Efficacy of an oral, 10-day course of high-dose calciferol in correcting vitamin D deficiency

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Abstract

Aim Treatment of vitamin D deficiency is an important aspect of the management of osteoporosis, particularly in the elderly. Most well-described regimens in current use involve daily dosing and thus require long-term compliance to be effective. In New Zealand, no preparation containing only low-dose vitamin D suitable for daily use is available. We describe a high-dose regimen for rapid correction of vitamin D deficiency, which makes use of the calciferol 50 000 international unit (IU) tablets available in this country.

Methods Thirty two women (mean age 76 ± 4 years; range 67–84 years) with serum 25-hydroxyvitamin D concentrations ≤10 µg/l were treated with oral calciferol 50 000 IU daily for 10 days.

Results At an average time after treatment of four months, serum 25-hydroxyvitamin D increased from 8 ± 1 µg/l to 21 ± 5 µg/l, bringing all but one patient within the reference range (14–76 µg/l). Serum parathyroid hormone level decreased after treatment by 0.7 ± 1.7 pmol/l (p <0.05), and alkaline phosphatase activity decreased by 5 ± 11 u/l (p <0.05). Serum calcium increased by 0.06 ± 0.08 mmol/l (p <0.001), but all values were within the reference range. Data collected from a separate cohort of elderly inpatients showed that similar increases could be achieved with a single 300 000 IU dose, and suggested that serum 25-hydroxyvitamin D levels decline with a half-life of 90 days.

Conclusions This regimen provides a simple, safe and effective way of managing vitamin D deficiency. Its short-term nature may result in higher compliance than daily dosing regimens.

Vitamin D deficiency leads to secondary hyperparathyroidism, increased bone turnover and bone loss, predisposing to osteoporosis and osteoporotic fractures.\(^1\) Overt rickets and osteomalacia are now uncommon in Western populations, but subclinical vitamin D deficiency is widespread amongst older individuals, especially those in nursing homes or who are housebound. It is also common in healthy older individuals living independently.\(^2,3\) Correction of vitamin D deficiency is associated with rapid improvement in bone density,\(^2\) and may reduce fracture risk.\(^4,5\) Hence, treating vitamin D deficiency is important in the prevention and treatment of osteoporosis.

Vitamin D is usually administered daily in low doses, but because of its sequestration in adipose tissue and long half-life such regimens are slow to replenish vitamin D stores and require long-term compliance. Also, in some countries including New Zealand there are no satisfactory vitamin D preparations available for daily use. In
this study we have examined the only preparation containing vitamin D alone available in this country, a 50 000 international unit (IU) tablet. Its efficacy in correcting vitamin D deficiency when given as a single course or dose is reported.

**Methods**

Thirty two asymptomatic, postmenopausal women (mean age 76 ± 4 years; range 67–84 years), with serum 25-hydroxyvitamin D ≤10 µg/l were given a daily calciferol 50 000 IU tablet (PSM Healthcare, Auckland) for 10 days. These women were all independently mobile, free living, and had no diseases nor were taking medications that influenced vitamin D or calcium metabolism. They are referred to as the ‘outpatient’ cohort. Serum calcium, phosphate, alkaline phosphatase, 25-hydroxyvitamin D (Diasorin radioimmunoassay, Stillwater, MN, USA), and intact parathyroid hormone (Nichols Institute radioimmunometric assay, San Juan Capistrano, CA, USA) were measured before and after treatment. The prospectively collected data were complemented by data collated from hospital records of six men and 43 women (mean age 84 ± 5 years; range 69–94 years) admitted to the geriatrics service of Auckland Hospital (‘inpatient’ cohort). They received a single dose of 300 000 IU and had re-measurement of serum 25-hydroxyvitamin D at variable intervals thereafter. Thus, it was possible to study the decline in serum 25-hydroxyvitamin D levels following use of this regimen. Variables were assessed using Student’s paired t tests (two tailed), and data are presented as mean ± SD.

**Results**

**Outpatient cohort** Figure 1 shows the pre- and post-treatment levels of serum hormonal and biochemical analyses. The post-treatment levels were measured at 17 ± 7 weeks (range 5–31 weeks). The mean pre- and post-treatment 25-hydroxyvitamin D levels were 8 ± 1 µg/l and 21 ± 5 µg/l respectively (range 9–32 µg/l, post-treatment). All patients, except one, had post-treatment levels within the reference range (14–76 µg/l). The average increase following treatment was 13 ± 6 µg/l. There was no difference in the 25-hydroxyvitamin D increase after treatment between those treated during either summer or winter.

The mean serum parathyroid hormone level decreased after treatment by 0.7 ± 1.7 pmol/l (p <0.05). The mean serum calcium increased after treatment by 0.06 ± 0.08 mmol/l (p <0.001), but no post-treatment calcium concentration exceeded the reference range. Serum alkaline phosphatase activity decreased by 5 ± 11 u/l (p <0.05), indicating reduced bone turnover. Serum phosphate concentrations were unchanged.

**Inpatient cohort** At baseline, serum 25-hydroxyvitamin D was 7 ± 4 µg/l (range 2–16 µg/l). Following vitamin D dosing, levels of 25-hydroxyvitamin D increased to 25 ± 11 µg/l at an average interval of 17 weeks. The maximum value recorded was 51 µg/l. The change in serum 25-hydroxyvitamin D according to the time since dosing is shown in Figure 2. It can be seen that the levels peaked between 13 and 21 days, then declining with a half-life of 90 days.
Figure 1. Serum hormonal and biochemical indices before and after treatment of vitamin-D-deficient women with calciferol 50 000 units daily for 10 days (mean values are shown with a horizontal line, and p values are for the change from baseline)

- **Serum 25-hydroxyvitamin D (μg/L)**
  - Mean values are shown with a horizontal line.
  - p < 0.001

- **Serum calcium (mmol/L)**
  - Mean values are shown with a horizontal line.
  - p < 0.001

- **Serum parathyroid hormone (pmol/L)**
  - Mean values are shown with a horizontal line.
  - p < 0.05
Figure 2. Change in serum 25-hydroxyvitamin D concentrations (in µg/l) as a function of the time since treatment with a single dose of calciferol 300 000 IU (the time intervals shown are quintiles and data are mean ± SD)

Discussion

We have shown that a 10-day course of high-dose oral calciferol is both safe and effective in correcting vitamin D deficiency. It is a simple, cheap, well-tolerated method of replacement that is convenient for both in- and outpatient settings. There were no significant side effects, and no patients had post-treatment serum 25-hydroxyvitamin D or calcium levels exceeding the reference range. These results are complemented by the finding that a single dose of 300 000 IU produces comparable results, in terms of both safety and efficacy. In fact, we have now treated many patients giving 500 000 IU at one time, without loss of efficacy or safety.

The increase in 25-hydroxyvitamin D was modest. Some patients still had borderline deficiency, as reflected by the persistent elevation of parathyroid hormone levels and marginal concentrations of 25-hydroxyvitamin D. Trials of higher dosing regimens are needed, aiming to restore 25-hydroxyvitamin D levels to the 20–40 µg/l range or higher, which is increasingly regarded as the optimal range.

This study represents observations derived from patients coming through a clinical service, and is not a formal randomised trial with a comparator group. Despite this, we believe that the data are a valid description of the effects of this vitamin-D dosing regimen. All the assays used are well established, both internationally and in routine clinical use in our laboratory, so it is most unlikely that the results obtained are the product of assay drift or other laboratory artefact. The fact that the patients’ samples were assessed over a period of months in a number of different assays makes the potential for these confounders to skew the results even more unlikely. The results are
biologically consistent, in that there is an increase in serum 25-hydroxyvitamin D and calcium on the one hand, and a fall in parathyroid hormone and alkaline phosphatase on the other. These results are also typical of what we have seen clinically with many hundreds of patients managed with this regimen, though the full biochemical evaluation presented here is not available in all those.

The results from the inpatient cohort make clear that some ongoing vitamin D supplementation is necessary to maintain normal levels. This has not been explored in the present study, but it could consist of repetitions of one of the present dosing regimens, or of more frequent smaller doses. We have found, over a number of years, that one 50 000 IU tablet per month is adequate to maintain normal 25-hydroxyvitamin D concentrations in most patients.

In conclusion, doses of 300 000–500 000 IU of calciferol represent a safe and effective regimen that can be initiated while the patient is in hospital, ensuring that the major problem of vitamin D deficiency has been adequately addressed.

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**Acknowledgements:** This study was supported by the Health Research Council of New Zealand

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**References:**


