



Vitamin D Intoxication with Hypercalcemia Due to Overuse of Supplement

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ABSTRACT

We describe a patient with hypercalcemia associated with the injection of high doses vitamin D as supplement for a period of six months. A 76-year-old woman had been taking an intramuscular injection of vitamin D 300,000 IU every ten days for six months. She was hospitalized with symptoms of hypercalcemia: chronic constipation, unstable gait, a chronic generalized musculoskeletal pain and increased fatigue. On admission her 25 (OH) vitamin D and Calcium levels were 559 nmol/L and 13.85 mg/dL respectively, and Parathyroid Hormone (PTH) level was 7.1 pg/mL. Immediately she received diuresis therapy with saline and furosemide in conjunction with calcitonin and pamidronate. At discharge her serum calcium level was 11.5 mg/dL. To lower endogenous overproduction of calcitriol, prednisolone 20 mg/day for 10 days was administered at discharge time.

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Introduction

For many people the word “vitamin” expresses a beneficial and essential component for healthy life (1) and some like to take supplements including vitamin D without a physician order. While vitamin D toxicity is rare (2), most of reported cases are due to oversupplementation. In order to avoid vitamin D intoxication health care providers and pharmacists should encourage patients to use supplements containing vitamin D exclusively by physician order required.

We present a patient who developed hypercalcemia after arbitrary administration of 300,000 international units (IU) vitamin D every ten days as intramuscular (IM) route for six months.

Case Presentation

A 76-year-old woman was admitted in Dr. Shariati

hospital affiliated to Tehran University of Medical Sciences (TUMS) with chief complaining of lack of appetite and constipation for two weeks. Her past medical history included diabetes from 15 years ago along with hypertension, stage 4 chronic kidney disease and heart failure with New York Heart Association (NYHA) functional class III. Review of systems was significant for abdominal pain, chronic constipation, loss of strength in legs with unstable gait, a chronic generalized musculoskeletal pain, increased fatigue, and polyuria. Her family history was unremarkable. Her drug history included Atenolol 100 mg once a day, Triamterene/Hydrochlorothiazide 50/25 mg once a day, Aspirin 80 mg once a day, Isosorbide dinitrate 40 mg once a day, Losartan 50 mg once a day, Atorvastatin 40 mg once a day, Metformin 500 mg three times a day, and Calcium (as carbonate) 500 mg once a day. On examination, her blood pressure was 130/80 mmHg and she was afebrile. The rest of her physical examination was unremarkable.

Since 6 months prior to her admission, she had been taking 300,000 IU Cholecalciferol injections every ten days without any medical advice. She had no history

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of smoking or alcohol consumption. Upon admission her fasting blood glucose was 220 mg/dL. Laboratory analysis revealed normal serum level of Sodium (141 mg/dL), Potassium (4.1 mg/dL) and Phosphorus (3.2 mg/dL) but there was a rise in serum level of Calcium (13.85 mg/dL) and Creatinine (2.85 mg/dL; estimated glomerular filtration rate: 17 mL/min/1.73 m²). High serum level of 25 (OH) Vitamin D (559 nmol/l) was detected along with intact Parathormone level of 7.1 pg/mL (normal range 10-65 pg/mL) and raised Alkaline Phosphatase level (571 IU/L). Complete blood count parameters were within normal reference range. She had normal findings on chest radiography, computed tomography of the chest, neck, and abdomen. The patient was diagnosed with vitamin D intoxication on the basis of the medical history, clinical and laboratory findings. Her hypercalcemia was a result of hypervitaminosis D and deteriorated by calcium-induced diuresis, hypovolemia, and renal insufficiency.

Patient was managed by normal saline 200 mL every 2 hours for first 24 hours and then 1000 mL daily. Since the patient was prone to volume overload as a result of reduced renal function, furosemide 80 mg every 2 hours was also initiated and continued for 24 hours, which could also facilitate calcium excretion. Saline and diuretic therapy is an effective modality in treatment of hypercalcemia. Calcium level fell to 13.12 mg/dL after 24 hours saline and diuretic therapy. For rapid reduction of serum calcium concentration, six hours after saline/diuretic therapy calcitonin was added. In the second day of treatment calcium level was 12.88 mg/dL, since calcitonin effectiveness lasts for up to 48 hours, pamidronate was added to the regimen. The administered calcitonin dose was 4 IU/kg (200 IU for this patient) Intramuscular (IM) every 12 hours for 2 days along with a single dose pamidronate 90 mg IV over 2 hours (3, 4). Twenty four hours after pamidronate infusion, her muscle strength improved.

Level of calcium was measured every 6 hours. After 6 days level of calcium dropped to 11.5 mg/dL. On the seventh day, patient was discharged with prednisolone 20 mg/day for 10 days.

Discussion

Vitamin D is an important pro-hormone which plays important role in calcium homeostasis and bone mineral metabolism. Vitamin D appears to have effects on a wide range of biological functions in cell differentiation, inhibition of cell growth and immune modulation (5). The adult Recommended Daily Allowance (RDA) is 15 mcg (600 IU) which increasing to 20 mcg (800 IU) after age 71 and "tolerable upper intake level" (UL) for vitamin D is 100 mcg (4000 IU) daily for healthy adults (6). The beneficial amount is more likely to be 10-12.5 mcg (800-1000 IU) per day, on the basis of bone density measurements and fracture prevention in the elderly (7-9). For vitamin D, No

Observed Adverse Effect Level (NOAEL) is defined as the highest 25(OH) D concentration which may not cause hypercalciuria in healthy subjects. There is no evidence of adverse effects with serum 25(OH) D concentrations < 140 nmol/L, which require a total vitamin D supply of 250 mcg (10 000 IU) per day to attain (10, 11).

Many reports of vitamin D toxicity have been explained a daily intake of >1000 mcg (40 000 IU) can cause an evidence of hypercalcemia. This dosage could result in a serum 25 (OH) vitamin D concentration above 200 nmol/l which has been considered as Lowest Observed Adverse Effect Level (LOAEL) (12-15).

Excessive vitamin D intake is associated with additional significant clinical adverse effects, including pain, conjunctivitis, anorexia, fever, chills, thirst, vomiting, and weight loss. These are all due to hypercalcemia and occur only at very high vitamin D intakes (16). Hypervitaminosis D is characterized by high serum levels of 25-hydroxyvitamin D, hypercalcemia, hypercalciuria, and hyperphosphatemia (17). Serum parathyroid hormone levels are inversely correlated with 25(OH) vitamin D levels (18).

Our case was taken 300,000 IU Cholecalciferol injections every ten days for six months. The patient was diagnosed with vitamin D intoxication on the basis of the medical history, clinical and laboratory findings. She needed an emergent treatment. She received normal saline as intravenous hydration and furosemide to further increase urinary excretion (19, 20). Calcitonin was added to diuresis therapy for rapid reduction of calcium level by increasing renal calcium excretion and decreasing bone resorption via interference with osteoclast maturation (21-23). In symptomatic patients with moderate hypercalcemia, concurrent therapy with a bisphosphonate with or without calcitonin is necessary, which binds to bone hydroxyapatite and inhibits calcium release by interfering with osteoclast-mediated bone resorption (24, 25). To reduce calcium effectively, pamidronate was administered in conjunction with normal saline, furosemide and calcitonin. Onset of action for saline, calcitonin and bisphosphonate is few hours, 4 to 6 hours and 24 to 72 hours, respectively. Accordingly calcium excretion initiates at first hours of treatment and maximizes during 72 hours after starting of treatment. The duration of action of bisphosphonates is as long as 2 to 4 weeks (26).

In the current case, serum calcium level was 11.5 mg/dL at discharge. To lower endogenous overproduction of calcitriol prednisolone 20 mg/day for 10 days was administered at discharge. Prednisolone will usually reduce serum calcium concentrations within two to five days by decreasing calcitriol production and increasing renal calcium excretion. Effects of glucocorticoids on serum calcium last from days to weeks (26).

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