FPIN's Clinical Inquiries

Pharmacologic Therapy for Vitamin D Deficiency

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Clinical Inquiries provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/?o=1025).

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Clinical Question

What is the best treatment regimen for vitamin D deficiency?

Evidence-Based Answer

Cholecalciferol (vitamin D_3) supplementation should be used for vitamin D repletion because it may be more effective in preventing nonvertebral fractures. (Strength of Recommendation [SOR]: B, based on subgroup analysis of randomized controlled trials [RCTs].) Cholecalciferol produces higher serum 25-hydroxyvitamin D levels than ergocalciferol (vitamin D_2). Vitamin D therapy may be given daily or weekly with equal effectiveness; the dosage depends on the degree of deficiency. (SOR: C, based on an RCT and cohort study.) The cumulative dosage is more important than dosing frequency, so the choice of daily, weekly, or monthly dosing can be based on patient preference. (SOR: C, based on an RCT.) Vitamin D levels should be rechecked after three months to ensure adequate response. (SOR: C, based on an observational study.)

Evidence Summary

There is no consensus on an adequate vitamin D level, but most experts recommend a level greater than 30 ng per mL (74.88 nmol per L) for optimal musculoskeletal and metabolic health.[1] However, a report from the Institute of Medicine states that a level greater than 20 ng per mL (49.92 nmol per L) is sufficient.[2] Exposure to sunlight corrects some deficiencies, but adequate dosing depends on latitude, skin pigmentation, and age.[1]

TYPE OF SUPPLEMENTATION

A meta-analysis of nine RCTs evaluated 33,265 patients older than 65 years who took vitamin D supplements or placebo (14,470 patients received 482 to 770 IU of cholecalciferol daily, and 2,038 received 800 to 1,000 IU of ergocalciferol daily).[3] After 12 to 84 months of follow-up, cholecalciferol supplementation was associated with a significant reduction in nonvertebral fractures (relative risk [RR] = 0.77; 95% confidence interval [CI], 0.70 to 0.85), but ergocalciferol supplementation was not (RR = 0.90; 95% CI, 0.71 to 1.15).

An RCT of 32 women 66 to 97 years of age who were deficient in vitamin D (levels of less than 25 ng per mL [62.4 nmol per L]) compared a single dose of cholecalciferol (300,000 IU) with an equivalent single dose of ergocalciferol.[4] At 30 days, vitamin D levels in the cholecalciferol group increased by 47.8 ± 7.3 ng per mL (119.31 ± 18.22 nmol per L) compared with 17.34 ± 4.78 ng per mL (43.28 ± 11.93 nmol per L) in the ergocalciferol group ($P < .001$).

ROUTE OF ADMINISTRATION

In the same RCT of 32 vitamin D–deficient participants who received 300,000 IU of cholecalciferol, oral administration increased 25-hydroxyvitamin D levels by 47.8 ± 7.3 ng per mL (119.31 ± 18.22 nmol per L) compared with 15.9 ± 11.3 ng per mL (39.69 ± 28.20 nmol per L) with intramuscular cholecalciferol administration ($P < .001$).[4] A small cohort study of 17 patients showed a 50 percent increase in serum vitamin D levels (independent of dosage) when the supplement was taken with a fatty meal as opposed to on an empty stomach or with a small meal.[5]

DOSAGE

A review of two RCTs on vitamin D repletion concluded that daily oral dosages of 1,160 to 2,200 IU (depending on the degree of defi-

Table 1. Cholecalciferol Dosages for Vitamin D Repletion

Initial serum 25-hydroxyvitamin D level (ng per mL [nmol per L])	Daily oral dosage (IU)	
	Based on Heaney[1]*	Based on van Groningen, et al.[6]*
8 to < 16 (19.97 to < 39.94)	2,200	1,875 to 2,750 (based on 40 × [75–initial serum 25-hydroxyvitamin D level in nmol per L] × body weight in kg)
16 to ≤ 24 (39.94 to < 59.90)	1,800	750 to 1,875
24 to 32 (59.90 to 79.87)	1,160	Up to 750

*—Estimated dosages needed over eight weeks to achieve a serum 25-hydroxyvitamin D level greater than 30 ng per mL (74.88 nmol per L) in a person weighing 154 lb (70 kg).

Information from references 1 and 6.

ciency) are needed to reach and maintain serum levels greater than 30 ng per mL[1] (*Table 1*[1,6]). A prospective cohort study of 208 vitamin D–deficient patients 18 to 88 years of age found that, based on body weight and degree of deficiency, almost equivalent dosages of cholecalciferol were needed to produce a serum level greater than 30 ng per mL.[6]

An RCT of 48 women 73 to 89 years of age compared daily (1,500 IU), weekly (10,500 IU), and monthly (45,000 IU) cholecalciferol repletion therapy with the same cumulative dose of 90,000 IU over two months.[7] At two months, there was no significant difference among groups in the final vitamin D level (33.2 ± 8.5 ng per mL [82.87 ± 21.22 nmol per L], 29.2 ± 8.9 ng per mL [72.88 ± 22.21 nmol per L], and 37.1 ± 10.3 ng per mL [92.60 ± 25.71 nmol per L], respectively). A second RCT of 338 older adults receiving cumulative doses equivalent to 600 IU of cholecalciferol per day for more than four months found that mean serum vitamin D levels were greatest with daily dosing compared with weekly and monthly dosing (69.9 ng per mL [174.47 nmol per L], 67.2 ng per mL [167.73 nmol per L], and 53.1 ng per mL [132.54 nmol per L], respectively; $P < .001$ in all groups).[8] However, the authors concluded that there was likely no clinical significance between daily and weekly dosing, and that the lower cumulative dose may have accounted for the differences between dosing intervals.

RECHECKING VITAMIN D LEVELS

An RCT of 61 men and women 32 to 50 years of age who were randomized to 1,000 IU or 4,000 IU of vitamin D daily found that levels peaked at three months, regardless of dosage.[9]

Recommendations from Others

The Endocrine Society recommends that adults who are deficient in vitamin D receive 50,000 IU of ergocalciferol or cholecalciferol weekly for eight weeks, based on a study of 38 patients who received ergocalciferol.[10]

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