Case Study: An Accidental Overdose of Ergocalciferol

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Introduction

This article examines the case study of an elderly gentleman on hemodialysis who mistakenly took high dose ergocalciferol daily over a two month period of time. This subsequently resulted in a 25(OH) vitamin D level of 307 ng/mL.

Case Study

DW is an 84 year old Caucasian male who was diagnosed with chronic kidney disease (CKD) Stage 5 and started maintenance hemodialysis in late November of 2008. He has a medical history of hypertension, dyslipidemia, type 2 diabetes mellitus (diagnosed 2007), prostate cancer with radiation therapy treatment, gout, dementia, and anemia secondary to CKD (treated with an erythropoiesis-stimulating agent). DW and his spouse are very interested in his medical care. He is generally compliant with his prescribed medications and specialized diet.

Upon admission to the dialysis unit, he underwent a nutrition evaluation by the dietitian. Though DW gardens as a hobby, he was deemed at risk for vitamin D deficiency due to limited sun exposure. While working outdoors, the patient wears full-length trousers and has only minor skin exposure to the sun. The dietitian recommended a start of over-the-counter (OTC) 1,000 IU cholecalciferol given twice daily by mouth. DW preferred the specific prescription information, regarding OTC vitamin D, be sent to his pharmacy, so it was faxed there on December 11, 2008.

This patient was hospitalized from January 22 to January 28, 2009 with a right lower lobe pneumonia. He was treated with antimicrobial therapy. No other major medical events occurred between mid-December 2008 and mid-February 2009.

On February 13, 2009, DW's 25(OH) vitamin D, vitamin D2, and vitamin D3 levels were tested. The total vitamin D level was 307 ng/mL with vitamin D2 of 307 ng/mL and vitamin D3 of < 4 ng/mL. The average level of 25(OH) vitamin D for patients in DW's dialysis unit was 33 ng/mL. It is inconceivable DW could have consumed enough vitamin D2 in his diet alone to achieve these high levels. Additionally, his sun exposure was sparse and would increase vitamin D3 levels, not vitamin D2 levels. After interviewing the patient, the dietitian contacted the head pharmacist at the patient's drug store. The pharmacist reviewed the patient's prescriptions and stated DW had incorrectly received 50,000 IU ergocalciferol tabs in place of the 1,000 IU cholecalciferol tabs.

DW had taken 2 tabs of ergocalciferol daily since mid-December of 2008. That is 100,000 IU ergocalciferol daily for almost two months. His vitamin D supplement was subsequently discontinued.

During this period, DW's calcium levels ranged from 8.8 – 10.0 mg/dL. He was taking a calcium-based phosphate binder, 667 mg calcium acetate, 2 tabs by mouth with meals. The patient did not receive any vitamin D analogs during this period. Table 1 shows the patient's laboratory chemistries with the lightly shaded area indicating the period of his ergocalciferol use.

Discussion

Vitamin D deficiency, a 25(OH) vitamin D level < 30 ng/mL, is widespread among dialysis patients. In a cross-sectional analysis of 825 CKD Stage 5 patients, it was reported 78% of the population suffered from this deficiency (1). Inadequate serum 25(OH) vitamin D has been associated with cardiovascular disease risk factors (2) and increased mortality (1). In the case of deficiency, vitamin D supplementation is the prudent course of action, yet one concern is the safety of this vitamin. In an *American Journal of Clinical Nutrition* 2008 article, Glenville Jones has suggested a vitamin D toxicity threshold of 300 ng/mL 25(OH) vitamin D (3). Additionally, Tokmak et al, examined the effect of high dose cholecalciferol, 20,000 IU, on a randomized treatment group of hemodialysis patients over fifteen months in comparison with a control group who were supplemented for only nine months. They found no negative effects of the high dose supplementation suggesting that increased levels may be needed to replenish vitamin D levels (4).

If hypercalcemia is the chief criterion for vitamin D toxicity (5), then DW did not achieve a harmful level of 25(OH) vitamin D. Dr. Reinhold Vieth, a leading researcher of vitamin D has noted "Vitamin D toxicity is the result of excessive levels of 'free' 1,25-$(OH)_2$D displaced from its carrier protein, vitamin

Table 1
DW's Laboratory Values

	Lab Norm	12/1/08	12/16/08	1/6/09	1/20/09	2/3/09	2/17/09	3/3/09	3/17/09
Calcium (mg/dL)	8.5-10.5	9.8	8.8	9.4	10	9.9	9.8	9.1	9.3
Corrected Calcium (mg/dL)	8.4-10.2	9.8		9.4		10		9.3	
Albumin (g/dL)	3.5-4.7	4.3		4.0		3.9		3.7	
Intact PTH (ng/L)	150-300	66		66		30		70	
Alkaline Phosphatase (U/L)	38-126	36		35		36		30	
Creatinine (mg/dL)	0.7-1.5	3.91		3.74		5.36		8.09	
Hemoglobin (g/dL)	11-12	11.1	11.3	12.1	11.7	12.5	13.2	12.8	12.4
Epoetin Dose (units)	hemoglobin dependent	7700				6600	5500	HOLD	

*lab norms may vary by facility.

D-binding protein, when there is a vast excess of other vitamin D metabolites" (6).

1,25-$(OH)_2$ vitamin D (calcitriol) and vitamin D analogs have an exponentially greater effect upon serum calcium levels than 25(OH) vitamin D, though circulating levels of the latter are approximately 1,000 fold greater than that of the former. Calcitriol is a potent agent for increasing intestinal calcium absorption which can lead to hypercalcemia. ESRD patients convert very little 25(OH) vitamin D to 1,25-$(OH)_2$ vitamin D at the endocrine level. However, these patients will continue to use 25(OH) vitamin D as a substrate for 1,25-$(OH)_2$ vitamin D production at the autocrine and/or paracrine level with influence by the parathyroid hormone (7).

Given the diminished ability of CKD Stage 5 patients to produce 1-alpha-hydroxylase at the endocrine level, the tolerable upper level of vitamin D in this population may be higher than that of the general population. A study by Frohling et al, which involved administration of 600,000 IU ergocalciferol weekly over several months, concluded that patients with renal impairment handle high doses of vitamin D differently than normal subjects (8).

Conclusion

In our patient, a gradual high intake of ergocalciferol over two months did not appear to cause toxicity. Given the relative safety of this vitamin, the ease of monitoring toxicity via bimonthly calcium testing, and its potential for reduction of mortality and co-morbidity rates, 25(OH) vitamin D levels should be tested annually in the CKD Stage 5 population. Vitamin D supplementation, a relatively inexpensive intervention, for those with 25(OH) vitamin D levels < 30 ng/mL, should be recommended. ◆

References

1. Wolf M, Shah A, Gutierrez O, et al. Vitamin D levels and early mortality among incident hemodialysis patients. *Kidney Int.* 2007;72(8):1004-1013.
2. Martins D, Wolf M, Pan D, et al. Prevalence of cardiovascular risk factors and the serum levels of 25-hydroxyvitamin D in the United States: data from the Third National Health and Nutrition Examination Survey. *Arch Intern Med.* 2007;167(11):1159-1165.
3. Jones G. Pharmacokinetics of vitamin D toxicity. *Am J Clin Nutr.* 2008;88(2):582S-586S.
4. Tokmak F, Quack I, Schieren G, et al. High-dose cholecalciferol to correct vitamin D deficiency in hemodialysis patients. *Nephrol Dial Transplant.* 2008;23(12):4016-4020.
5. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. *1997 Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington D.C. USA:National Academy Press; 1997.
6. Vieth R. The mechanisms of vitamin D toxicity. *Bone Miner.* 1990;11:267-272.
7. Vander A, Sherman J and Luciano D. *Human Physiology: The Mechanisms of Body Function.* 8th ed. New York, NY: McGraw-Hill Companies, Inc; 2001:541-542.
8. Frohling P, Kokot F, Vetter K, Kuska J, Kaschube I and Pietrek J. Serum 25-Hydroxyvitamin D in Patients with Chronic Renal Failure on Long-Term Treatment with High Doses of Vitamin D2. *Nephron.* 1980;26:116-120.