HK J Paediatr (new series) 2011;**16**:180-183

The Importance of Dietary Therapy in Acute Vitamin D Intoxication

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Abstract A previously healthy 9-month-old girl was brought to our clinic after falling from a height. She was restless and mildly dehydrated. She had been given 300,000 units of vitamin D in the previous 10 days. The levels of serum calcium, 25(OH) D vitamin, and parathyroid hormone were 17.1 mg/dl [reference 8.0-10.2], 892.9 ng/ml [reference 7.4-53.3], and 9.8 pg/mL [reference 9-65], respectively. She was treated with intravenous fluids, furosemide, calcitonin, steroid, and a diet containing minimal amounts of calcium and vitamin D. The daily dietary intake was 148 mg calcium and 8 units of vitamin D. Thirty-five days later, the serum vitamin D level had returned to a safe level. The effect of vitamin D can last for months, since it is fat-soluble. The recommended drug therapy inhibits calcium absorption. A diet with reduced calcium and vitamin D shortens the duration of therapy. This article emphasizes the importance of dietary treatment.

Key words Diet; Hypervitaminosis D; Treatment; Vitamin D intoxication

Introduction

Vitamin D is used for prophylaxis of vitamin D deficiency and treatment of rachitism. However, inappropriate treatment or supplementation with high dose vitamin D can lead to life-threatening intoxications.[1-3] At extreme doses, vitamin D is the most important reason for hypercalcemia in children. In most cases, hypercalcemia is accidentally found in asymptomatic patients. Clinical findings may be related to the neuromuscular, gastrointestinal, renal, skeletal and cardiovascular systems.[2-5] Renal and cardiovascular problems in particular, can be life threatening.

The diagnosis of vitamin D intoxication is considered when there is a rise in serum calcium and phosphorus, normal or low parathyroid hormone (PTH) level, and increased calcification in bones.[6,7]

Calcitonin is a hormone that lowers the serum calcium and phosphorus levels and suppresses the osteoclastic activity. It increases the excretion of calcium from the kidneys. It is used in vitamin D intoxication due to these properties.[2,3,5,8] Like the other fat-soluble vitamins, vitamin D is stored in fat tissue and its effect continues for a long time. For this reasons, the duration of therapy and the follow-up can be prolonged in intoxication cases. Moreover, limiting the dietary intake of vitamin D and calcium is an important detail that positively contributes to shortening the duration of therapy and it should not be forgotten.

Case Report

A 9-month-old girl with a body weight of 6300 grams (<3rd percentile), height of 65 cm (<3rd percentile); head circumference of 44 cm (50th percentile), weight z-score

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Received December 20, 2010

of -2.26, and height z-score of -2.18 and with no previous complaints had suffered from a fall on the back from her bed, which was 1 meter in height. Although she was cheerful for three days after falling, the child began to cry continuously and refuse feeding, and displayed apparent behavioral changes. At another medical facility she was treated as having a respiratory tract infection. An oral antipyretic was prescribed and she was discharged. However, when no recovery occurred on the 3rd day after discharge, she was admitted to our clinic. On physical examination, the anterior fontanel was found to be 2x3 cm and sunken. The eyes were sunken and she was restless. Heart rate was 180/min. There were no additional cardiac sounds or murmurs. Blood pressure was 85/55 mmHg. Electrocardiogram showed only sinus tachycardia but no QT shortening or arrhythmia. She had lost 500 grams in weight compared to a week before (7% weight loss). Neurological examination was normal. There were no special characteristics in other system examinations. In a detailed history, it was learnt that upon the recommendation of a retired nurse to prevent rickets and improve general well being, her mother had given her 300,000 units of vitamin D3 daily in the last 10 days before this admission.

According to the newly acquired information, the serum calcium level was found to be 17.1 mg/dL [reference: 8.0-10.2], phosphate was 4.8 mg/dL [reference: 3.8-6.5], blood urea nitrogen was 12.5 mg/dL [reference: 5-18], aspartate transaminase was 20 U/L [reference: 15-55], alanine transaminase was 10 U/L [reference: 5-45], 25(OH) D vitamin was 892.9 ng/mL[reference: 7.4-53.3], and PTH was 9.8 pico gr/mL [reference: 9-65]. Urinary Calcium/creatinine ratio was 0.71 mg/mg [reference: 0-0.21]. On ultrasonography of the urinary system, a first degree increase in echogenicity of the right and left kidney parenchyma was observed.

After hospitalisation, therapy for hypercalcemia was begun immediately. Intravenous (IV) infusion of ¼ isotonic saline with 5% Dextrose at rate of 150 mL/kg/day was given. Two doses of 1 mg/kg/dose intravenous Furosemide, and 2 U/kg/dose of subcutaneous calcitonin for every 6 hours were administered to the patient for 4 days. In addition, 2 doses of 1 mg/kg/dose prednisolone were started. Vitamins were ceased and a calcium-deprived diet was started. The clinical and laboratory course of the patient was summarised in Table 1. On the 10th day, the patient was discharged, prednisolone was slowly tapered and discontinued on the 20th day and a calcium-deprived diet was maintained till serum calcium and vitamin D levels decreased to the normal range. On the 25th day, serum vitamin D level was found to be 405.9 ng/mL (elevated). Apart from our recommendations, it was learnt that the mother had given the girl an egg every day (equivalent to adding 52 units of vitamin D) to her diet. The amount of the calcium and vitamin D free infant formula that had been

Table 1 The clinical and laboratory course of the patient

Days	Intervention	Serum phosphate level (mg/dL)	Vitamin D in diet (units/day)	Calcium in diet (mg)	Calcium in serum (mg/dL)	Vitamin D in serum (ng/mL)
1	Started immediate hypercalcemia treatment	4.8	300,000		17.1	892.9
2		5.1	8	148	13	
4	Diuretic therapy and calcitonin were stopped	4	8	148	10.9	
10	Steroid was slowly tapered and patient was discharged	5.1	8	148	10.8	
20	Steroid was stopped	5.6	8	148	9.5	368
25	Addition of vitamin D to diet by her mother		60	170	10	405.8
35		5.1	8	222	10	147
50	Her diet was changed to regular diet	5.9	8	222	10.3	53
60		6			8.5	52.7

added to the therapy was increased and the parents were subsequently re-informed about not to add any food without our permission. The diet was arranged as two meals with 200 grams vegetable puree with meat, one meal with fruit puree and three meals with 180 ml calcium- and vitamin D-deprived diet (consisting of 700 kcal/day energy, 222 mg/day calcium, 8 units vitamin D)(totally 6 meals per day). On the 35th day, the serum vitamin D3 level was found to be 147 ng/mL; calcium level was 10 mg/dl, and phosphorus level was 4 mg/dL. Renal USG revealed medullary nephrocalcinosis. Hypercalciuria lasted for 1 month after discharge.

Discussion

It is recommended that all exclusively breast-fed children be given vitamin D 400 U/day and formula-fed children be given 200 U/day.[1,9] The use of parenteral forms can easily lead to vitamin D intoxication, even with a doctor's prescription. It is more dangerous given as self-medication, by the parents to the child.[2-4] In our country, doctors use parenteral forms of vitamin D in 80% of the cases of vitamin D-deficient or -dependent rickets.[2] In our case, although the recommendation was given by a retired nurse to prevent rickets and to improve general wellbeing; due to missing information, her mother administered vitamin D3 for 10 days without knowing the adverse effects. Although the sale of the ampoule form of vitamin D without a prescription is forbidden by the Ministry of Health in Turkey,[1] the parents were able to purchase the drug easily and use it in an uncontrolled manner. There is thought to be a lack of additional information given by pharmacies.

The median lethal dose of vitamin D is 21 mg/kg, and all organs are affected at this dose.[5] Our patient received a total dose of 11.9 mg/kg (1 µg = 40 U) (10). The reported upper limit of normal for the serum vitamin D is 60 ng/mL (150 nmol/L), and the reported dangerous dose limit is 300 ng/mL (750 nmol/L).[4,10] Adverse effects occur due to hypercalcemia. Early findings of hypercalcemia are a loss of appetite, nausea, vomiting, fatigue, constipation, and nonspecific pain. At a more advanced stage, renal dysfunction due to nephrocalcinosis and vascular calcification-related renal hypertension may develop. In our patient, most of the signs and symptoms of vitamin D toxicity were observed.

In treating vitamin D intoxication, immediate cessation of the vitamin, an increase in hydration with intravenous fluids, loop diuretics except hypercalcemia-causing thiazides, glucocorticoids that block the action of vitamin D and calcium reabsorption, and a diet with low calcium are used. Moreover, glucocorticoids also increase the excretion of calcium via the renal tubules. Although the serum calcium level was within normal range, the serum 25(OH) D vitamin level was still high. Prescribing a steroid at discharge could block the action of vitamin D.

If the calcitonin that is used in the therapy is of animal origin, it can cause allergic reactions. Although bisphosphonates have been used in some cases, the safety of their long-term use in children is controversial.[5,8] With extremely high calcium levels in the presence of renal insufficiency, hemodialysis can be used for hypercalcemia therapy.[3,5,8,9] Dialysis and bisphosphonates were not used in our case.

Vitamin D is a fat-soluble vitamin and is stored in the adipose tissue; it can be effective for more than two months. In our patient, the hypercalcemia dropped to a normal level on the 5th day. The vitamin D level decreased by 33% within 10 days. An increase in the serum vitamin D3 level was noted on the 25th day. We believe that this increase was due to adding vitamin D to her diet; it was not a laboratory error because the vitamin D3 coefficient variation was 4.2% on the day that the test was performed. With our treatment, the level dropped below the dangerous level in 35 days (Table 1). Vitamin D has an important role in calcium homeostasis; most humans depend on sun exposure to meet their requirement for vitamin D. If the sun exposure is high in a patient with vitamin D intoxication, an unintended increase in the serum vitamin D level could occur, contradicting intoxication treatment.

A patient put on a long-term diet low in calcium and vitamin D could develop vitamin D deficiency. When the patient's serum vitamin D and calcium levels reach normal levels, a normal diet should be started as soon as possible. Although drug therapy has been discussed in detail in case reports and reviews, diet is discussed only briefly or not mentioned at all, despite the fact that the primary aim in the treatment of intoxication is to reduce the body level of the toxic substance. If vitamin D and calcium, which causes the most important side effects, are not omitted from the patient's diet, drug therapy only, which is used to remove the excess vitamin D and calcium from the body, becomes less effective.

In conclusion, a diet with reduced amounts of vitamin D and calcium is an important component of the treatment of life-threatening hypercalcemia due to vitamin D intoxication. Clinicians can shorten the duration of drug therapy with such a diet.

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