



## Case Report

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# Elevated Vitamin D Levels and Hypercalcaemia on Maintenance Dose of Calcium and Vitamin D

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## Abstract

We report a 74-year-old woman with elevated vitamin D levels and hypercalcaemia seemingly caused by long term use of maintenance dose vitamin D, in the form of Adcal-D3 chewable tablets. Using the tablet after a right hip fracture lead to an asymptomatic but significant raise in Serum 25-hydroxyvitamin D3 as well as an abnormal bone profile; withholding treatment normalised the patient's biochemistry four weeks later. We discuss here the potential for vitamin D supplementation in the older person to cause biochemical abnormalities.

## Introduction

Vitamin D is a prohormone that plays a significant role in calcium haemostasis and regulation of bone mineral density. It also participates in biological processes such as cell differentiation and modulation of the immune system. Vitamin D deficiency is a common occurrence in the elderly population (defined as aged 65 years and older) with a prevalence of around 15% [1] This has led to greater awareness and a rise in the usage of vitamin D [2,3].

The extensive use of both medical prescriptions and over the counter preparations may influence the incidence of Vitamin D Toxicity (VDT) as well as cases of hypervitaminosis D [4,5]. The clinical signs of significantly elevated vitamin D are often caused by the subsequent hypercalcaemia that ensues. Symptoms can include: weakness, fatigue, nausea, vomiting and constipation.

## Case Report

A 74-year-old woman was admitted to a rehabilitation ward after a fall; this resulted in a fracture to the right hip which was managed with intramedullary nail. Her past medical history is: Factor XI deficiency, atrial fibrillation, migraine, peptic ulcer, and pseudo-gout. She was diagnosed with osteoporosis in 2013. The patient's serum 25-hydroxyvitamin D3 was low at 19 nmol/L (Vitamin deficiency defined as <25 nmol/L). High dose vitamin

D treatment was commenced and after which time, Adcal-D3 chewable tablets was prescribed as maintenance, 1 tablet twice a day.

Post discharge from hospital during her admission to an intermediate care unit a set of abnormal bloods were noted on bone profile, as shown in the following table (Figure 1).

Corrected Serum Calcium	2.99 mmol/L [2.20-2.60 mmol/L]
Serum 25-hydroxyvitamin D3	195 nmol/L [<140 nmol/L]
Phosphate	2.20 mmol/L [0.18- 1.5 mmol/L]
Parathyroid Hormone	1.0 pmol/L [1.6-6.9 pmol/L]

**Figure 1:** A table demonstrating the abnormal biochemistry of the patient.

Other biochemical parameters including: serum angiotensin converting enzyme, myeloma screen (serum and urine electrophoresis), full blood count, liver function, renal, C-reactive protein, erythrocyte sedimentation rate and thyroid function were found to be normal.

The patient did not report any symptoms typical of hypercalcaemia such as weakness, fatigue, nausea, vomiting or constipation and clinical examination was unremarkable. Dietetic

review confirmed that the patient had been consuming a healthy diet; the patient also denied taking any over the counter vitamin supplements. Primary care records showed that she has not had any high dose vitamin D since 2013 except maintenance dose on Adcal D3. Her serum calcium was first noted to be slightly elevated three months before her fracture. Adcal-D3 was stopped and four weeks after cessation the patient's serum calcium, phosphate, vitamin D and parathyroid hormone level normalised. Since withholding calcium and vitamin D, her calcium and vitamin D level has remained within the normal range over the last two years and her general health remains good. It is likely that her elevated vitamin D and hypercalcaemia was due to long term use of Adcal-D3.

## Discussion

Excess supplementation of vitamin D is a leading cause elevated levels of vitamin D and vitamin D toxicity. Vitamin D toxicity is an extreme form of hypervitaminosis D, the level at which risk is clinically significant defined at  $>250\text{nmol/L}$  [6]. The main causes of vitamin D toxicity were due to ingestion through supplementation or fortification. One of the most common reasons was due to formulation or compounding error in the manufacture of supplementation. As [7] noted in their case report, a laboratory error in dilution lead to a patient taking capsules at a strength 2000-fold higher than was prescribed [7]. Though an extreme case, this type of error in calculation and manufacture is not isolated occurring in both the fortification of foodstuffs like milk [8] as well as errors in production of medication [9].

Inappropriate prescription of vitamin D supplements has also been implicated for some cases of raised vitamin D [10]. Evidence suggests that dosage  $<10,000$  IU per day does not cause VDT, however, very high dose formulations ( $>60,000$  IU) are popular and have been given in error on several occasions which has led to VDT [11]. The common factor in these cases is that patients have been exposed to toxic or at least high doses of vitamin D before the manifestation of hypervitaminosis D. The body's homeostatic mechanisms are normally robust enough to regulate levels otherwise. Indeed, this is the reason why VDT is rare from dietary intake alone or sun exposure as homeostatic mechanisms regulate the amount of vitamin D produced in skin from sun light or absorption from diet [12].

It is most unusual to develop hypercalcaemia and elevated vitamin D levels on maintenance dosing of calcium and vitamin D (Adcal tablets contain 500mg of calcium and 400iu of cholecalciferol). However, endogenous production of 1,25-dihydroxyvitamin D<sub>3</sub>, the hormonally active metabolite of vitamin D, can occur in patients with lymphoma, chronic granulomatous diseases such as sarcoidosis and in Wegener's granulomatosis [13]. Oestrogen replacement therapy can also potentially raise vitamin D levels via activation of the vitamin D receptor. The long term consequences of untreated vitamin D toxicity include renal stones, ectopic soft tissue calcification and cardiac arrhythmias.

We are not aware of any reports on an elevated vitamin D and hypercalcaemia whilst on maintenance dose of calcium and vitamin D. Although this patient had no signs and symptoms of VDT, a vitamin D level of vitamin D of  $>140$  nmol/L may be associated increase mortality [14]. This case is notable for the very low level of vitamin D taken in order to address abnormal biochemistry and an elevated vitamin D level (400iu), the safe dose being  $<10,000$ iu per day. We feel it is important to highlight this because calcium and vitamin D is very commonly prescribed for the older person in falls clinics, often in conjunction with a bisphosphonate for osteoporosis or post fracture. Although not specific for elevated vitamin D, a mildly elevated serum calcium level should trigger the clinician to complete a vitamin D assay in addition to searching for other causes of hypercalcaemia.

## Acknowledgements

The authors declare to conflict of interest.

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