OH-D should guide treatment for these patients, who may require vitamin D supplements at dosages exceeding 2000 IU daily.

Vitamin D3 is the preferred supplement for adults. Calcitriol has a narrow safety index and should not be used for routine supplementation.

Discussion

These recommendations are built on evidence and take into account important variables, such as the differential synthesis of vitamin D across the population and the aging of the population as a whole. Although they advocate more aggressive supplementation with vitamin D than what is currently recommended, Osteoporosis Canada's guidelines seem reasonable.

It is therefore remarkable how these recommendations differ from those of the Institute of Medicine.[8] The Committee to Review Dietary Reference Intakes for Vitamin D and Calcium evaluated over 1000 studies and considered the full potential of vitamin D to improve health and decided that there was little to recommend supplementation with calcium and vitamin D other than maintenance of bone health. The evidence for vitamin D in the prevention of other health outcomes, such as falls and cancer, was considered mixed and inconclusive.

The Committee was not only less enthusiastic regarding the benefits of vitamin D, but they were also more sanguine about the potential epidemic of vitamin D deficiency in North America. Even among persons with minimal sun exposure, they recommend supplementation at a dose of 400 IU per day, with a dose as high as 800 IU reserved for persons 71 years and older.

However, the Committee also notes that the risk for harms in vitamin D supplementation do not increase until the dose surpasses 4000 IU per day. And this wide range of doses, from 400-4000 IU daily, allows physicians and patients to follow their own conclusions regarding the best dose of vitamin D supplementation. Some physicians will examine the evidence for themselves, conclude that vitamin D levels seem to be important determinants in a number of health outcomes, and recommend high-dose supplementation with vitamin D. Other physicians will agree that the evidence regarding the efficacy of vitamin D supplementation in preventing disease unrelated to bone health is mixed, and they may recommend less aggressive supplementation. There does not seem to be a single correct answer when it comes to vitamin D, but the broad safety index of these supplements allows room for physicians to follow more aggressive or conservative approaches to therapy.

Regardless of the treatment decision, it is important that physicians remain aware of vitamin D and its role in health and disease. Patients are monitoring the debates regarding vitamin D and are sure to have questions. It is up to all of us to provide reasonable, albeit possibly divergent, answers.

Clinical Pearls

- Many adults, particularly those at the highest risk for fracture, have evidence of vitamin D deficiency.
- Vitamin D supplements seem to be important in the maintenance of bone health, although doses of 400 IU or less may not be effective in preventing fracture.

- The current guidelines from Osteoporosis Canada call for vitamin D supplementation with 400-1000 IU per day among low-risk adults. There is no need to monitor 25-OH-D levels in these patients.
- The Osteoporosis Canada guidelines also recommend vitamin D supplementation at 800-2000 IU per day among moderate-risk individuals, with possibly higher doses for high-risk individuals.
- The guidelines regarding vitamin D supplementation from Osteoporosis Canada contrast with those from the Institute of Medicine, which recommends a dose of 400 IU daily for most adults.

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