Hypercalcaemic Crisis — A Case Study of Three Unusual Cases of Iatrogenic Vitamin D and Calcium Intoxication

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Abstract
Severe hypercalcaemia is potentially life-threatening complication of several diseases. Most commonly it is caused by cancers that enhance bone resorption. Though rare, Vitamin D intoxication is an important cause of hypercalcaemia. Massive doses of ergocalciferol continue to be prescribed inappropriately or without adequate supervision and the dangers to this therapy are still not appreciated. We studied such three unusual cases of Vitamin D and calcium intoxication due to overcorrection of osteoporosis treatment.

Introduction
Hypervitaminosis D is a well known cause of morbidity and mortality. The adequate intake is 5 micrograms (200 IU) daily for all individuals (males, females, pregnant/lactating women) under the age of 50 years, 10 micrograms daily (400 IU) for all individuals from 50-70 years, and 15 micrograms daily (600 IU) for those who are over the age of 70 years. The recommended dose 1200 mg/day of elemental calcium and Vitamin 400 – 800 IU/day, is an amount which is effective in prophylaxis and treatment of Vitamin D deficiency especially in osteoporotic patients. However higher prescribed doses may lead to severe hypercalcaemia which is potentially life-threatening. There is little relationship between symptoms of hypercalcaemia and the actual level of blood calcium. Hence early and rapid diagnosis of symptoms of hypercalcaemia though difficult, is important.

Case Report
Case 1
An 80 yr old male, known hypertensive was admitted with chief complaints of nausea, loss of appetite, constipation and progressive weakness. On examination patient’s general and systemic examination was normal. Investigations revealed Calcium – 18.5 mg/dl, Creatinine – 2.70 mg/dl, Albumin – 3.2 gm%, Vitamin D – 150 ng/dl, Plasma PTH – 0.15 pg/ml.

Urea – 50 mg %. Alkaline Phosphatase – 66 mu /dl. Treatment was started immediately with infusion of I.V Isotonic saline (500 ml /6 hrs) over 24 hrs followed by loop diuretics. A single dose of Bisphosphonates i.e. I.V Zolendronate 4 mg diluted in100 ml of 0.9 % NaCl was given followed by Inj Calcitonin 100 mg i.m 8 hrly. During the hospital stay patient developed vomiting, oliguria with fluid retention and bronchospasm. Appropriate I.C.U management with diuretics, bronchodilators improved the condition. Repeat Calcium levels were reduced. On discharge patient was asked to stop calcium supplements. Repeated calcium, PTH and urine analysis report were found to be normal. Detailed history revealed, patient had taken 18 injections of Vitamin D for bone pain.

Case 2
A 67 yr postmenopausal female admitted with complaints of nausea, vomiting, loss of appetite and low back pain. General and systemic examination was

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normal. Biochemistry showed Calcium – 16.7 mg%, Creatinine – 1.8 mg/dl, Albumin – 3.10 mg%, Alkaline phosphatase-64 mu/dl Plasma P.T.H – 8.67 pg/dl. Immediate treatment with isotonic saline infusion, Calcitonin along with single dose of Bisphosphonates (Pamidronate) 90 mg in 100 ml of 0.9% NaCl started. Patient responded well to this treatment vomiting stopped and appetite was improved. Repeat calcium levels were normal serially. On discharge, patient was advised to stop calcium supplements and low calcium diet was prescribed. On follow up patient’s calcium reports which were found to be normal. Detailed history that patient had taken 3 Vitamin D injections from orthopaedic doctor for backache.

Case 3

A 74 yr old, postmenopausal female was admitted with complaints of generalized weakness, anorexia and mental confusion. She was a known case of hypertension, diabetes, ischaemic heart disease, chronic kidney disease and hyperthyroidism on treatment. She also had a history of multiple compression fractures between D2 – D12 levels. On examination she was drowsy but oriented with bradycardia. Systemic examination essentially normal. On investigating, the Serum calcium – 15.10 mg/dl Creatinine – 2.9 mg/dl , Urea – 158 mg %, Albumin – 1.7 mg, Vitamin D3 – 145 ng/dl ( normal < 75 ng/dl) with normal PTH levels and thyroid function test. CT Scan of Brain was also normal. Patient was shifted to I.C.U. and immediate treatment for hypercalcaemia was started with isotonic saline infusion, followed by diuretics. Calcitonin and Bisphosphonates (Zolendronate) was administered under close cardiac monitoring. With this management the serum calcium gradually reverted to normal over next 24 to 48 hours and the patient’s general condition stabilized. Subsequently the patient developed fever and septicemia (ESBL producing Klebsiella was cultured from blood). As her O₂ saturation and B.P dropped, she had to be intubated and placed on ventilatory support with inotropic infusion. The azotaemia was managed with dialysis. Despite energetic and continued management, the patient continued to deteriorate with multiorgan failure and finally succumbed to her illness.

Discussion

Calcium plays an important role in cellular mechanism that control processes such as nerve conduction, muscle contraction, coagulation, electrolyte and enzyme regulation, hormone release etc. Hypercalcaemia is an elevated calcium level in the blood (Normal range: 9-10.5 mg/dL or 2.2-2.6 mmol/L). It can be due to excessive skeletal calcium release, increased intestinal calcium absorption, or decreased renal calcium excretion. Hyperparathyroidism and malignancy account for ~90% of cases. Other causes include Vitamin-D metabolic disorders (e.g. vitamin D intoxication, sarcoidosis and other granulomatous diseases with elevated 1,25(OH)₂D), disorders related to high bone-turnover rates (like hyperthyroidism, prolonged immobilization, thiazide use, vitamin A intoxication, Paget’s disease of the bone) renal failure (e.g. severe secondary hyperparathyroidism), lithium use.\(^1\)

Hypercalcemia can present as fatigue, depression, confusion, anorexia, nausea, vomiting, constipation, pancreatitis or increased urination; Severe hypercalcaemia (above 15-16 mg/dL) is potentially life threatening.\(^2\) At these levels, coma and cardiac arrest can result.

The symptoms of hypercalcaemia can however mislead like in our cases where the patient’s clinical symptoms didn’t correlate with the blood levels of calcium. Hypervitaminosis D is a well known cause of mortality and morbidity and should be suspected when some of the above symptoms develop in a patient receiving vitamin D.\(^3\) Excess vitamin D leads to increased absorption of calcium from the gastrointestinal tract and enhanced bone resorption, as well as there is consequent loss of renal concentrating ability causing hypercalcaemia. Also an increase in albumin of 1 g/dL over normal increases measure total calcium by 0.8 mg/dL.\(^4\) The serum
phosphorus and alkaline phosphatase levels in hypervitaminosis D are normal, which distinguishes it from primary hyperparathyroidism.

Treatment of vitamin intoxication consists of discontinuing treatment with vitamin D, a low-calcium diet. Hydration is needed because many patients are dehydrated due to vomiting or renal defects in concentrating urine. After rehydration, a loop diuretic such as furosemide can be given to permit continued large volume intravenous salt and water replacement while minimizing the risk of blood volume overload. In addition, loop diuretics tend to depress renal calcium reabsorption thereby helping to lower blood calcium levels by 1-3 mg/dL within 24 hours. Bisphosphonates are pyrophosphate analogues with high affinity for bone, especially areas of high bone-turnover. They are relatively contraindicated in renal failure. Calcitonin blocks bone resorption and also increases urinary calcium excretion by inhibiting renal calcium reabsorption.

**Conclusion**

This case report is to sensitize about the overcorrection of osteoporosis with Vitamin D and Calcium leading to hypercalcemia. Massive doses of ergocalciferol continued to be prescribed without adequate supervision and the dangers of this therapy are still not generally appreciated. A vigorous emphasis on the use of Vitamin D and calcium as of other vitamins, implies several risk and must be prescribed only when needed and under strict medical supervision.

**References**


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**TREATING ACUTE MYOCARDIAL INFARCTION : SOMETHING IN THE WIND?**

The preservation of healthy myocardium during a heart attack is the holy grail of contemporary cardiology. Primary angioplasty to restore perfusion is an important advance but room for improvement remains. Over the past 40 years, hundreds of experimental interventions have been reported to protect the myocardium in animal models, but except for early reperfusion, none have translated into clinical practice.

J-WIND-ANP studied atrial natriuretic peptide (ANP) and I-WIND-KATP studied nicorandil. By contrast, intravenous nicorandil showed no acute benefits.