

QUESTION: Which Adults Should be Tested or Treated for Vitamin D Deficiency?

Audra Fox, MD (PGYE) and Shyama Gandhi, MD (PGY2); Cheryl B. Aspy, PhD; James W. Mold, MD, MPH

ANSWER AND LEVEL OF EVIDENCE:

- Sunlight deprived individuals [A]
- Post-menopausal women and others with Glucocorticoid-induced osteoporosis [B]
- Dark-skinned adults, patients with diabetes mellitus, the elderly, those affected by autoimmune and rheumatologic disorders and the morbidly obese [C]

PROGRAM: University of Oklahoma Health Sciences Center, Family Medicine Residency Program, Oklahoma City, OK

SUMMARY OF ISSUES

Once foods were fortified with vitamin D, rickets appeared to have been conquered and many health care professionals thought the major health problems resulting from vitamin D deficiency had been resolved.¹ However, rickets can be considered the tip of the vitamin D-deficiency iceberg. In fact, vitamin D deficiency remains common in children and adults.²⁻⁴ In utero and during childhood, vitamin D deficiency can cause growth retardation and skeletal deformities and may increase the risk of hip fracture later in life. Vitamin D deficiency in adults can cause or exacerbate osteopenia and osteomalacia as well as muscle weakness. It is also associated with other conditions including autoimmune diseases (rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus [SLE], and diabetes mellitus [DM] type I), cardiovascular disease and some types of cancer.⁵ Improved professional guidance is needed regarding when to measure 25-(OH)D, whom to treat without testing, when to retest, and how to interpret test results.

Most experts agree that a serum 25(OH)D of < 20 ng/mL represents overt vitamin D deficiency, and levels of 21-29 ng/mL are considered to be insufficient for optimal metabolism.⁶ The goal should be to maintain both children and adults at a level > 30 ng/mL to take full advantage of all the health benefits that vitamin D provides. However, the assays used by different laboratories show significant variability. For example, one commonly used lab assay (from Nichols) significantly underestimates the amount of vitamin D₂ derived from dietary and pharmaceutical sources. (Vitamin D₃ is mainly derived from the action of ultraviolet light on the skin.) A vitamin-D assay that accurately identifies both D₂ and D₃ components of 25-hydroxyvitamin D should therefore be used.

Multiple preparations of vitamin D and its metabolites are available. Two commonly available forms are: cholecalciferol (D₃) and ergocalciferol (D₂). Some studies suggest that vitamin D₃ increases serum 25(OH)D more efficiently than does vitamin

D₂. Cholecalciferol is available in 400, 1000, 5000 and 50,000 IU capsules and Ergocalciferol in 400 and 50,000 IU capsules. Calcitriol (1, 25 dihydroxyvitamin D), which is available in 0.25 and 0.5 mcg capsules, is most useful in patients with liver disease. Dihydrotachysterol (DHT), available in 0.124, 0.2, and 0.5 mg tablets, has a rapid onset and a relatively short duration of action, and is most useful in chronic renal failure or in type I vitamin D dependent rickets.

SUMMARY OF EVIDENCE

Sunlight-deprived individuals - Sunlight exposure increases serum 25-OHD levels by increasing vitamin D receptor levels especially after UVB exposure. Hospitalized, rehabilitation center, and long-term care facility patients, elderly patients with Alzheimer's disease, stroke patients and immigrants often have inadequate exposure to sunlight.

In a randomized, controlled trial, Alzheimer's disease patients were assigned to regular sunlight exposure (n=132) or sunlight deprivation (n=132) and followed for one year. Serum 25(OH)D level increased by 2.2 fold in sunlight-exposed group. Eleven patients sustained fractures in the sunlight-deprived group, and three fractures occurred among sunlight-exposed group (p=0.0362; odds ratio=3.7).⁷ Another 12-month randomized trial of stroke patients concluded that sunlight exposure can increase the bone mineral density of vitamin D deficient bone by increasing 25-OHD concentration.⁸ [A]

Glucocorticoid-induced osteoporosis - Active vitamin D₃ analogues not only preserve bone during glucocorticoid therapy more effectively than no treatment (placebo), plain vitamin D₃, and/or calcium, but are also more effective in decreasing the risk of vertebral fractures.

A meta-analysis of 54 articles was performed to determine if there is evidence for using activated forms of vitamin D₃ to treat or prevent glucocorticoid-induced osteoporosis, and to compare the effect of active vitamin D₃ metabolites with other anti-osteoporosis therapies. Studies concluded that active vitamin D₃ analogues helped preserve bone during glucocorticoid therapy. For example, when bone mineral density was compared across treatments, the pooled effect size of active vitamin D₃ analogues compared with no treatment, placebo, plain vitamin D₃ and/or calcium was 0.35 (95% confidence interval, 0.18, 0.52). Compared with bisphosphonates, the pooled effect size was -1.03 (95% CI -1.71, -0.36). The pooled estimate of the relative risk for vertebral fractures of active vitamin D₃ analogues compared with no treatment, placebo, plain vitamin D₃ and/or calcium was 0.56 (95% CI 0.34, 0.92) and compared with bisphosphonates it was 1.20 (95% CI 0.32, 4.55).⁹ [B]

Post-menopausal women - In a systematic review of publications in the past 10 years reporting prevalence estimates for vitamin D inadequacy, reported as serum 25(OH)D values below various levels, 30 published studies in the English language were identified from January 1994 through April 2004. In post-menopausal women, the prevalence of 25(OH) vitamin D concentrations ≤ 20 ng/ml ranged from 1.6% to 86% for community-living and institutionalized older women, respectively.¹⁰ [B]

Dark-skinned adults - A cross sectional analyses of serum vitamin D levels in 637 participants in Southern Arizona concluded that despite residing in a region with high chronic sun exposure, adults are commonly (42% in black women age-15-49) deficient in vitamin D, particularly blacks and Hispanics.¹¹ [C]

Diabetes mellitus - Evidence from trials with vitamin D and/or calcium supplementation suggests that combined vitamin D and calcium supplementation may have a role in the prevention of DM type 2 in populations at high risk (i.e., glucose intolerance). The available evidence is limited because most studies were cross-sectional and did not adjust for important confounders, whereas intervention studies were short in duration, included few subjects, used a variety of formulations of vitamin D and calcium, or did *post hoc* analyses. Observational studies show a relatively consistent association between low vitamin D status, calcium or dairy intake, and prevalent DM type 2 or metabolic syndrome. The Odds Ratio (OR, 95% confidence interval) for DM type 2 prevalence was 0.36 (0.16–0.80) among nonblacks for highest vs. lowest 25-hydroxyvitamin D. For metabolic syndrome prevalence, the OR was 0.71 (0.57–0.89) for highest vs. lowest dairy intake.¹² [C]

Elderly - Older people (> 80) in residential care can reduce their incidence of falls if they take a vitamin D supplement for two years even if they are not initially vitamin D deficient. In men and women 65 years of age or older who are living in community, dietary supplementation with calcium and vitamin D moderately reduced bone loss measured in total body over a three-year study period and reduced the incidence of nonvertebral fractures.¹³⁻¹⁴ [C]

Autoimmune and rheumatologic disease - Cross-sectional study including patients fulfilling the American College of Rheumatology criteria for the classification of SLE. Serum 25(OH)D levels at 30 and 10 ng/ml were the cut-off values for vitamin D insufficiency and vitamin D deficiency, respectively concluded that vitamin D insufficiency and deficiency are common (75% patients with vitamin D insufficiency and 15% had vitamin D deficiency) in patients with SLE and are associated with sun avoidance. Hydroxychloroquine prevented vitamin D deficiency. Vitamin D deficiency was related to a higher degree of fatigue. Vitamin D levels were not associated with SLE severity.¹⁵ [C]

Morbid obesity - Hypovitaminosis D with secondary hyperparathyroidism due to low Calcidiol bio-availability should be added to the crowded list of sequelae of morbid obesity. A cross sectional study involving 144 patients was done with 80 patients who had not undergone bariatric surgery and 64 who had undergone surgery. Eighty percent of the patients presented low vitamin D levels and mild secondary hyperparathyroidism. Previous surgery or the presence of diabetes did not influence Calcidiol levels. Corrected serum calcium, phosphorus, alkaline

phosphatase, iPTH and Calcidiol were similar between subjects with and without surgery.¹⁶ [C]

COMMENTS

No specific guidelines or official recommendations regarding who should be tested or treated for vitamin D deficiency are available currently so until more data is available, clinical judgment should be used before testing individuals. If you are more than likely to treat a patient because they fall within one of the above mentioned categories, it is understandable to forgo the test and start the patient on adequate supplementation. However it is evident that more research on vitamin D needs to take place in this regard.

SEARCH TERMS

Vitamin D deficiency, test, screen, English, Humans, Cancer, autoimmune disorders, cardiovascular risk factors, elderly.

INCLUSION AND EXCLUSION CRITERIA

Excluded were articles relating to children, infants, pregnant and lactating women, adults with chronic kidney disease and kidney transplants.

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