




# Risks of Supplementation with Excessive Doses of Vitamin D

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## ABSTRACT

Vitamin D poisoning was not frequent in Brazil until its increasing use in the last decade. In this article, we report a case of intoxication by intentional prescription of vitamin D in a much higher dose than the literature recommends, in order to prevent diseases via "hormonal modulation". The case described in this report was an elderly woman, previously healthy patient that was submitted to an unregulated treatment without scientific support, leading to symptoms such as nausea and vomiting, in addition to weight loss, lack of appetite, polyuria and asthenia over the months. Through the history and laboratory testing, vitamin D intoxication and acute kidney injury were diagnosed. After treatment, there was a complete remission of the symptoms. "Hormonal modulation" is a practice condemned by the Federal Councils of Medicine and Dentistry and by the Brazilian Society of Endocrinology and Metabology. The act of prescribing is of great ethical and technical responsibility and it must be based on scientific evidence. Thus, the patient can receive the best possible treatment, for either preventive or curative nature, by respecting the recommendations of the competent authorities and, therefore, minimizing risks and damages to patients.

**Keywords:** Ethics professional, Geriatrics, Acute kidney injury, Drug-related side Effects and adverse reactions, Vitamin D.

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## INTRODUCTION

Of singular importance to the endocrine system, vitamin D [25(OH)D] is a pro-hormone, which acts as a regulator of osteomineral physiology, especially of calcium metabolism and phosphorus balance, in addition to intervening in other physiological functions, such as the modulation of muscle function, growth and cell differentiation.<sup>1,2</sup>

Vitamin D poisoning was uncommon in Brazil until its increasing use in the last decade<sup>3</sup>. Several reports in the literature highlight accidental poisoning, especially in the elderly, due to error in intake, in the administration by caregivers, lack of understanding of the prescription or error in the formulation.<sup>4,5</sup>

In this article, we report a case of poisoning in which there was an intentional prescription of a dosage much higher than recommended in the literature, to prevent diseases, with the subterfuge of a "hormonal modulation", a practice condemned by the Federal Council of Medicine (CFM), Brazilian Society of Endocrinology and Metabolism (SBEM) and Federal Council of Dentistry (CFO).<sup>6-8</sup>

## CASE REPORT

A 67-year-old female patient seeks medical care with nausea, vomiting, constipation alternating with diarrhea and severe weakness, of inaccurate onset, lasting three to four months and progressively worsening. In addition to polyuria, weight loss, inappetence and insomnia.

She denies comorbidities, a history of cataract surgeries and varicose veins. The patient only mentions the use of medications prescribed by a non-medical professional for preventive "hormonal modulation", as she was aging and both daughters were recently treated for cancer (melanoma and breast cancer). The medications were handled and, according to the packages brought to the consultation, one of the preparations contained 50,000 IU Vitamin D per drop, and the instruction to use 2 drops daily.

In addition to another preparation containing Vitamin A 4000 IU/day, Vitamin K2 240 mcg/day, sublingual Oxytocin 10 IU/day and Zinc 15mg.

She had done physical exercises for several years, recently suspended due to intense asthenia.

On physical examination, the patient was underweight, with a BMI of 18.7 kg/m<sup>2</sup>, weight 44.5 kg and height 1.54 m, with no other changes.

Complementary exams performed in the week before diagnosis, requested by another professional, showed vitamin D above 210 ng/ml. With suspicion of vitamin D intoxication, calcium, potassium and renal function measurements were requested to confirm the diagnosis. In addition to the recommendation for hydration, immediate suspension of the use of vitamin D.

With the diagnostic confirmation of hypercalcemia (total corrected calcium 12.9 mg/dL) an emergency admission was performed.

During hospitalization, vigorous intravenous hydration was performed, and oral water intake was stimulated, on a calcium-restricted diet. After adequating blood volume, the use of furosemide and prednisone was started. She presented good clinical and laboratory evolution. Two days after admission, she was discharged from the hospital with prednisone for six days and outpatient follow-up.

After five days of diagnosis, the patient presented progressive improvement of symptoms - weakness, constipation, appetite and good laboratory evolution (Chart 1).

In the outpatient follow-up, bone densitometry was performed, which showed osteoporosis, and weekly doses of alendronate were prescribed to treat this condition and help maintain serum calcium.

Four months after stopping the use of vitamin supplements, the patient showed complete improvement in symptoms, regained weight (47.25 kg) and returned to her physical exercise routine. She maintained high levels of Vitamin D.

In accordance with circular letter n° 166/2018-CONEP/SECNS/MS, this case report was approved by CEP/SCS/UFPR, embodied opinion number 4.161.100.

## DISCUSSION

In the case reported, the patient searched for preventive treatments, thinking about her aging and the fact that her two daughters have recently been diagnosed with different and severe forms of cancer, being currently assisted by a professional who guided her to perform "hormonal modulation".

SBEM has already issued an official opinion clarifying that "(...) there is no specialist in Hormone

**Chart 1** Test results by date. Toledo, PR, 2019/2020.

	<b>Creatinine (mg/dL)</b>	<b>Total Calcium (mg/dL)</b>	<b>Ionized Calcium (mmol/L)</b>	<b>PTH (pg/mL)</b>	<b>Vit D 25(OH)D (ng/mL)</b>	<b>Urea (mg/dL)</b>	<b>Phosphorus (mg/dL)</b>
<b>Reference</b>	0,5 - 1,0	8,5 - 10,2	1,05 - 1,30	15 - 65	30 - 60	15 - 45	2,5 -4,8
<b>Pre Replacement</b>		9,8		69,4	*		
<b>Diagnosis</b>	<b>1,37</b>	<b>13,4</b>	<b>1,59</b>	28,4	> 210	<b>66</b>	4
<b>Internment</b>	0,89	9,02				47,41	2,85
<b>4 days **</b>	0,96	11	1,34			<b>61</b>	
<b>1 week**</b>	0,88	10,6				42	
<b>1 month**</b>	0,69	9,2	1,2			32	
<b>5 months**</b>	0,99		1,2	57,7	89,03	48,11	

**Source:** Laboratory, 2019/2020. \* dosage of 1.25 OH Vit D: 47,9 (ref 19,9 - 79,3) \*\* After discharge

Replacement and is not recognized by the CFM as a specialty entitled "Hormonal Modulation". Hormone replacement is a medical act and can only be done by medical professionals. The specialty that deals with hormonal changes is Endocrinology and Metabolism. The replacement of any hormone must be made based on its deficiency, with specialized medical supervision, observing the risks and benefits of its use; there is no support in the medical literature for the use of hormonal preparations to delay aging. (...).<sup>7</sup> In addition to SBEM, other entities have already taken a stand against this practice, such as the CFO, through RESOLUTION CFO-199, of January 29<sup>th</sup>, 2019, which states: "(...) The prescription is prohibited for dentists and the dissemination of therapies called modulation and/or replacement and/or supplementation and/or hormonal physiology, as well as the use of any other terms not scientifically recognized, outside its area of competence and performance".<sup>8</sup>

Besides the hormonal modulation not being a practice accepted by the class councils, the medication prescribed to the patient contained the hormone Oxytocin and high doses of vitamins with values higher than those recommended by ANVISA in RDC number 269/2005, which establishes norms for daily dosage levels of vitamins and minerals in medicines.<sup>9</sup>

The CMF resolution nº 1999/2012 regulates and limits the use of hormonal therapies with the aim of delaying, modulating or preventing the aging process. This resolution also prohibits the use of vitamins and antioxidants referred to as anti-aging, anti-arteriosclerosis, anti-cancer therapy or aimed at

the treatment of chronic-degenerative diseases; except in cases of deficiencies with a confirmed diagnosis, whose replacement has scientifically proven benefits.<sup>6</sup>

There is still no consensus in the literature regarding the role of vitamin D in preventing mortality, reducing cardiovascular risk, cancer and autoimmune diseases. The probable extra-skeletal effects of vitamin D are of great scientific interest; however, so far, there is no scientific support for the prescription of supplementation of high doses of this substance aiming at effects beyond bone health.<sup>10-12</sup>

Therefore, we understand that the prescription given to the patient is in disagreement with the legislation and the literature, since there are no proven benefits in relation to the prescribed dosage, but rather several risks. Therefore, the professional acted with malpractice and recklessness.<sup>6,13</sup>

The presentation of vitamin D toxicity can range from asymptomatic to severe, life-threatening symptoms, mostly due to hypercalcemia.<sup>12</sup> They may be neuropsychiatric (confusion, psychosis, stupor or coma), cardiovascular (complications with the QT interval, ST-segment elevation, bradyarrhythmias) or gastrointestinal manifestations, as in the case described: abdominal pain, nausea, polydipsia, anorexia and constipation.<sup>5,14</sup> The patient also had renal complications: acute kidney injury (calculated clearance 31.7) and dehydration.

The diagnosis of intoxication is established by increasing 25(OH)D concentrations above 100 ng/ml, followed by hypercalcemia, severe hypercalciuria and a decline or undetectable activity of parathyroid hormone (PTH).<sup>14</sup>

In this case, the patient was indicated for screening for vitamin D deficiency, with the dosage of 25(OH)D concentration. This was an elderly patient with low weight and risk factors for osteoporosis, which was confirmed during the investigation. Supplementation focusing on bone health should only be performed after confirmation of levels below the recommended level.<sup>15</sup>

The guideline in cases of vitamin D 25[OH] D insufficiency (values below 20ng/mL) is vitamin D supplementation through cholecalciferol (D3) or ergocalciferol (D2) with a loading dose of 50,000 IU/week or 7,000 IU/day for eight weeks, followed by a support dose between 1,000 and 2,000 IU/day.<sup>5,16</sup>

The patient was prescribed a dose of 700,000 IU/week, 14 times higher than the loading dose, with no recommendation on the time of use, and no dosage prior to prescription.

The treatment strategy for vitamin D poisoning consists of pausing supplementation, reducing calcium intake, administering isotonic sodium chloride solution to restore kidney function and correct dehydration as soon as the volume is restored and maintained. Loop diuretics and glucocorticoids can be added to help lower plasma calcium levels, as performed in the case reported.<sup>14</sup> In severe cases of hypercalcemia, antiresorptive therapy using calcitonin and bisphosphonates may be helpful.<sup>17-19</sup>

To reduce the concentration of 25(OH)D in the body, phenobarbital, aminoquinolines (chloroquine, hydrochloroquine), ketoconazole, rifampicin, or specific inhibitors of CYP27B1 (1 $\alpha$ -hydroxylase) could be used. All drugs with many unwanted side effects and numerous drug interactions, should be avoided, especially in the elderly population.<sup>14</sup>

The consequences of supplementation with excessive doses of vitamin D are considerable, leading to intoxication with severe complications, such as kidney damage and potentially fatal outcomes. The competent authorities condemn treatments without scientific evidence with promises of eternal youth and miraculous cures. It is worth noting that the prescription of the substance, often considered harmless by some, culminated in this case in specialized care and hospitalization, generating unnecessary costs to the health system, since the patient was previously healthy. The act of prescribing is of great responsibility, the professional must be responsible (ethically and technically) not only for the prescription, but also for patient care throughout the process, monitoring the outcomes, and adverse effects or complications if they occur, performing the prompt treatment of these.

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