CASE REPORT

VITAMIN D INTOXICATION IN 7-MONTH-OLD INFANT WITH RECOMMENDED DAILY INTAKE OF VITAMIN D

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Over the past decade there is increased use of vitamin D supplementation because of its benefits on bone health. It is a fat-soluble vitamin and cannot be excreted from the body. There is need for monitoring 25-hydroxyvitamin D levels in infants and children who receive long-term vitamin D supplementation at or above the upper level intake that is currently recommended. Vitamin D intoxication can present from mild ignorable to severe life-threatening symptoms. We present a 7-month-old infant with vitamin D intoxication at recommended daily doses of vitamin D.

Keywords: Hypervitaminosis D; Recommended daily allowance; Hypercalcemia, Vitamin D

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INTRODUCTION

Vitamin D also called sun vitamin exists in three inactive forms, Ergocalciferol (vitamin D2), Cholecalciferol (vitamin D3) and 7-dehydrocholesterol (Vitamin D3). Ergocalciferol and Cholecalciferol are found in various foods and as dietary supplements. 7-dehydrocholesterol is produced endogenously in skin via sun exposure.

These inactive forms are converted to 25OHD in the liver while in kidney final hydroxylation to 1, 25 (OH) 2D occurs which is active form of Vit D. The active vitamin D form binds to the vitamin D receptors (VDR) to increase intestinal calcium absorption and exert the other vitamin D-related actions. It is a fat-soluble vitamin and excess amount is stored in the body and leads Vit D intoxication. In Vit D intoxication high concentrations of either 25OHD or free 1, 25(OH) 2D lead to hypercalcemia by increasing intestinal calcium absorption and bone resorption. This hypercalcemia results in increase load over kidneys leading to increased calcium excretion in the distal tubule causing hypercalciuria. Persistently elevated serum calcium concentrations impair the concentrating ability of kidneys and cause polyuria and dehydration. It can also result in nephrocalcinosis. We present 7-month-old infant with Vit D intoxication.

CASE

A 7-months-old boy presented to consultant gastroenterologist with lethargy, vomiting, constipation and polyuria for last 3 months. Being a product of consanguineous marriage, he was delivered by uneventful SVD at hospital having 3.2 kg birth weight. He was discharged from hospital on very next day without any laboratory parameters. He was breast fed along with supplemented formula milk. History revealed that mother was on regular Vitamin D supplementation pre and post pregnancy as advised by her obstetrician without knowing her serum Vitamin D level. Baby since 2nd day of birth was on Vitamin D drops (400 IU/day) along with multivitamin drops, which also had vitamin D (400) in it. He remained well up to 4 months of life when he developed vomiting and lethargy. His vomiting was non-bilious and non-projectile contains milk and associated with lethargy and polyuria. Mother noticed that he is not passing stool as per routine. He visited multiple paediatricians for these complaints and thoroughly worked up for hypertrophic pyloric stenosis and renal tubular acidosis to no avail.

It was at this time he was referred to us for vomiting. On examination young infant weighing 6.6 kg @ 10thcentiles, length 65 cms 25th@ centiles and FOC 44 cms @ 2SD, sunken eyes, depressed anterior fontanelle and dry mucous membranes. He was unable to hold his neck. His pulse rate was 116/min; respiratory rate was 28/min and temperature 99 °F. There was no visceromegaly and bilateral equal air entry with normal vesicular breathing. He was conscious but lethargic with depressed deep tendon reflexes. His base line laboratory investigation showed normal complete blood count, normal renal and liver profile, Na=134 meq/dl, K=3.9 meq/dl, Cl=94 meq/dl, HCO3= 20.6 and Ca =25 mg/dl. Spot Urinary electrolytes showed K=10.4 meq/ml Na= 45 meq/ml Cl= 41 meq/ml Ca=11.2 meq/ml and urinary creatinine to Ca ratio was more than 2.17 suggestive of hypercalcemia with hypercalciuria. Urine output was 11ml/kg/hr. USG (ultra-sonogram) KUB (kidney & urinary bladder) showed bilateral nephrocalcinosis with cystitis. Urine complete examination showed numerous WBC casts and culture sensitivity was negative. Serum Vit D level measured to be more than 150ug/dl which were in

toxic range and parathyroid hormone were not detectable. So, he was labelled as a case of Vit D intoxication.

He was managed for his symptomatic hypercalcemia in consultation with endocrinologist. All sources of vitamin D and calcium were stopped except his mother feed. Mothers vitamin D level and serum calcium were in normal range. Intravenous fluid resuscitation with normal saline at 1.5–2.5 maintenance combined with furosemide at 1–2 mg/kg/d was started to increase the glomerular filtration rate and calcium excretion. We monitored him with improvement in symptomatology, strict intake/out-put record electrocardiogram and serum calcium level. At 24 hours of fluid therapy serum calcium level was still above 20 mg/dl hence intravenous Pamidronate at dose 0.5 mg/kg/dose was added. Two doses were given and serum calcium decreased to 17mg/dl at 72 hours and further decreased to 13 mg/dl at 96 hours. Intravenous fluid resuscitation was continued for a week and serum calcium further dropped to 10 mg/dl. He improved symptomatically and became active alert, achieved sitting with support; constipation and polyuria also are settled. His nephrocalcinosis however persisted on ultra-sonogram (USG KUB) but his RFTs and renal excretory functions are in normal range. Now he is doing very well on calcium and Vit D restricted diet.

DISCUSSION

The diagnosis of vitamin D intoxication is based on elevated serum 25OHD concentrations associated with hypercalcemia, hypercalciuria, normal serum 1,25(OH)2D and suppressed PTH levels. Paediatric endocrine society has accepted the cut-off serum concentration more than 150 ng/mL to define Vit D intoxication.[1] All recommended dosages regimens for the treatment of Vitamin D deficiency maintains 25 (OH) D levels between 30–100 ng/ml. Our index case had level exceeding 150 ng/ml.[2] The amount of vitamin D intake that results in excess or intoxication and the severity of corresponding hypercalcemia have not been clearly established in paediatrics. Index case did not take any mega dose of Vit D but he was taking 400 IU/day as Vit drops and additional 400IU/day in disguise of multivitamin drops. He was breast fed and his mother was vitamin D sufficient plus formula milk supplemented with vitamin D. So collectively he was taking 1200–1600 IU/day for 4 months lead to toxic levels of Vit D this is first ever case report of Vit D intoxication resulting from daily dose in hundreds for a longer duration. Reports published in literature on vitamin D intoxication in infants and young children has described cases that received extremely large doses in the range of 240 000–4 500 000 IU either accidentally or misunderstood dose.[3] The maximum calcium levels described in literature are as high as 20 mg/dL and we found 25 mg/dl in our case. The role of genetic make-up of an individual on vitamin D metabolism and response to supplementation also has been described in the literature. Genetic polymorphism regulates the synthesis and metabolism of vitamin D as well as the synthesis of vitamin D binding protein (DBP). So, the variability in the amount of vitamin D taken and the resulting serum 25OHD concentrations along with severity of hypercalcemia may be explained by differences in genetics.[4] The symptoms of vitamin D intoxication described in literature were present in our index case about 25% of patients with Vit D intoxication can develop nephrocalcinosis that was found in our index case. Metastatic vascular calcifications have also been reported but not found in our case.[5]

Most effective therapy to achieve normokalaemia is fluid resuscitation with normal saline at1.5–2.5 maintenance combined with loop diuretics to increase glomerular filtration and calcium excretion.[6] Bone resorption is increased in vitamin D intoxication to antagonize this antiresorptive therapy with bisphosphonates, i.e., pamidronate 0.5–1 mg/kg/dose is second most effective therapy. Our index case was an infant and calcium level was dangerously elevated so we started both therapies and calcium dropped to 17 mg/dl followed by 13 mg/dl in 96 hours. Study done by Sezer *et al* reported same that therapy with bisphosphonates achieved normokalaemia four times faster than steroids.[7] Vitamin D has a long half-life so serum 25OHD concentrations may remain elevated despite all measures; therefore, it is recommended to monitor symptoms and serum calcium concentrations rather than 25OHD levels.

CONCLUSION

Vit D is good for bone health. Before prescribing vitamin D to any infant it is mandatory to inquire parents about child's formula milk supplemented with vitamin D and any multivitamin containing vitamin D. There is need to monitor serum vitamin D level infants who are taking RDA of Vit D for a long period.

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