



## Vitamin D intoxication through errors in administration: a case report

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### Abstract

Vitamin D intoxication caused by the irregular consumption of medications is a major concern in geriatric health. Due to errors in administering such vitamins and medical malpractice, many patients lack the proper management of vitamin supplementation, considering what is actually prescribed. The present study, which aims to report on intoxication by this vitamin, describes an elderly couple who lived alone and divided their household tasks. The wife, who is the main focus of the report, was lucid but suffered musculoskeletal disorders and used a wheelchair, while the husband could function physically. The wife was hospitalized with a clinical profile of delirium. Intoxication is a major cause of metabolic encephalopathy, which explains how the case developed. The co-adjutant was the husband, who suffered apparent mild cognitive impairment, and modified the doctor's dosage of vitamin D alone, contradicting the guidance of the family. The family monitored the health status of the couple through weekly telephone calls to check if their medications were being taken properly. After investigation with new anamneses and a review of medical records, intoxication was confirmed due to an error in the amount of the drug administered over a prolonged period. It is extremely important to be aware of the clinical profile of hypercalcemia and how to treat the same. In geriatrics, diagnosis should involve both clinical treatment and special care to understand the daily routine of elderly persons in order to avoid further repercussions.

**Keywords:** Vitamin D.  
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## INTRODUCTION

Brazil is undergoing an increase in the life expectancy of its population, contributing to a greater incidence of aggravations caused by senescence and senility. Hydroelectrolytic disorders involving calcium, which represent a significant number of such events, are often caused by the excess or insufficient intake and absorption of vitamin D<sup>1</sup>.

When vitamin D is lacking, supplementation aims to avoid and treat diseases such as osteomalacia, osteopenia and osteoporosis, as well as secondary hyperparathyroidism, conditions which are involved in the increase of morbidity and mortality in this age group<sup>2</sup>.

We have identified cases of vitamin D poisoning associated with high daily doses due to errors in formulations, prescriptions or administration, as in the case described in this article.

Hypervitaminosis D is a rare cause of hypercalcemia and renal injury. However, high doses of either vitamin D<sub>2</sub> (ergocalciferol) or vitamin D<sub>3</sub> (cholecalciferol) may be more prevalent, both in prescribed and exaggerated administration<sup>3</sup>.

Fat-soluble vitamins provide benefits at physiological levels but can be dangerous when taken in excessive quantities. For many people, the word "vitamin" indicates something beneficial and essential, not potentially toxic<sup>4</sup>.

It is said that the diet of more than a third of the population of the USA involves supplements. However, data also exists to show that the diets of more than 50% of Americans feature supplements, often of more than one type. Between 60-70% of patients fail to report the use of these supplements to their physicians<sup>5</sup>. Clinical research carried out prior to the completion of diagnosis of intoxication is often flawed or prolonged. The case described in the present article shows the importance of knowledge of the properties of calcium in the body and its repercussions. Profiles of delirium as a consequence of metabolic encephalopathy<sup>6</sup>, as occurred with the patient here, also require attention.

In geriatrics, detailed anamnesis is the key to many conditions, emphasizing the importance of

an integrated approach to the health of the elderly, ranging from knowledge of the patient's daily life to the appropriate treatment for specific diseases<sup>7</sup>.

In this scenario, questions to caregivers should also be clarified: to what extent are they necessary or dispensable, and are family and medical orders followed correctly. The objective of the present study is to report a case of vitamin D intoxication caused by administration error, as well as to discuss the possibilities of adverse effects attributable to the management of this medication.

## METHOD

The initiative behind the project was based on the increase of vitamin replacement prescriptions observed both in a local geriatrics outpatient clinic and in hospitalizations, with the majority of patients receiving formulas containing cholecalciferol. We therefore began to study the phenomenon of an increase in supplementation, and found articles that described not only an increase in scientific publications on vitamin D of more than 250%, but also an increase in the use of this vitamin in primary care prescriptions in England of 8,000% and an increase in costs of 5,000% since 2008<sup>2</sup>. In this specific case, the research team had no contact with the patient, who had died three years previously. All data were obtained by reviewing medical records, interviews with relatives after the death of the patient, and with the geriatric doctor responsible for her during hospitalizations.

Firstly, we obtained authorization from the relatives of the patient to obtain post-mortem information and carry out data collection for scientific research. The case doctor contacted the patient's children by telephone and explained our interest in reporting the incident, explaining that no one would be identified at any time, and thus obtained consent. A review of medical records obtained from a teaching hospital of the public health system in the municipality of Catanduva, São Paulo, Brazil was then carried out.

The doctor responsible for the case signed a Consent Form in relation to this work and assisted us with interviews regarding the course of the case during the period in which it actually occurred. Meetings were also held during the production of

the work to clarify visits and hospitalizations, which were also checked against the medical records.

The present study was approved by the Research Ethics Committee of the Faculdades Integradas Padre Albino (Approval No.: 1.644.191), in accordance with resolution nº 466/2012 of the National Health Council.

## RESULTS

The patient was an 84-year-old female pacemaker user with a history of hypertension, dyslipidemia, hypothyroidism, congestive heart failure, coronary artery disease with acute myocardial infarction, a stroke, chronic non-dialytic renal disease, and spine and hip osteoarthritis.

She was hospitalized in January 2013, 15 days after undergoing a behavioral change towards aggressive and mental confusion, combined with pain in the whole body, nausea, vomiting and inappetence.

She was taken to the emergency room by her husband and daughter-in-law, who also brought a medical prescription which included the medications shown in Chart 1.

At the initial physical examination the following information was recorded: weight 83kg, height 1.55m, blood pressure 140x90 mmHg, heart rate 85bpm and mild prior right-sided hemiparesis.

In terms of tests carried out, an electrocardiogram was ordered to rule out the possibility of a new episode of acute myocardial infarction and a chest radiography to check for pulmonary alterations, neither of which revealed acute pathological signs. A skull tomography for the investigation of mental confusion showed a sequelae lesion in the left insula, physiological basal nuclei calcification, but no other disorders.

The biochemical tests requested were related to the diagnostic hypotheses of infection, hydroelectrolytic disorders and especially delirium. On the first day of hospitalization, complete blood count, urine 1, sodium, potassium, calcium, phosphorus, magnesium, urea and creatinine tests were requested to verify renal function and chronic kidney disease activity, and transaminases were used to check liver function due to the daily use of so many medications.

The results of these initial exams are shown in chart 2.

**Chart 1.** Medications of daily use, dose and posology. Catanduva, São Paulo, 2013.

| Medication    | Dose    | Quantity (pills) | Time            |
|---------------|---------|------------------|-----------------|
| Levothyroxine | 50 µg   | 1                | Morning         |
| Omeprazole    | 20 mg   | 1                | Morning         |
| Losartan      | 25 mg   | ½                | Morning         |
| Furosemide    | 40 mg   | ½                | Morning         |
| Venlafaxine   | 37,5 mg | 1                | After breakfast |
| AAS           | 100 mg  | 1                | After lunch     |
| Flunitrazepam | 2 mg    | ½                | Night           |
| Simvastatin   | 20 mg   | 1                | Night           |
| Complex 46    | -       | 2                | Night           |
| Amitriptyline | 75 mg   | 1                | Night           |
| Alendronate   | 70 mg   | 1                | 1x week         |
| Metoprolol    | 25 mg   | 1                | Every 12h       |
| Vitamin D     | 7000 U  | 1 capsule        | 1x week         |

Source: Public hospital geriatrics ward, Catanduva, São Paulo 2013.

**Chart 2.** Exams, results and reference values. Catanduva, São Paulo, 2013.

| Exams                             | Results     | Reference               |                                 |
|-----------------------------------|-------------|-------------------------|---------------------------------|
| Blood count                       | Hemoglobin  | 12.1 g/dL               | 13-16 g/dL                      |
|                                   | Hematocrit  | 37.2%                   | 36-46%                          |
|                                   | Leukocytes  | 10.600/mm <sup>3</sup>  | 4.000-10.000/mL                 |
|                                   | Basophils   | 4%                      | 0-2%                            |
|                                   | Neutrophils | 68%                     | 45-75%                          |
|                                   | Eosinophils | 0                       | 0-5%                            |
|                                   | Lymphocytes | 22%                     | 22-40%                          |
|                                   | Platelets   | 382.000/mm <sup>3</sup> | 130.000-370.000/mm <sup>3</sup> |
| Sodium                            | 136 mEq/l   | 135-145 mmol/L          |                                 |
| Potassium                         | 4,2 mEq/l   | 3.5-5.5 mmol/L          |                                 |
| Urea                              | 68 mg/dl    | 16-40 mg/dL             |                                 |
| Creatinine                        | 2,3 mg/dl   | 0.6-1.2 mg/dL           |                                 |
| Urine I                           | Normal      | Normal                  |                                 |
| Ionic Calcium                     | 1,98 mEq/l  | 1.17 a 1.32 mEq/l       |                                 |
| Total Calcium                     | 16,8 mg/dl  | 8.5-10.2 mg/dL          |                                 |
| Phosphor                          | 3,6 mg/dl   | 2.5-4.8 mg/dL           |                                 |
| Magnesium                         | 1,6 mg/dl   | 1.9-2.5 mg/dl           |                                 |
| Glutamic oxaloacetic transaminase | 21 U/L      | 5-40 U/L                |                                 |
| Glutamic pyruvic transaminase     | 17 U/L      | 7-56 U/L                |                                 |

Source: Public Hospital Geriatrics Ward, Catanduva, São Paulo, 2013.

There were slight signs of infection in the blood count, while urea and creatinine were elevated as expected due to the patient's renal condition. The presence of hypercalcemia and hypokalemia were of greatest interest.

Parenteral hydration was started with 1000ml of 0.9% saline solution every 12 hours. For the hypercalcemia, 40 mg intravenous furosemide was administered every 12 hours, intravenous hydrocortisone 100 mg every eight hours and nasal calcitonin every 12 hours. The measures for hypokalemia were based on the intravenous replacement of 19.1% potassium chloride.

On the second day of hospitalization, with the cause of the potassium and calcium disorders still unknown, a new blood sample was collected with the same control tests, but this time with a

dosage of parathyroid hormone (PTH) and 25OH Vitamin D on suspicion of kidney malfunction. The results showed PTH 15pg/ml (reference 15-65pg/ml), inappropriately "normal" in the presence of hypercalcemia, and vitamin D 160ng/ml (reference 30-100ng/ml), confirming vitamin intoxication and excluding hyperparathyroidism.

On the eighth day of treatment without response to therapy, 60 mg of pamidronate was administered for two days, with an evident improvement in ionic calcium levels to a value of 1.66mEq/l, in addition to the initial therapy. Hyperhydration and the diuretic were continued for a further six days with dose and posology reduction until normalization of the serum levels of the ionizable calcium. The patient was discharged after 14 days of hospitalization, with the diagnostic hypothesis of hypervitaminosis D, and replacement was suspended.

Three months after discharge, the patient returned to the emergency room with the same complaints and serum calcium concentration again increased to a value of 1.90mEq/l. Subsequent exams again revealed PTH below normal and vitamin D elevated to levels above the gauging ability of this method.

As medication was suspended on the first hospitalization, the relatives were invited to a meeting to carry out a new anamnesis. The conversation with the family lasted approximately 40 minutes in an attempt to identify the possibilities behind the clinical picture. It was discovered that the elderly couple lived alone and were visited every fortnight by their family, who organized the medicines into charts and calendars.

During the anamnesis, it was found that while the woman's 90-year-old husband administered the pills to his wife, he did not appear to have a complete understanding of the situation, presenting mild cognitive deficits such as being easily distracted and failing to understand the seriousness of the case. The family explained that the husband played the role of "functioning body" and the wife the role of "lucid mind" so that the couple could live together without assistance, sharing household chores.

The children of the couple were asked to bring the medication schedule and packaging the next day for verification purposes. It was noticed that vitamin D was not scheduled for the days of the week and the reason for this was asked. The children explained that since the prescription was only once a week, they telephoned on Saturdays to remind the husband to get the bottle of vitamins and administer the supplement, until the medication was suspended during the first hospitalization.

At this point, the husband said that he thought his wife was too weak and for the last two years had been administering the vitamin every day to "strengthen" her, assuming that she would improve. This continued even after the suspension of the vitamin three months earlier.

The patient took a tablet of 7,000 IU of vitamin D per day for two years, when the recommended dose was one tablet per week. The 90-year-old husband continued this situation for a prolonged period, resulting in irreversible hypercalcemia in his wife

upon arrival at hospital. The patient died two days after the second hospitalization, with respiratory sepsis.

## DISCUSSION

Symptoms of severe vitamin D poisoning are evidenced mainly by hypercalcemia, changes in bone metabolism, and disturbances in the amounts of phosphorus and calcium in the serum<sup>8</sup>.

There are few previous reports of such cases in literature, since hypercalcemia suggests other diagnostic hypotheses. This condition tends to be associated with primary hyperparathyroidism, multiple myeloma, or other neoplasms. The diagnosis of vitamin D intoxication is not usual in cases of hypercalcemia, as it is infrequent, especially prior to the advent of vitamin D supplementation. In recent times, the number of reported cases has increased as this vitamin has been prescribed more frequently due to hypovitaminosis D treatment<sup>2</sup>.

Calcium is essential for processes intrinsic to the human body, such as action potentials and bone formation. Serum concentrations fluctuate through the regulation of three main sites responsible for the transport and storage of calcium: the intestine, kidney and the bones. Low serum levels of vitamin D are a well-known risk factor for osteoporotic diseases and have been associated with the occurrence of a variety of other common chronic diseases such as hypertension, cardiovascular diseases, diabetes mellitus, various cancers, infections and various autoimmune conditions<sup>10</sup>.

Recent reviews have concluded that vitamin D3 supplementation can prevent a number of premature deaths, but further studies are needed to assess the levels required to reduce levels of mortality<sup>10</sup>. Treatment with vitamins with very high doses of cholecalciferol should be avoided, but are tolerated at low daily, weekly or monthly doses<sup>11</sup>.

Normal total serum calcium levels are between 8.8 and 10.4mg/d. Hypercalcemia occurs when there is an imbalance between calcium absorption and excretion from the kidney and its deposition in the bone<sup>1</sup>.

The clinical symptoms of hypercalcemia include anorexia, nausea, vomiting, polyuria, polydipsia,

constipation, weakness and changes in mental status, and cases can be fatal. The patient may develop cognitive problems, go into a coma, and cardiac arrhythmias and renal failure may occur. There are recent reports in literature of potentially fatal complications of vitamin D toxicity with severe hypercalcemia and renal failure due to errors in manufacturing and the labeling of supplementation<sup>12</sup>. Every year, one in three people aged 65 or older experiences at least one fall, with 9% of these occurrences leading to an emergency room visit and 5-6% resulting in a fracture. Doses of 700 IU to 1,000 IU of supplemental vitamin D per day can reduce falls by 19% or, with vitamin D<sub>3</sub>, by up to 26%. This benefit was found to be significant within two to five months of treatment and lasted beyond 12 months of treatment<sup>13</sup>.

The estimated toxic dose of vitamin D is more than 100,000 IU per day over a period of at least one month<sup>9</sup>. In the present report, the dose used was more than double that recommended, and the situation continued for two years.

With intense daily media advertising of products based on multivitamins and microelements that supposedly improve physical and mental performance, poisoning by such substances has become a considerable risk for patients. Such findings underpin the latest recommendation that those 65 years or older should receive around 800 IU of vitamin D per day. It should also be remembered that an intake of calcium supplements of 1,000 mg per day or more, combined with a high dose of vitamin D ( $\geq 800$  IU per day), may be harmful<sup>14</sup>.

Finally, well-balanced vitamin D levels are essential for maintaining the structural integrity

of bones and other processes of homeostasis of the human body<sup>15</sup>. Integrated health care for the elderly is required, considering all the variables that can interfere with the patient's condition between diagnosis and appropriate treatment. The case described herein is a useful example, as the important variable was the caregiver, who interfered with good intentions but caused irreversible harm to the patient. Communication must always be carefully established and monitored.

Even though the diagnosis of the case is described, the present study has limitations, such as the fact that the patient died a few years before publication, making it impossible for the team to obtain additional information, and resulting in reliance on retrospective interviews of an old case.

## CONCLUSION

The aim of the present study was to report a case of exaggerated vitamin D dosage due to failures in administration by the caregiver, and thus to alert physicians, patients and family members about the risks involved in the management of this supplementation.

Vitamin D replacement should be closely monitored, especially in geriatric cases, due to its potential risk of intoxication. Adequate monitoring is the responsibility of the patient, the family, and the medical staff.

With the increase in the use of this medicine, along with the aging population, hypercalcemia has become an increasingly common profile for medical care professionals in Brazil.

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