High-dose oral vitamin D3 supplementation in rheumatology patients with severe vitamin D3 deficiency

Cord von Restorff a,⁎, Heike A. Bischoff-Ferrari b, Robert Theiler a

a Triemli Hospital, Zurich, Switzerland
b Department of Rheumatology and Institute of Physical Medicine, University Hospital Zurich, Zurich, Switzerland

A B S T R A C T

Objectives: Recent large trials indicate that adherence associated with a daily regimen of vitamin D is low and limits anti-fracture efficacy with vitamin D supplementation. The aim of this report is to describe changes of 25-hydroxyvitamin D (25(OH)D) serum concentrations achieved with a single oral dose of 300000 IU vitamin D3.

Methods: Over a course of 4 months, we identified 33 elderly with severe vitamin D deficiency (25(OH)D<25 nmol/l) on admission to acute care. Patients were admitted for musculoskeletal pain, bone disease, or gait abnormalities. The mean age was 80.5 years (SD±6.1). All patients were treated with a single oral dose of 300000 IU D3 in combination with 500–1000 mg calcium supplements per day depending on their dietary calcium intake.

Results: Baseline mean 25(OH)D serum concentrations were 15 nmol/l (SD±5.5). Mean 25(OH)D serum concentrations increased to 81.4 nmol/l (SD±29.7) at 3 months (29 patients) and were still 69.0 nmol/l (SD±17.9) at 6 months (26 patients). Mean serum calcium levels were 2.24 mmol/l (SD±0.11) at baseline, 2.28 mmol/l (SD±0.18) at 3 months, and 2.28 mmol/l (SD±0.13) at 6 months. Two patients with mild hypercalcemia (2.69 mmol/l) at 3 months had normal values at 6 months.

Conclusion: Based on our observations, a single oral dose of 300000 IU vitamin D3 raises mean 25(OH)D serum concentrations to the target mean of above 75 nmol/l at 3 months and a mean level of 69 nmol/l at 6 months. As calcium absorption is enhanced with higher 25(OH)D serum concentrations, calcium supplementation may need downward adjustment with this regimen to avoid mild hypercalcemia.

Introduction

Vitamin D deficiency is a significant risk factor in the development and progression of osteoporosis. Despite a documented 25% reduction in hip and any non-vertebral fractures [1] plus a 35 to 65% reduction of falls [2,3] from randomized controlled trials with oral 700–800 IU vitamin D3, guideline practice of vitamin D supplementation is still low, and the prevalence of vitamin D deficiency is still high [4]. Adding further support to vitamin D supplementation, higher 25-hydroxyvitamin D levels have been associated with a lower incidence of hypertension [5], cancer [6], diabetes [7], multiple sclerosis [8], and other chronic diseases [9].

Most vulnerable to vitamin D deficiency are older individuals, individuals with a darker skin tone, and individuals living in northern latitudes with prolonged winters [10]. From a public health perspective, recent large trials with vitamin D for the prevention of fractures among older individuals suggested that only about 50% of older individuals adhere to a daily oral vitamin D regimen [11,12], which reduced fracture efficacy documented in these trials. Thus, alternative strategies that help improve adherence to treatment with the aim of long-term vitamin D repletion are of clinical interest. We report on 33 older patients at our clinic identified with severe vitamin D deficiency (25-hydroxyvitamin D levels<25 nmol/l) who received oral 300000 IU D3 once (Streuli®, 300000 IU) with a follow-up at 3 and 6 months.

Methods

Between December 2006 and April 2007, we screened patients age 70 years and older for their serum 25-hydroxyvitamin D serum concentrations (DiaSorin RIA Assay 25-Hydroxyvitamin D 125 I Radio-immunoassay. DiaSorin Stillwater, USA. Sensitivity 3.75 nmol/l; coefficient of variation 4.9% at a level of 41.75 nmol/l and 7.8% at a level of 113 nmol/l) on admission to the rheumatology in patient clinic of one large hospital center (Triemli Hospital, Zurich). Patients were sent to the clinic for evaluation and treatment of acute or chronic pain, osteoporotic fractures, or elective surgery of the spine, hip or knee.
Many of these patients were immobile, had insufficient sunlight exposure, and malnutrition.

Exclusion criteria from high-dose vitamin D supplementation were a creatinine clearance below 30 ml/min, hepatic insufficiency, primary hyperparathyroidism, sarcoidosis, and hypercalcemia. Patients without exclusion criteria received a single oral dose of an unctuous suspension of highly concentrated vitamin D for breakfast (Streuli®, 300 000 IU). No patient was on bisphosphonates prior to our report. A total of 33 patients was treated. The oral vitamin D suspension in a dose of 300 000 IU vitamin D3 has been approved by Swissmedic for treating vitamin D deficiency in Switzerland. Patients were informed if severe vitamin D deficiency defined as 25-hydroxyvitamin D serum concentrations of less than 25 nmol/l was diagnosed.

Depending on the dietary report of the patient, additional calcium supplementation between 500 and 1000 mg per day was prescribed at day 4 after the high-dose vitamin D treatment. Follow-up blood samples for serum calcium, parathyroid hormone, phosphate, albumin, creatinine, alkaline phosphatase, and 25-hydroxyvitamin D were performed 3 and 6 months following high-dose vitamin D treatment. When patients had their ambulatory follow-up at our clinic, they were asked for any experienced side effects, and their heart rate was screened for arrhythmia.

Results

Table 1 shows the baseline data of the 33 patients, 29 of whom were female and 4 male. Serum 25-hydroxyvitamin D concentrations increased 3 months after oral supplementation in all patients (Fig. 1). 50 nmol/l 25-hydroxyvitamin D was reached in 27 out of 29 patients (93%) after 3 months. Levels over 75 nmol/l were reached in 14 of 29 patients (48%) at 3 months [13,14]. One of the two patients who did not achieve 25-hydroxyvitamin D serum concentrations of at least 50 nmol/l at 3 months died due to severe sepsis unrelated to vitamin D treatment, the second patient had the lowest starting level with 4.5 nmol/l prior to treatment. One other patient accidentally received a second dose of our highly concentrated unctuous vitamin D3 supplementation during the second hospitalization. She had the highest 25-hydroxyvitamin D serum concentration at 3 months with 167 nmol/l, and her serum 25-hydroxyvitamin D concentration was 85.8 nmol/l at 6 months. Two patients had mild hypercalcemia at 3 months, which normalized at 6 months.

At 6 months 92% of all patients had 25-hydroxyvitamin D serum concentrations above 50 nmol/l and 35% had desirable serum concentrations of 75 nmol/l. PTH levels decreased by 22% within 3 months and remained suppressed at 6 months.

None of the treated patients reported significant side effects that may have been caused by vitamin D supplementation and the clinical heart rate check revealed no arrhythmia. Few patients (about 5%) complained of mild constipation or headaches, which may have been related to their calcium supplement intake [11]. No rehospitalizations were recorded.

Discussion

Based on this clinical observation among 33 patients with severe vitamin D deficiency a single oral dose of 300 000 IU vitamin D3 increased 25-hydroxyvitamin D serum concentration in most patients to at least 50 nmol/l and 48% of patients reached the desirable range of at least 75 nmol/l at 3 months. Despite a decline at 6 months, mean 25-hydroxyvitamin D serum concentrations were still more than 4 times higher compared to baseline.

Raising 25-hydroxyvitamin D levels in older individuals permanently and effectively is a challenge for many clinicians. According to this clinical observation, a single oral dose of 300 000 IU D3 may safely replete 25-hydroxyvitamin D serum concentrations for up to 6 months.

A strength of the study is the use of a high intermittent oral dose of vitamin D including a prospective assessment of 25-hydroxyvitamin D levels among frail older individuals at risk of vitamin D deficiency. The study also has several limitations, including its uncontrolled design as a clinical case study and its small size. Another limitation of our report is that the baseline assessment was during winter season, while the 3 and 6 month checks occurred between March and October, which may have led to an overestimation of the treatment benefit at

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline Variables</th>
<th>After 3 Months</th>
<th>After 6 Months</th>
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<tbody>
<tr>
<td><strong>25-hydroxyvitamin D (nmol/l)</strong></td>
<td>15.0±5.4 44.0 4.5–24.5</td>
<td>18.4±29.7 73.8 36–167.3</td>
<td>69.0±27.9 65.4 36.0–115.5</td>
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<tr>
<td><strong>Creatinine (mmol/l)</strong></td>
<td>74.0±22.7 69.0 44–128</td>
<td>78.8±213.7 75.0 47–130</td>
<td>81.8±228.9 80.0 49–144</td>
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<tr>
<td><strong>Calcium (mmol/l)</strong></td>
<td>2.24±0.11 2.22 2.09–2.60</td>
<td>2.28±0.18 2.30 1.91–2.69</td>
<td>2.2±0.13 2.30 1.93–2.47</td>
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<tr>
<td><strong>Phosphate (mmol/l)</strong></td>
<td>1.04±0.12 1.00 0.85–1.38</td>
<td>1.05±0.14 1.05 0.77–1.28</td>
<td>1.07±0.16 1.08 0.71–1.50</td>
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<td><strong>Albumin (g/dl)</strong></td>
<td>36.8±3.5 37.0 29–45</td>
<td>39.0±4.9 40.0 27–46</td>
<td>39.4±4.7 41.0 23.0–46.7</td>
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<tr>
<td><strong>PTH (ng/l)</strong></td>
<td>75.9±86.9 45.1 12.8–390</td>
<td>58.9±39.8 49.6 17.3–159</td>
<td>60.0±42.7 42.7 19.3–181.5</td>
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<td><strong>Alkaline phosphatase (U/l)</strong></td>
<td>95.3±48.8 83.0 81–252</td>
<td>93.3±60.0 74.0 15–346</td>
<td>92.4±50.3 80.0 23–296</td>
</tr>
<tr>
<td><strong>TSH</strong>&lt;sub&gt;12&lt;/sub&gt; (mU/l)</td>
<td>1.4±0.8 1.29 0.1–3.76</td>
<td>3.2</td>
<td>2.4</td>
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This table shows serum levels at baseline, and after 3, and 6 months following oral supplementation with the highly concentrated unctuous vitamin D3 suspension (300 000 IU cholecalciferol). TSH was only measured at baseline. n = number of patients, SD = standard deviation, PTH = parathyroid hormone, TSH = thyroid-stimulating hormone.
6 months. However, we have shown recently that the seasonal swing in 25(OH)D levels is small in frail older individuals as they tend to avoid the sun, have decreased dermal production of vitamin D or are institutionalized [4].

References


