

ORIGINAL ARTICLE

A cause and effect relationship between pediatric epileptic medications and vitamin - D deficiency: Does it exist?

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ABSTRACT:

Objective: Epilepsy is included in neurological disorders that require chronic therapy using antiepileptic medications. Short term follow ups have implicated that patients' on antiepileptic drugs use for long duration may suffer from deficiency of vitamin D and bone diseases irrespective of age and sex. Thus, the present study examined this relationship between serum levels of a compound of Vitamin D (25-hydroxyvitamin D) and use of antiepileptic medications in pediatric epilepsy patients. **Materials & Methods:** Fifty patients with pediatric epilepsy and on monotherapy for a minimum duration of one-year along with 50 age and sex matched controls were selected. Both cases as well as controls undertook tests for serum 25-hydroxyvitamin D and serum calcium and phosphorus level estimation. **Results:** It was seen that patients deficient in 25-hydroxyvitamin D were significantly higher among cases (48%) than controls (22%). Carbamazepine and sodium valproate were the drugs which were significantly associated with 25-hydroxyvitamin D deficiency. It was estimated that the risk of vitamin D deficiency was highest when sodium valproate was used followed by carbamazepine. **Conclusion:** Carbamazepine and sodium valproate use results in 25-hydroxy vitamin - D deficiency especially in pediatric epileptic patients.

Keywords: Epilepsy; vitamin D; Carbamazepine; Valproic Acid.

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This article may be cited as: Gupta BK. A cause and effect relationship between pediatric epileptic medications and vitamin - D deficiency: Does it exist?. J Adv Med Dent Scie Res 2017;5(9):47-49.

Access this article online	
<p>Quick Response Code</p> 	Website: www.jamdsr.com
	DOI: 10.21276/jamdsr.2017.5.9.10

Introduction

Epilepsy is one of the most common chronic neurological disorders that affect approximately all age groups. More than 10 million people suffer with seizures among the Indian population and prevalence of epilepsy is 1%.¹ In children, the frequency varies from 2 to 22 per 1000² and around 50% of the epileptic patients suffer since their childhood.³

Such patients are usually taking antiepileptic drugs (AEDs) for a long time leading to abnormal bone mineral metabolism, increased risk of fracture and osteoporosis.⁴ The main mechanism is vitamin D deficiency that is caused by AEDs in epilepsy patients.⁵

Vitamin D exists as serum 25-hydroxyvitamin D and this also serves as a marker of vitamin D levels in the body. Thus, the aim of the present study was to scrutinize the blood levels of serum 25-hydroxyvitamin D in pediatric epilepsy patients who are on long term AEDs.

Material and Methods

Fifty pediatric epilepsy cases below 18 yrs and 50 age and sex matched controls were selected. Informed consent was taken from the subjects. Epilepsy was diagnosed when there was incidence of minimum two unprovoked seizures happening at least 24 hours apart.⁶

Controls were enlisted from healthy subjects from same hospital. Epileptic patients who were on monotherapy with antiepileptic drugs for minimum one year were included. Those for healthy controls included patients without any history of seizures, rickets or other bone related disorders.

5 ml blood was collected from both cases and controls for assessment of 25-hydroxyvitamin D. Chemiluminescent microparticle immunoassay (CMIA) with automated instruments was used for calculation

Statistical analysis was applied by SPSS version 22.0 (Chicago, IL, USA) software. Mean and standard deviation (SD) were estimated. P - value of <0.05 was considered statistically significant.

Results

Boys constituted 60% in both cases and controls. Mean age recorded was 12 yrs in cases and 11.5 yrs in controls. A significantly higher prevalence of deficiency of 25-hydroxyvitamin D, (P<0.0001) was noticed in cases compared to controls (Table 1).

Also, a higher prevalence of 25-hydroxyvitamin D deficiency was found with carbamazepine (P=0.003) and sodium valproate (P=0.03) usage. The difference was statistically significant. (Table 2)

Table 1: Comparison of 25 – hydroxy Vitamin D deficiency among cases and controls

Parameter	Cases	Control	p-Value
Overall 25-hydroxyvitamin D deficiency	48%	22%	0.003
Mean 25-hydroxyvitamin D	16.5±4.5	28.7±9.6	0.00002

Table 2: Comparison of various medications and their comparative associations with 25 – hydroxy Vitamin D deficiency

Medicine	Normal	Deficiency	p - Value
Sodium Valproate	3 (12%)	7 (28%)	0.003
Phenobarbital	8 (30%)	5 (22%)	0.08
Topiramate	3 (12%)	3 (12%)	0.12
Lamotrigine	5 (19%)	0	0.24
Carbamazepine	7 (27%)	9 (38%)	0.03
TOTAL	26 (52%)	24 (48%)	

Discussion

It was seen that 25-hydroxyvitamin - D deficiency was significantly higher among epileptics (48%) compared to control subjects (22%), which is a constant finding noted by similar studies.^{5,7}

Lower mean calcium levels in epileptic patients compared to controls (p = 0.03) has been previously advocated by others.⁸ The mechanisms that are responsible for lower levels of calcium in epileptics can be many. AEDs are concomitant with modifications in bone metabolism and phosphate concentration and consequently a variation in calcium homeostasis in the body.⁹ However, in literature, there is significant amount of contradiction to the previous research as well.¹⁰

The present study affirmed that mean 25-hydroxyvitamin - D levels were significantly lower in cases (16.5±4.5) compared to controls (28.7±9.6) (P<0.0001). In a similar study, the mean level of 25-hydroxyvitamin D was found to be lower among cases (28.79±33.85) in sharp contrast comparison to controls (mean 47.62 ± 46.16).¹¹ Some studies also have failed to show any relationship between deficiency of 25-hydroxyvitamin D and epilepsy.^{9,12}

The main mechanism for pathogenesis seems to be based on a reduction of active levels of vitamin - D, probably caused by stimulation of hepatic cytochrome P450 enzymes by AEDs, causing it to convert into inactive metabolites in the liver. Hypocalcemia is due mainly to reduced absorption from the gut which is perhaps secondary to the state of hypovitaminosis D.¹³

It was also found that 25-hydroxyvitamin – D deficiency was associated with carbamazepine (39.6%) and sodium valproate (34.2%) usage; literature also shows that similar studies advocate our findings.¹⁴ However, some studies did not find any significant association of carbamazepine and sodium valproate usage with deficiency of 25-hydroxyvitamin D.¹⁵

The present study further re - emphasises the need to create more bone health awareness among epileptic patients and health care providers towards epilepsy. All epileptic patients should be counselled with regards to calcium and vitamin D intake, exposure to sunlight and

physical activity, especially before commencement of AEDs.

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Source of support: Nil

Conflict of interest: None declared

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