Treatment for vitamin D deficiency: here and there do not mean everywhere

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The optimal levels of vitamin D and the best treatment for vitamin D deficiency are the object of intense discussion. As for the threshold value of 25-hydroxyvitamin D (25(OH)D) defining a sufficient vitamin D status, a dedicated Committee of the Institute of Medicine recently stated that a serum concentration of at least 50 nmol/L meets the needs of at least 97.5% of the population [1, 2]. The corresponding recommended dietary allowance (RDA) in adults is 600 IU per day up to 70 years of age and 800 IU daily thereafter. Notably, these intakes are based on an assumption of minimal or no sun exposure. The IOM Committee’s members considered bone health as the only outcome consistently and causally linked to vitamin D and concluded that studies about the potential positive effects of vitamin D on calcium absorption and balance, physical performance, and risk of falls are still inconclusive as to causality. However, many experts deem the evidence that vitamin D supplementation improves calcium metabolism and skeletal muscle strength and function (with ensuing reduced risk of falls) strong enough to include calcium and muscle health among the outcomes influenced by vitamin D [3, 4]. In addition, serum parathyroid hormone plateaus in adults when 25(OH)D concentration is higher than 78 nmol/L [5] and mineralization defects of bone are not found in iliac crest biopsies from patients with serum 25(OH)D higher than 75 nmol/L [6]. Guidelines thus appeared where it is criticized the IOM position and suggested to target a 25(OH)D value above 75 nmol/L to maximize vitamin D’s effect on bone, calcium, and muscle [3]. Nevertheless, there is general agreement that minimum levels of 25(OH)D must be higher than 50 nmol/L, in order to prevent rickets and osteomalacia [1–3].

In this Journal, Toss and Magnusson present the results of a randomized controlled trial performed in Sweden, at 58° North latitude [7]. They report that 1,600 IU vitamin D₃ given throughout the year raised 25(OH)D concentration above 50 nmol/L in 22 community-dwelling, 55 to 85-year-old people. Most of the increase in serum 25(OH)D occurred within the first 3 months of treatment (mean values at baseline and 3 months 50.4 nmol/L and 81.8 nmol/L, respectively), with small individual fluctuations during the following 9 months (−16 to 32 nmol/L, mean 8 nmol/L). In 6 out of 22 subjects (27%), 25(OH)D levels remained below 75 nmol/L.

The Authors conclude that 1,600 IU vitamin D₃ is sufficient to obtain 25(OH)D concentrations above 50 nmol/L in community-dwelling elderly Swedish and acknowledge that the 25(OH)D increment they observed was somehow modest, despite a relatively high dose of cholecalciferol. This weak response is attributed to the mildness of patients’ vitamin D deficiency at study entry.

Location of any vitamin D supplementation study should be primarily taken into account when interpreting the results. Sunlight is pivotal in determining vitamin D levels, because of the catalytic action of UVB rays on the conversion of 7-dehydrocholesterol to previtamin D₃ in the upper layer of the skin. Latitude, season of the year, or time of day can dramatically influence the skin’s production of vitamin D₃ by modifying the zenith angle of the sun [3]. It is noteworthy that delivery to the liver is slower, and thus increase in circulating 25(OH)D more sustained, for skin-derived than ingested vitamin D [8].

From last April to September, we treated 16 vitamin D-deficient internal medicine outpatients in Genova, Italy, latitude 44° North. They initially came to observation for
follow-up visits of stable or recovering medical conditions, and none of them had diseases or was on drugs known to affect vitamin D status. Baseline serum 25(OH)D was below 50 nmol/L in all. Vitamin D was prescribed as an oral solution to be taken once a week (Abiogen Pharma, Pisa, Italy), since the same cumulative dose of vitamin D has been shown to achieve equal 25(OH)D values if given daily or weekly [9]. Six patients were prescribed 5,000 IU vitamin D$_3$ per week (slightly more than 700 IU per day) and ten 7,000 IU per week. Serum levels of 25(OH)D were assessed before and 3 months after starting vitamin D supplementation. Six more subjects, who did not receive vitamin D because their 25(OH)D values were close to or above 75 nmol/L, were also evaluated (controls). No lifestyle or dietary indications were given for the treatment period, but to avoid over-the-counter vitamin supplements.

As shown in Table 1, 5,000 and 7,000 IU vitamin D$_3$ per week significantly increased 25(OH)D concentrations by 44 and 43 nmol/L, respectively ($p < 0.01$), with no difference between the two dosages. Thirteen out of 16 patients (81.25%) reached a 25(OH)D value above 50 nmol/L. Therefore, in 3 months, we observed a sharper increase in 25(OH)D levels and a higher percentage of cases with serum 25(OH)D above 50 nmol/L than those reported by Toss and Magnusson, although the daily dose of cholecalciferol given to patients was roughly half to two-thirds of 1,600 IU. Remarkably, 8/16 (50%) subjects of our series were obese and expected to respond less to vitamin D supplementation because of the sequestration of cholecalciferol in the adipose tissue [3]. Serum 25(OH)D significantly increased also in controls by 21 nmol/L (Table 1).

The discrepancies between our and Toss and Magnusson’s data may be explained by the combined effect of sunlight and oral cholecalciferol on our patients’ vitamin D levels. Based on the trend seen in controls, in a sea city in Italy, 44° North latitude, in Spring and Summer, sun exposure during outdoor activities of everyday life may account for a net increase in serum 25(OH)D by as much as 21 nmol/L. Such an increment is doubled by adding a mean of 700–1,000 IU oral cholecalciferol per day.

Two unsolved issues are fuelling the debate about vitamin D deficiency: what should be the target serum 25(OH)D value, and how much vitamin D patients need. The answer to the latter question must be addressed by as many intervention studies as the populations with significantly different exposure to the light of the sun.

References

