Vitamin D Intoxication: Consequence of Misconception - A Case Report

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ABSTRACT

Introduction: Among 4 fat soluble vitamins vitamin D is considered as wonder drug as number of studies showed its deficiency is associated with cardiovascular diseases, metabolic diseases, abdominal obesity, hyperglycemia, asthma etc., but on the other hand unsupervised, inadvertent use of vit D also leads to its toxicity.

Case Report: An 11 years and 6 months old girl was presented with 15days history of burning abdominal pain mainly in epigastric region, constipation, decreased appetite followed by several episodes of vomiting. There was history of administration of total 12 doses of intramuscular injection of Vitamin D (600,000IU/dose) for improvement of her height following which features of Vitamin D intoxication manifested. On examination her height was below 3rd centile (though her height velocity was within target range) and blood pressure was above 99th centile, no other significant finding was there on systemic examination. On laboratory studies renal function tests were deranged, hypercalcemia, increased level of serum 25-hydroxy D, decreased serum parathormone (PTH), GFR were noted. USG abdomen, fundus examination reports were normal. Hydration therapy, oral diuretic, oral bisphosphonate therapy were started. Symptomatic improvements was noted after 48hours, and blood pressure, laboratory parameters came to within normal level over next 2 weeks.

Conclusion: Due to awareness of vit D deficiency the common practice of overzealous vit D supplementation should be avoided to prevent the consequences of its toxicities. Vit D3 metabolic profiling and safety parameters must be evaluated before initiation of therapy.

Keywords: Hypervitaminosis D, Hypercalcemia

INTRODUCTION

Among the four fat soluble vitamins vitamin D regulates the calcium homeostasis. Recommendation and concerns over vitamin D deficiency has led to widespread use of vitamin D supplements, containing upto 60,000IU/unit dose in practice from infantile age. In recent years vitamin D deficiency has been considered as the most common nutritional deficiency in health and disease and hence, there has been an increase in the use of vitamin D.[1] Doses more than 50,000 IU/day raise levels of 25(OH) vit D to more than 150 ng/ml and are associated with hypercalcemia and hyperphosphatemia.[2]

Various Studies have documented the role of Vit D in various pathological states and it is now being considered as a wonder drug. Framingham Offspring Study found a significant association between low serum 25OHD levels and incidence of Cardiovascular disease.[3] A trial in New Zealand found a significant improvement in insulin sensitivity on Vit D supplementation compared with those in the placebo group after 6 months.[4] Low serum 25OHD levels have been implicated in metabolic syndrome, abdominal obesity, and hyperglycemia. Vitamin D deficiency has been linked to asthma incidence in the developing fetus and in young children.[5] There is innumerable data on the beneficial effects of Vit D supplementation, but there is other side of spectrum also where inadvertent or unsupervised use of Vit D can lead to its toxicity.

Vitamin D toxicity usually occurs over a time period and presents with hypercalcemia. Unintentional vitamin D poisoning is associated with over fortification of milk, adulteration of table sugar, contamination of cooking oil, with use of over the counter supplement. Hypervitaminosis D can also result from excessive intake of synthetic vitamin D analogs (25-D, 1,25-D). We hereby present a case scenario in which unsupervised parentral intake of Vit D led to its toxic effect in an 11.5 yr old girl.

CASE REPORT

11.5 years old female patient was admitted in JNMCH, AMU, Aligarh with complaints of burning abdominal pain in epigastric region, constipation, decreased appetite for 15days and vomiting (multiple episodes in a day) for last 12days. Pain was not associated with feed intake and not relieved after any medication and gradually increasing in intensity. After 3 days of onset of pain vomiting started which was non-projectile, non-bilious and not associated with blood, and associated with nausea and loss of appetite. There was history of multiple intramuscular vitamin D injections (600,000IU per injection) prior to development of the symptoms. The medication was prescribed for the complaint of short stature and each injection was given every 3rd day. After administration of 3rd dose the complaints started but the injectable medication was not stopped and total 12 injections were given prior to admission. No CNS complaint was there.

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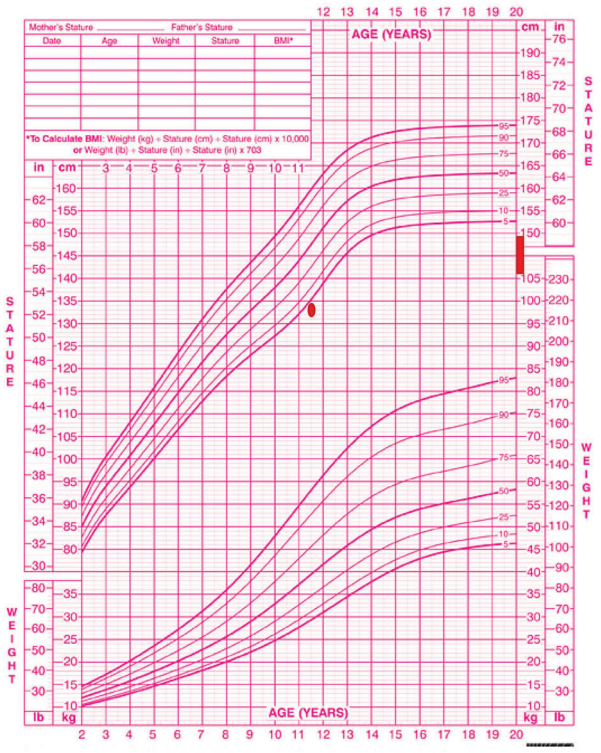

Figure-1: Growth chart of the patient showed that the patient's height was below 3rd centile (marked by red circle) and target height is also below 3rd centile (marked by red bar) and her height velocity is within the target range

Anthropometry: Her length was 134.5 cm, (<-2SD) weight was 31.5kg, BMI 17kg/m^2 (<median), US: LS 0.9. Mid parental height: 147cm.

When the height was plotted in the graph (Figure 1) it was observed that her height is below 3rd centile for her age, and her mid-parental height was also below 3rd centile, According to the graph her height velocity graph for her final height within the target range.

SMR was 2, menarche was not attained. On examination blood pressure was above 99th centile.

General examination: Pallor, cyanosis, icterus, clubbing, edema, lymphadenopathy – absent.

Other head to toe examination: Within normal limit.

Systemic examination

Higher function: Intact. No apparent cranial nerve palsy, no signs of meningeal irritation was there. Pupil bilateral normal size normally reacting.

Sensory system: Intact.

Motor system: Bulk, posture, tone normal, no abnormal movement was there, power 5/5.

Reflexes: Superficial, deep: normal Planter- Bilateral Flexor. Coordination, stance & gait: normal.

Cerebellar sign: Absent.

Autonomic: No abnormality detected.

Abdomen: Inspection: Not distended, not scaphoid, umbilicus: central, all quadrants moving equally with respiration. Palpation: soft, non-tender, no organomegaly. Percussion: tympanic. Auscultation: bowel sound within normal limit. Hernial orifices: no abnormalities detected. Genitourinary system: no abnormality detected.

CVS: Inspection: precordium: normal. Apex: left 5th intercostal space 2.5cm medial to mid-clavicular line. S1,S2-normal, no murmur. Respiratory system: Inspection: bilateral chest movement normal, equal. No visible vein/ pulsation/ scar mark present. Palpation: bilateral chest movement equal, no local rise of temperature. Percussion: resonant in all lung field. Auscultation: bilateral air entry equal, normal vesicular breath sound was heard.

Laboratory reports showed:

	Observed value	Normal range
Serum Calcium	14mg/dl	8.8-10.8mg/dl
Serum 25 Hydroxy D	255.10ng/ml	30-100ng/dl
Serum Phosphorus	5.3mg/dl	3.3-5.4mg/dl
Serum PTH	0.23pg/ml	14-72pg/ml
Blood urea	58mg/dl	14-36mg/dl
Serum creatinine	1.88mg/dl	0.55-1.30mg/dl
Urine calcium	15mg/dl	
GFR	40ml/min/1.73m^2	

On Ultrasonography no nephrolithiasis was noted. Fundus examination was not suggestive of raised intracranial pressure.

Since there was a clear history of high dose of Vit D intake with all the laboratory parameters favouring the diagnosis, the child was kept as a case of hypervitaminosis D and treatment was started. Hydration therapy was started along with oral diuretic and bisphosphonate tablets. After 48 hours of starting of treatment symptomatic improvement was noticed, renal function parameters started to decline, though still in higher range (Blood urea 42mg/dl, Serum creatinine 1.14mg/dl). After next 72hours the parameters came in normal range (Blood urea 32mg/dl, Serum creatinine 0.95mg/dl) and serum calcium level became 13.8mg/dl which was still high. Blood pressure also started to fall and it was between 90th and 95th centile and after 2weeks blood urea, serum creatinine, and serum calcium level became 22.92mg/dl,0.62mg/dl and 10.71mg/dl respectively. Blood pressure was at 90th centile.

DISCUSSION

The first reported case of vitamin D toxicity documented in 1931 resulting from an overdose of vitamin D supplement in a 2-year-old male infant.[6] Serum calcium concentration of 18–19mg/dL and a serum 25(OH)D concentration of >600 ng/mL have been reported in infants and adults. In contrast the highest serum 25(OH)D concentration reported in a patient due to prolonged sunshine exposure was 90 ng/mL (225 nmol/L).[7] Death of two infants due to daily administration (over 8–12 months) of irradiated ergosterol containing approximately 30,000–40,000 IU of vitamin D2 has also been reported. Accidental overdose has also occurred in several cases due to milk over-fortified with vitamin D at 600 times (>50 IU/100 g) the targeted dose.[8] With availability

of oral vitamin D preparations, intramuscular preparations do not offer any advantage unless severe malabsorption is present. In the present case, patient was given multiple injections of vitamin D without any documentation of serum vitamin D deficiency to accelerate growth velocity and to attain tall stature. As Vitamin D is stored in fat, toxicity once occurs, takes a very long and unpredictable time to resolve. As in our case, patient presented with symptoms of hypercalcemia. This patient received cumulative dose of 7200000IU over 18days (400000IU/day). Prolonged hypercalcemia, hyperphosphatemia, hypercalciuria can result in nephrocalcinosis, nephrolithiasis, bone resorption and tissue calcification. Serum 25(OH)D3 is a marker of vitamin D3 status. Quantitation of serum 25(OH)D3 concentration is a first step to evaluate of hypercalcemia due to suspected vitamin D3 associated toxicity[9] In our patient over dosage on vitamin D resulted in serum 25 OH D levels of 255 ng/ml. Levels above which vitamin D toxicity occurs has been described are 150 ng/ml. An upper limit of 10,000 IU/d of vitamin D for adults has been described safe.[10] Other causes of hypercalcemia include primary hyperparathyroidism and granulomatous diseases such as sarcoidosis, granulomatous tuberculosis and certain lymphomas where extra renal expression of 1a-hydroxylase by tumors has been the cause of excessive production of $1,25(OH)_2D3$ and resulting hypersensitivity to vitamin D.[9]

CONCLUSION

Due to awareness regarding vitamin D deficiency overzealous supplementation with vitamin D3 supplements has become common which may lead to vitamin D3 toxicity. Vitamin D3 metabolic profiling is of value for evaluating such cases and to exclude certain genetic causes. Safety parameters have to be established for long term supplementation especially for high dose vitamin D3 supplementation. Thus, vitamin D deficiency, although common, needs to be treated with caution and inadvertent use of vitamin D supplements should be avoided.

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