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Hypercalcemia in a Weight Lifter on Nutritional Supplements

Beslenme Takviyeleri Alan Bir Haltercide Hiperkalsemi

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Abstract

Hypercalcemia commonly occurs secondary to hyperparathyroidism or malignancy. We describe a case of a young weightlifter who had been consuming over the counter multivitamin pills containing vitamin A and D and was detected to have hypercalcemia, metastatic calcification and renal insufficiency. The relevant literature on vitamin A and D intoxication and hypercalcemia is reviewed. *Turk Jem 2015; 19: 31-33*
Key words: Hypercalcemia, vitamin A, vitamin D

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Özet

Hiperkalsemi sıklıkla hiperparatiroidzm veya maligniteye sekonder oluşur. Bu yazıda, reçetesiz satılan A ve D vitaminleri içerikli multivitamin hapları kullanan ve hiperkalsemi, metastatik kalsifikasyon ve böbrek yetmezliği olduğu tespit edilen bir genç halterci sunulmaktadır. Vitamin A ve D intoksikasyonu ve hiperkalsemi ile ilgili literatür gözden geçirilmiştir. *Turk Jem 2015; 19: 31-33*
Anahtar kelimeler: Hiperkalsemi, A vitamini, D vitamini

Çıkar Çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemiştir.

Introduction

Athletes, amateur or professional, use dietary supplements to enhance performance. Among the list of supplements considered legal, the commonly used ones include multi-vitamins, vitamin C, minerals, protein powder/bar, iron, calcium, and creatine (1). There is a renewed interest in use of vitamin D by athletes due to reports of deficiency in those involved in indoor sports and trials showing improvement in muscular performance after supplementation (2). However, unsupervised consumption of vitamins exceeding the tolerable upper limit can occasionally be counterproductive. We report the case of a weightlifter who developed features of hypercalcemia and acute kidney injury after self-medication with over the counter preparation of multi-vitamins.

Case Report

A 22-year-old amateur weightlifter was detected to have elevated blood pressure when he reported for routine medical examination. He gave no history of headache, seizures, vomiting, visual blurring, angina, and dyspnea. There was no history of episodic palpitations, headache, sweating, weight gain or loss, or ankle swelling. He denied history of intake of any banned performance-enhancing drugs, such as anabolic steroids, growth hormone, diuretics or erythropoietin. However, he admitted to using protein supplements and over the counter multi-vitamin pills. On examination, he was of athletic build, with Body mass index (BMI) of 21.3 kg/m^2. Blood pressure was 160-180 /110-124 mmHg, pulse -78/min; all pulses were palpable and felt equally. On fundus examination there were no changes of hypertension or papilledema. Systemic examination and haemogram were normal. Urine RE/ME showed presence of calcium oxalate crystals. Blood urea and serum creatinine levels were 69 mg/dL (10.4-28) and 3.4 mg/dL (0.7-1.1), respectively. Serum calcium (corrected for albumin) was found to be elevated [13.7 mg/dL (8.6-10.6)]. Serum phosphate [3.7 mg/dL (2.5-4.6)] and alkaline phosphatase [61U/L (39-117)] levels were normal. Electrocardiography showed convex 2 mm ST elevation in leads V1-V3, abdominal ultrasound showed normal-sized kidneys, increased echotexture, loss of corticomedullary differentiation and multiple 5-7 mm nonobstructive renal calculi. Multiple foci of calcification were noted in the pancreas. Renal dynamic scan showed total GFR of 53.7 ml/min (85-125). In view of hypercalcemia, evidence of metastatic calcification with renal impairment, further tests were conducted to establish the etiology. Twenty-four hour urine was collected and analyzed for calcium, which revealed hypercalciuria

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[324 mg (normal upper limit 4 mg/kg)]. Serum parathormone was suppressed [4.80 pg/mL (15.6-68.0)]. In view of the history of intake of vitamin supplement and suppressed PTH, the level of 25 hydroxy cholecalciferol [25 (OH) D_3] was estimated and found to be 375 nmol/L (75-250). When confronted with the results of his tests showing 25 (OH) D_3 levels in toxic ranges, he gave details of intake of vitamin pills (Table 1). He had been taking them for four months to boost physical strength.

Serum 1,25 dihydroxycholecalciferol [1,25 $(OH)_2$ D_3] and retinol levels could not be estimated due to lack of facility. The patient was diagnosed to have chronic vitamin A and D intoxication resulting in hypercalcemia, metastatic calcification and chronic kidney disease. The patient was advised to refrain from taking any further vitamin supplement. He was asked to increase fluid intake and was started on furosemide and amlodipine tablets. Repeat evaluation two months later showed normalization of blood pressure. Serum calcium (10.5 mg/dL) and urea (25 mg/dL) had normalized, however, serum creatinine (2.5 mg/dL) remained elevated.

Discussion

The presentation of hypercalcemia is protean ranging from incidental biochemical abnormality to multiorgan presentation involving musculoskeletal, gastrointestinal, renal, central nervous system and cardiovascular systems. Hyperparathyroidism and malignancy account for majority of cases of hypercalcemia (3). Less common causes of hypercalcemia include vitamin D intoxication, sarcoidosis, tuberculosis, fungal infections and milk-alkali syndrome among others (4).

The US Institute of Medicine has designated 15 µg/day (600 IU) and 100 µg/day (4000 IU) as recommended dietary allowance (RDA) and tolerable upper limit of intake of vitamin D intake in adults. These are doses which cause no hypercalcemia, hypercalciuria or ectopic calcification (5). Vitamin D increases calcium absorption from the gut through the action of its active metabolite 1,25 di-hydroxy vitamin D_3 [1,25 $(OH)_2D_3$]. 1,25 $(OH)_2$ D_3 increases transcellular calcium transport in the columnar cells of the intestine by increasing the expression of luminal calcium channels and calbindins (6). The mechanism of hypercalcemia in patients with vitamin D intoxication is postulated to be increased in the production of 1,25 $(OH)_2$ D_3 due to increase in serum levels of precursor 25(OH) D_3. However, two more mechanisms have been proposed: direct binding of precursor 25(OH) D_3 to vitamin D responsive elements in the nucleus of target cells and displacement of 1,25 $(OH)_2$ D_3 from vitamin D-binding protein and leading the "free form" to act on the nuclear receptors. Jones, after reviewing case reports of vitamin D intoxications, concluded that 25(OH) D_3 alone was a good biomarker for vitamin D intoxication. Hypercalcemia due to vitamin D intoxication occurs only when 25 (OH) cholecalciferol levels are higher than 375-500 nmol/L (7).

Table 1. Daily intake of Vitamin A, Vitamin D & Calcium by the patient (see text for RDA)

Name of Formulation	Tablets consumed per day	Daily intake Vitamin A (IU)[a]	Dailyintake Vitamin D (IU)[b]	Elemental Calcium (mg)
Supradyn	2	20000	2000	20
Revital	2	4000	400	150
Actymin Forte	2	5000	400	5
Shelcal	2	-	500	1000 mg
Multivitamin	2	-	400	-
Total		29000	3700	1275

[a]: Multiply by 0.3 to get µg of Retinol equivalent. [b]: Multiply by 0.025 for µg

The RDA and tolerable upper limit of preformed vitamin A intake for adult males is 900 µg/day (3000 IU) and 3000 µg/day (10000 IU) respectively (5). Acute hypervitaminosis A occurs due to consumption of 100xRDA over short duration lasting few days and is characterized by headache, vertigo, nausea, vomiting, peeling of skin and convulsions. Chronic toxicity has been reported to occur due to consumption of more than 25.000 IU/day of retinol esters for more than six years or more than 100.000 IU for six months. Prolonged intake of excess vitamin A leads to osteoporosis and pathological fractures (8). This loss of bone mass has been attributed to stimulation of osteoclasts on periosteal surface of cortical bone by vitamin A. Hypercalcemia has been documented in patients with chronic hypervitaminosis A. Most cases have occurred due to prescription errors, supplementation of vitamin A in patients with renal insufficiency and in those treated with all-trans-retinoic acid for acute promyelocytic anemia (9,10).

Our patient was consuming over the counter preparation of multivitamins with total vitamin A in doses twice the tolerable upper limit for four months prior to presentation and which resulted in hypercalcemia. That one of the preparations had vitamin A at tolerable upper limit cannot be overlooked and could be the one which contributed significantly to the over dosage. The total vitamin D intake was above the RDA but below the tolerable upper level of daily intake. It also contributed to hypercalcemia as serum 25(OH) D_3 level was elevated. The renal insufficiency resulting from hypercalcemia may have contributed further to the toxicity of vitamin A, as renal insufficiency is known to reduce conversion of retinol to retinoic acid, and to increasing levels of retinol binding protein (11). We, however, did not have the facility to estimate serum retinol levels. Rocha et al. have reported a case of hypercalcemia and acute kidney injury in a young individual who was self injecting a veterinary formulation of vitamin A and D for improving physical appearance (12). This case highlights the growing need to educate those pursuing athletics and power sports that over the counter multivitamin preparations which are considered legal for enhancing performance can be harmful if taken without guidance.

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