

Question: I use 8 wks of high dose (50,000 units) vitamin D for people with levels below 20. Some people are using 12 wks instead. Is there evidence for this?

The most recent clinical practice guideline for the evaluation, treatment and prevention of vitamin D deficiency, published by The Endocrine Society in 2011, defines vitamin D deficiency as serum circulating 25-hydroxyvitamin D (25(OH)D) concentrations <20 ng/mL (50 nmol/L) and vitamin D insufficiency as 25(OH)D concentrations 21-29 ng/mL (525-725 nmol/L).¹ To develop their recommendations, an appointed Task Force conducted 2 systematic reviews of the literature and used a grading system to define both the strength (strong or weak) and quality of evidence (very low, low, moderate, or high). According to this grading system, their recommendation for treatment of vitamin D deficiency was based on weak but high quality evidence from the literature. For context, all of the treatment recommendations received the same grade for evidence and only recommendations related to diagnostic criteria for vitamin D deficiency were based on what was considered strong evidence.

The guideline recommends that all adults with vitamin D deficiency receive treatment with 50,000 IU of either vitamin D₂ or vitamin D₃ once a week for 8 weeks (or its equivalent of 6,000 IU daily) to reach a target concentration of >30 ng/mL 25(OH)D.¹ This should be followed by maintenance therapy with a daily dose of 1,500 – 2,000 IU. While there is no mention of extending treatment to 12 weeks, the guideline describes the strategy of continuing to treat with 50,000 IU of vitamin D every other week to prevent recurrence of deficiency. These recommendations were based on results of 2 published studies.

An observational cohort study conducted by Malabanan et al evaluated the effect of increasing 25(OH)D concentrations above 25 nmol/L on circulating parathyroid hormone (PTH) in patients with vitamin D deficiency.² Investigators selected the first 35 patients with 25(OH)D concentrations >25 nmol/L and <62.5 nmol/L and without evidence of malabsorption, hypercalcemia, or alcohol abuse. These patients were treated with 50,000 IU of oral vitamin D₂ once weekly for 8 weeks along with 1000-1500 mg calcium daily. Serum 25(OH)D and PTH were measured before and after treatment. Results indicated a mean age of 67 years (range 49-83 years) and a 109% increase in mean [SE] 25(OH)D concentrations from 42.5 [2.5] nmol/L to 87.5 [2.5] nmol/L, with a corresponding 22% decrease in mean PTH concentrations from 63 [5] to 45 [3] pg/mL. Calcium levels did not change. Authors concluded that 8 weeks of 50,000 IU oral vitamin D₂ once weekly was safe and effective for correcting 25(OH)D deficiency/insufficiency and secondary hyperparathyroidism.

The second study was a retrospective chart review conducted by Pietras et al on patients in a clinic specializing in metabolic bone disease.³ The purpose of the study was to evaluate the effectiveness of a long term maintenance therapy strategy to prevent recurrence of vitamin D deficiency or maintain adequate vitamin D concentrations. Subjects included were ≥ 18 years of age with 2 or more measured 25(OH)D levels, who were receiving maintenance therapy with 50,000 IU oral vitamin D₂ every other week. Results indicated that 86 patients (mean age of 61 [range 18-91] years and 79% female) received treatment for a mean duration of 26 (range 5-72) months. Of these patients, 92% had 25(OH)D concentrations <30ng/mL prior to treatment with a mean (SD) of 23.4 (9.5) ng/mL. Mean (SD) concentration at the end of the study period was 47.0 (18.2) ng/mL (P<0.001).

Of the 86 patients studied, 41 who were vitamin D deficient or insufficient received 8 weeks of oral 50,000 IU of vitamin D₂ weekly prior to maintenance therapy.³ For these patients, the mean (SD) 25(OH)D level prior to treatment was 19.3 (6.2) ng/mL, which increased to 37.2 (13.0) ng/mL (P<0.001) after the 8 weeks of treatment. These patients were then continued on maintenance therapy with 50,000 IU vitamin D₂ every other week. The final mean (SD) 25(OH)D level was 46.9 (18.6) ng/mL (P<0.001). Authors noted that 16% of patients remained vitamin D deficient or insufficient and attributed this in most of the cases to medication non-adherence or other medication use (e.g., corticosteroid or anticonvulsant) which can affect vitamin D metabolism.

With regard to adverse events, no changes in serum calcium levels and no incidents of kidney stones or evidence of vitamin D intoxication were reported. Authors concluded that 50,000 IU of vitamin D₂ weekly for 8 weeks effectively corrected vitamin D deficiency and continued treatment with 50,000 IU vitamin D₂ every other week prevented recurrent vitamin D deficiency in most patients.

A recent literature search did not identify any studies that evaluated extending weekly treatment of vitamin D deficiency to 12 weeks with 50,000 IU vitamin D. However, 2 randomized controlled trials (RCT) published in 2015 evaluated different monthly treatment approaches. These may be of interest and are mentioned briefly for completeness.

One of these RCT was conducted in Belgium and compared 3 different monthly dosing strategies within an 8-week treatment window using oral vitamin D₃ to treat patients with vitamin D deficiency.⁴ A total of 150 subjects were randomized to receive loading doses of either 50,000 IU (group 1), 100,000 IU (group 2) or 200,000 IU (group 3) at week 0, followed by 25,000 IU, 50,000 IU or 100,000 IU, respectively, at weeks 4 and 8. Serum concentrations of 25(OH)D were measured at weeks 0, 4, 8 and 12. Overall mean \pm SD baseline concentration of 25(OH)D was 13.53 \pm 3.72 ng/mL. By week 12, 52%, 84% and 98% of subjects in groups 1, 2, and 3, respectively, reached the target of >20 ng/mL and 4%, 24% and 64%, respectively, reached the target of >30 ng/mL. Authors concluded that there was a dose-response relationship between the groups, with increases in 25(OH)D concentrations proportional to dose, and concluded that the loading dose of 200,000 IU followed by 2 monthly doses of 100,000 IU of vitamin D₃ safely and effectively improved vitamin D deficiency.

The second RCT evaluated dose-response with monthly vitamin D₃ supplementation in vitamin D deficient overweight/obese African Americans.⁵ A total of 70 subjects were randomized to receive either placebo or 18,000 IU, 60,000 IU, or 120,000 IU of oral vitamin D₃ monthly for 16 weeks. Baseline serum 25(OH)D overall was 14.77 \pm 0.6 ng/mL. Results indicated dose- and time-dependent increases in serum 25(OH)D concentrations. The group receiving the 18,000 IU monthly dose reached and maintained mean concentrations \sim 20 ng/mL at weeks 8 and 16, while those receiving 60,000 IU and 120,000 IU monthly doses reached and maintained mean concentrations >30 ng/mL at weeks 8 and 16. Authors concluded that the 60,000 IU monthly dose appeared to be sufficient to achieve a target 25(OH)D concentration of 30 ng/mL in this population.

The Endocrine Society guideline notes that obese patients and patients with malabsorption syndromes or taking medications that interfere with vitamin D metabolism (e.g., anticonvulsants, glucocorticoids and others) require 2 – 3 times more vitamin D to correct or prevent deficiency.¹ The guideline

recommends treating these patients with at least 6,000 – 10,000 IU/day to reach 25(OH)D concentrations >30 ng/mL, followed by maintenance therapy with at least 3,000-6,000 IU/day and continued monitoring with dose adjustments to ensure concentrations remain above 30 ng/mL. The guideline also notes that based on results of dose-ranging studies, vitamin D supplementation can be given 3 times a year, once a week, or once a day to maintain serum 25(OH)D concentrations.

While there are currently no published studies directly comparing different durations of treatment for vitamin D deficiency, the current treatment guideline from The Endocrine Society does support the strategy of continuing maintenance therapy with 50,000 IU of oral vitamin D₂ or D₃ every other week after completing an initial 8 week course of weekly treatment with 50,000 IU. As noted in the guideline, individual patient characteristics should be taken into account, with monitoring of 25(OH)D concentrations to achieve target concentrations >30 ng/mL and higher doses considered for obese patients, those with malabsorption syndromes, or those taking concurrent medications known to interfere with vitamin D metabolism.

References:

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