Hyper Vitaminosis D: Are we Overprescribing Vitamin D?

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Abstract

Vitamin D, the sunshine vitamin is now considered to be a hormone due to its important role in many physiological functions. Vitamin D deficiency has been associated with many disorders ranging from bone diseases, cardiovascular diseases to cancer. Hence, there is a recent surge in the empirical prescription of vitamin D for various disorders without documentation of vitamin D deficiency and monitoring the treatment. We report a case of iatrogenic hypercalcemia and acute kidney injury due to vitamin D toxicity after empirical and overzealous use of vitamin D and calcium supplements. We present this case to remind clinicians the importance of monitoring the patients treated with mega doses of vitamin D.

Keywords: Acute kidney injury, cholecalciferol, hyper vitaminosis D, iatrogenic hypercalcemia

Introduction

Activated vitamin D (1,25 OH vitamin D) plays a crucial role in a plethora of physiological functions. Vitamin D deficiency is associated with various illnesses other than disorders of calcium metabolism, including infectious diseases, autoimmune diseases, cardiovascular disease, type 2 diabetes mellitus, and some cancers.1 Hence, vitamin D is now a frequently
prescribed drug for various disorders. Unfortunately, there is lack of awareness of the various preparations and dosages of this hormone. This occasionally leads to avoidable errors in prescription, leading to unwanted side effects.

Case Report

A 46-year-old female patient was referred to the Department of Nephrology for evaluation of renal failure. She gave a history of low backache for the past 2 years. Since then, she has been on several medications. She denied history of reduced urine output or pedal edema. Her blood pressure was 110/80 mm of Hg. Neurological examination was significant for tenderness and bony step at the level of L5. Her motor and sensory examination was normal.

The laboratory investigations revealed the following results: Hemoglobin 9.4 g/dL, erythrocyte sedimentation rate 18 mm/1 h, urine analysis showed no proteinuria and no deposits, urea 120 mg/dL, creatinine 2.2 mg/dL, Na 130 mEq/L, potassium 3.6 mEq/L, calcium 13.7 mg/dL, phosphorus 3.0 mg/dL, serum bilirubin 0.9 mg/dL, albumin 3.2 g/dL, total protein 5.6 g/dL, alanine transaminase 38 IU/L, aspartate transaminase 42 IU/L, and alkaline phosphatase 155 IU/L. X-ray of spine showed lumbar spondylolisthesis of L5 over S1 and diffuse rarefaction of bone [Figure 1]. Magnetic resonance imaging of lumbosacral spine showed lumbar spondylolisthesis of L5 over S1 [Figure 2]. Bone mineral density by Dual-energy X-ray absorptiometry scan was suggestive of osteoporosis with a T score of −2.9 and Z score of −2.4.

The patient was managed by continuous saline infusion, diuretics, and bisphosphonates. Parathyroid hormone (PTH) was 13.54 pg/mL and vitamin D 25(OH) was >150 ng/mL. Retrospectively, while reviewing her previous medical prescriptions, it was found that she had received multiple prescriptions of oral calcium carbonate, oral cholecalciferol, and oral calcitriol over the last 2 years. Two months earlier, she had also received intramuscular injections of cholecalciferol 600,000 IU daily for 20 consecutive days. Serum and urine protein electrophoresis was negative for M protein. Malignancy screen was negative.

Patient was advised surgery for spondylolisthesis for which the relatives refused to. She was discharged after 2 weeks with serum calcium and creatinine of 12.1 mg/dL and 1.6 mg/dL, respectively. During her last follow-up, her calcium was 10.9 mg/dL and creatinine was 1.1 mg/dL. She was started on oral bisphosphonates for osteoporosis.

Discussion

Vitamin D has achieved increasing prominence over the past few decades in the research publications. 1,25(OH)₂D₃ is now considered to be a steroid hormone and functions the same way as other steroid hormones by interacting with its vitamin D receptor (VDR). Over the past several decades, various research has shown that the VDR is widely distributed among various body tissues than previously thought (intestine, bone, kidney, and parathyroid).[2] The pluripotent steroid hormone
1,25(OH)₂D₃ initiates the physiologic responses of at least 36 cell types that possess the VDR. In addition to the production of circulating 1,25(OH)₂D₃ in the kidneys, researchers have found a paracrine production of this steroid hormone in at least 10 extra renal organs.

Vitamin D has been found to have important role the adaptive immune system, the innate immune system, insulin secretion by the pancreatic β cell, myocardial functioning, blood pressure regulation, and brain and fetal development.[2] Vitamin D depletion has been associated with increased risk of osteoporosis, hip fracture in the elderly, hypertension, cardiovascular disease, and some types of malignancies.[1] Vitamin D deficiency prevails in epidemic proportions even in a tropical country like India, with a prevalence of 70%–100% in the general population.[3] Therefore, it is not surprising that vitamin D supplements are being prescribed for various diseases. Many patients are given vitamin D supplements empirically in doses much beyond the recommended doses, without the laboratory evidence of vitamin D deficiency and without monitoring.

In patients taking vitamin D preparations monitoring should be done by periodic estimation of 24-h urinary calcium excretion, which should not exceed 250 mg.[4] Vitamin D is toxic in huge doses and reports of vitamin D toxicity exist in literature.[5] Vitamin D intoxication usually occurs at levels of 25(OH) vitamin D > 150 ng/mL.[6] The clinical manifestations are kidney disorders (65.0%), renal insufficiency (51.0%), gastrointestinal tract disorders (23.0%), and arterial hypertension (52.0%).[7] The management of these patients includes withdrawal of the offending agent/s, intravenous volume expansion, furosemide, bisphosphonates and hydrocortisone in selected cases. Complete recovery of renal function can occur if the diagnosis is made early in the course of the disease.

In our patient, hypercalcemia was parathyroid independent, as the serum levels of PTH was low normal. The malignancy as the cause of hypercalcemia was ruled out by absence of clinical and laboratory evidence of malignancy.

Conclusion

The toxic potential of mega doses of vitamin D therapy is still not generally appreciated among health care providers. This case report highlights that large doses of vitamin D prescribed without adequate supervision can be potentially toxic despite its wide margin of safety. This case questions the rationale behind empirical treatment with vitamin D and calcium supplements. Vitamins are generally considered to be beneficial and not harmful. Nevertheless to say anything that is overdone becomes dangerous.

Footnotes

Source of Support: Nil.
Conflict of Interest: None declared.

References


Figures and Tables

Figure 1
X-ray lumbosacral spine spine lateral view showing spondylolisthesis of L5 over S1

**Figure 2**
Magnetic resonance imaging spine showing spondylolisthesis of L5 over S1