Acute Vitamin D Intoxication in a Child

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ABSTRACT. We present the unique case of a previously healthy, 2-year-old boy with resistant hypercalcemia and hypertension resulting from an unintentional overdose with an imported vitamin D supplement. The patient presented initially to the emergency department with colic and constipation and was discharged after a benign physical examination. The symptoms persisted and, on the second visit, the patient was found to have a serum calcium level of 14.4 mg/dL. Despite therapy with intravenously administered 5% dextrose solution at one-half normal strength, furosemide, calcitriol, and hydrocortisone, the calcium concentration increased to 15.0 mg/dL on the second hospital day and did not decrease until the fourth hospital day, when it fell to 13.9 mg/dL. The vitamin D concentration peaked at 470 ng/mL on hospital day 3. With additional questioning, the mother revealed that she had been giving her son a daily dose of 1 ampule of Raquiferol, an imported vitamin D supplement, instead of the recommended 2 drops per day. Each ampule contained 600 000 IU of vitamin D; therefore, the boy received a total of 2 400 000 IU over 4 days. The patient’s hypercalcemia persisted for 14 days and was complicated by persistent hypertension. No renal, cardiac, or neurologic complications were noted. At discharge, the vitamin D concentration was still elevated at 389 ng/mL and the total calcium level had decreased to 11 mg/dL. The boy made a complete clinical recovery. This case highlights the need for caution when using imported and/or unregulated medicines, as well as the dangers of parental dosing errors. Pediatrics 2005; 116:e453–e456. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-2580; vitamin D, overdose.

ABBREVIATION. AAP, American Academy of Pediatrics.

With the resurgence of breastfeeding in the United States, vitamin D supplementation is once again an important issue, especially considering the parallel increase in the number of reported cases of nutritional rickets.2–6 The American Academy of Pediatrics (AAP) recently issued a new policy on vitamin D supplementation that recommends that all breastfeeding infants and nonbreastfeeding infants who drink <500 mL (<16 1/3 oz) of vitamin D-fortified formula or milk per day should receive 200 IU of vitamin D per day.7 Although the skin has the ability to metabolize cholesterol to a vitamin D precursor, it is unclear exactly how much sunlight one needs daily to metabolize sufficient amounts of vitamin D effectively.8 In addition, health care providers and organizations, including the Centers for Disease Control and Prevention, have recommended decreased exposure to direct sunlight and the liberal use of sunscreens to prevent skin cancer.9 Because vitamin D is used so readily, it is important to understand how dosing errors can lead to overdoses with potentially life-threatening consequences. Vitamin D is 1 of 4 fat-soluble vitamins. With parathyroid hormone, it regulates calcium homeostasis tightly. When the serum calcium level is low, calcitriol, the biologically active form of vitamin D, restores homeostasis through increased dietary calcium absorption through the gut and through increased bone resorption. Dietary sources of vitamin D are limited to fish, oysters, and dairy products. In the United States, milk is fortified with vitamin D, and some forms of butter, margarine, cereals, and fruit juices also are fortified. Unfortunately, most individuals in the United States do not eat the necessary 2 servings of a vitamin D-fortified food in a day to ensure adequate dietary intake of vitamin D.10 To make up for this deficit, these people should rely on adequate sun exposure; however, if these patients adhere to the recommendation of the Centers for Disease Control and Prevention on decreasing direct sun exposure, then they would need a dietary supplement of vitamin D to ensure proper bone health.

Unintentional vitamin D poisoning has been associated with overfortification of milk,11,12 adulteration of table sugar,13 and contamination of cooking oil14–16 and with use of an over-the-counter supplement by an adult.17 We present the unique case of an unintentional vitamin D overdose in a child, caused by improper dosing with an imported vitamin D supplement.

CASE REPORT

A previously healthy, 2-year-old, Hispanic boy was brought to the emergency department by his mother because of constipation and abdominal pain. During the previous 3 days, he had experienced vomiting, constipation, lethargy, and abdominal pain. With the exception of slightly elevated blood pressure, his physical symptoms were mild. On presentation to the emergency department, the boy was afebrile, with a blood pressure of 90/50 mm Hg and a heart rate of 130 beats per minute. A complete blood count revealed a white blood cell count of 10 000/μL. The hematocrit was 38.0%, and the electrolytes were normal. The serum calcium level was 14.4 mg/dL. The boy was discharged home by his mother with instructions to return if symptoms persisted. On follow-up visit 1 day later, the parents reported no improvement in symptoms. The boy was readmitted and placed in the hospital. The patient was in no acute distress and answered questions appropriately. A urinalysis revealed no protein or casts. The renal ultrasounds were normal. The patient was discharged home on the second hospital day with a serum calcium level of 14.4 mg/dL. Despite therapy with intravenously administered 5% dextrose solution at one-half normal strength, furosemide, calcitriol, and hydrocortisone, the calcium concentration increased to 15.0 mg/dL on the second hospital day and did not decrease until the fourth hospital day, when it fell to 13.9 mg/dL. The vitamin D concentration peaked at 470 ng/mL on hospital day 3. With additional questioning, the mother revealed that she had been giving her son a daily dose of 1 ampule of Raquiferol, an imported vitamin D supplement, instead of the recommended 2 drops per day. Each ampule contained 600 000 IU of vitamin D; therefore, the boy received a total of 2 400 000 IU over 4 days. The patient’s hypercalcemia persisted for 14 days and was complicated by persistent hypertension. No renal, cardiac, or neurologic complications were noted. At discharge, the vitamin D concentration was still elevated at 389 ng/mL and the total calcium level had decreased to 11 mg/dL. The boy made a complete clinical recovery. This case highlights the need for caution when using imported and/or unregulated medicines, as well as the dangers of parental dosing errors.
examination results were benign. The patient was discharged with a diagnosis of constipation, and his mother was instructed to follow up with his pediatrician regarding his blood pressure. The boy was brought back to the emergency department the next day because of continued and worsening abdominal pain. The review of systems was significant for a loss of appetite but otherwise yielded negative results. The mother denied that the child had fever, diarrhea, or seizure-like activity. She indicated that the only medication her son had been taking was a vitamin D supplement, Raquiferol (Spedrog Caillon Laboratories), which is sold normally in Latin American countries and which she had obtained from a local bodega. She started giving him this medicine to promote good health and strong bones. The mother administered 1 ampule of Raquiferol per day for ~4 days, with the last dose being administered 8 days before admission. Each ampule contained 600 000 IU of vitamin D; therefore, the boy received a total of 2 400 000 IU over 4 days.

The physical examination revealed an age-appropriate young boy who was crying intermittently but could be consoled. He weighed 14.5 kg (90th percentile). Vital signs were as follows: blood pressure, 139/98 mm Hg; pulse, 88 beats per minute; respiratory rate, 16 breaths per minute; temperature, 97.6°F. Other significant findings in the physical examination included a nontender nondistended abdomen with normal active bowel sounds and nonfocal neurologic examination results.

Laboratory testing showed a serum Ca^{2+} concentration of 14.4 mg/dL (normal: 8.4–10.2 mg/dL). Complete blood count and electrolyte concentrations were within normal limits, as follows: Na^+, 139 mEq/L; K^+, 3.7 mEq/L; Cl^−, 102 mEq/L; CO_2, 28 mEq/L; blood urea nitrogen, 13 mg/dL; creatinine, 0.5 mg/dL; glucose, 107 mg/dL; Mg^{2+}, 1.3 mg/dL. An electrocardiogram showed normal sinus rhythm, with a regular rate and normal intervals.

With additional investigation, it was noted that the Raquiferol package instructions indicated that the recommended dosage was 2 drops from an ampule per day. On the basis of this history and the physical examination and laboratory investigation results, hypercalcemia caused by unintentional vitamin D overdose was diagnosed, and the patient was admitted to the PICU for treatment.

Additional testing at admission showed a vitamin D concentration of 106 ng/mL (normal: 10–68 ng/mL). The immunochemiluminometric assay that was used (LabCorp, Research Triangle Park, NC) measures 25-hydroxyvitamin D and its 24,25-, 25,26-, and 1,25-dihydroxy metabolites. The physiologic concentrations of these metabolites are insignificant and therefore do not affect the accuracy of the 25-hydroxyvitamin D measurements.

During his 2-week hospitalization, the patient was treated with intravenously administered fluids (5% dextrose solution at one-half normal strength at 1.5 times maintenance), furosemide, calcitonin, and intravenously administered hydrocortisone. Despite these therapies, the total calcium level increased to 15.0 mg/dL on hospital day 2 and did not decrease until the 4th hospital day, at which time it decreased to 13.9 mg/dL. The vitamin D concentration did not peak at 470 ng/mL until hospital day 3 (Fig 1) because the half-life of vitamin D is ~30 to 60 days. During his stay, the patient remained asymptomatic except for occasional colic and persistent hypertension. When he was discharged, his vitamin D level was still elevated at 389 ng/mL and his total calcium concentration was 11 mg/dL. His discharge instructions included avoidance of products containing vitamin D and use of sunscreen for 3 to 4 months. At the 3-month follow-up visit, his total serum calcium concentration was 12 mg/dL.

**DISCUSSION**

Guidelines issued by the AAP and the National Academy of Sciences indicate that all breastfeeding infants and nonbreastfeeding infants who drink <500 mL (<16½ oz) of vitamin D-fortified formula or milk per day should receive 200 IU of vitamin D per day. Vitamin D has a median lethal dose of 21 mg/kg.18 and, in overdose, affects all major organ systems. The symptoms of vitamin D toxicity stem from the deposition of calcium phosphate crystals in soft tissues throughout the body,19 which can occur once the calcium-phosphate product is >60 mg/dL. Early symptoms of hypercalcemia include anorexia, nausea, vomiting, weakness, lethargy, constipation, and nonspecific aches and pains. Renal function can become impaired as a result of nephrocalcinosis. Vascular calcification leads to renal hypertension. Because vitamin D is lipophilic and is stored in fat tissues, the effects of vitamin D toxicity can persist ≥2 months after the exogenous source is removed.

The patient described in this report was mistakenly given 600 000 IU of an imported vitamin D product each day for 4 days. Each drop contains
indications, such as acute or chronic renal failure and vitamin D intoxication, hemodialysis should be re-
ocemia and can lower serum calcium levels rapidly. Normal-
known. Hemodialysis can be used to treat hypercal-
side removal of the exogenous source, intravenous fluid hydration, loop diuretics (thiazides can pro-
ose abdominal bleeding. The use of bisphosphonates, such as pamidronate, is ac-
ponent received 3000 times the daily adequate intake of vitamin D. He received 300 times the daily toler-
required, and no benefit was noted. The patient responded to therapy with calcium gluco-
patients should make clinicians consider this condition in the differential diagnosis. Vitamin D supplements used for the treatment of rickets are too concentrated for use as a routine supplement. Although it is not nec-
the hands of the attending physician. A possible reason for the failure to detect calcites may be that the patient was on a dietary supplement containing calcium and vitamin D, which could have masked the laboratory evidence of hypercalcemia. The patient responded to therapy with oral calcium gluconate, and the serum calcium level returned to normal.
Treatments for hypercalcemia include the use of calcitonin and bisphosphonates. Calcitonin inhibits bone resorption and blocks the release of calcium and phosphate into the serum. The use of bisphosphonates, such as pamidronate, is accepted widely for adults, but use in children has been only anecdotal and thus the safety is unknown. Hemodialysis can be used to treat hypercalcemia and can lower serum calcium levels rapidly. Because rebound hypercalcemia is predictable after vitamin D intoxication, hemodialysis should be re-
formed to reverse the hypercalcemia. The patient responded well to therapy with oral calcium gluconate, and the serum calcium level returned to normal.

As awareness of the AAP guidelines increases in the general population, more people may start to use vitamin D supplements without physician supervision. As this case report demonstrates, acute intoxication can occur as a result of parental dosing errors. Vitamin D is a beneficial supplement and is safe when used correctly at its recommended doses (200–1000 IU for infants and 2000 IU for all others). Vitamin D toxicity occurs over days of ingesting thousands of international units of vitamin D; therefore, it is unlikely that patients will overdose with the doses of vitamin D found in daily multivitamins or foods fortified with vitamin D. However, if a patient presents with symptoms consistent with vitamin D toxicity, then strong clinical suspicion with a history that reveals the use of a vitamin D supplement

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Pediatrics 2005;116;e453
DOI: 10.1542/peds.2004-2580

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