

Research Article

A study of vitamin - D status in epileptic children in age group of 2-15 years

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ABSTRACT

Background: Epilepsy is a common neurological disorder of childhood frequently requiring prolonged use of anticonvulsants. This study was done to assess the levels of vitamin D epileptic children. We aimed to describe the prevalence of, and risk factors for vitamin D insufficiency among children with epilepsy.

Methods: This prospective observational study included 86 children with age group of 2 to 15 years with epilepsy subjecting them for assessment of 25 OH vitamin D levels by CLEA method.

Results: Of total of 86 patients, 65 children (75.5%) had vitamin D levels <20 ng/ml (deficiency). 15 (17.4%) children had vitamin D levels between 21-29ng/ml (insufficiency) and 6 (7.1%) children had vitamin D levels >30ng/ml (sufficiency). Males were more commonly deficient in vitamin D, and vitamin D levels were significantly low in indoor patients. The levels of vitamin D decreased as the duration of anticonvulsant usage increased. No significant correlation was found between monotherapy and polytherapy.

Conclusions: We found vitamin D insufficiency to be highly prevalent among our unselected cohort of children with epilepsy. Potential risk factors for low vitamin D were examined, and indoor ambulation and duration of anticonvulsant intake were found to be significant. For children with epilepsy, cerebral palsy and enzyme-inducing AEDs are often cited as risk factors for poor bone health. This high prevalence of hypovitaminosis D suggests that, almost all children with epilepsy are at risk.

Keywords: Vitamin d deficiency, Epilepsy, Anticonvulsants, Hypovitaminosis D

INTRODUCTION

Medical literature has recently focused attention on the impact of vitamin D on various aspects of health. The association between vitamin D, antiepileptic drugs (AEDs), and bone health in individuals with epilepsy has been recognized for more than thirty years.¹ Although few comparable data are available for children, adults with epilepsy are known to be at significantly increased risk for bone fractures, compared to the general population. Increasing age and duration of treatment are important risk factors.^{2,3}

Seizures themselves pose a risk for injury, including fractures; and the added co-morbidity of poor bone health increases this risk, especially in children whose seizures have major motor manifestations, as well as those with impaired motor function and coordination.

Many AEDs are inducers of hepatic CYP450 metabolism. It has been postulated that these AEDs result in increased hepatic metabolism of vitamin D, leading to low vitamin D levels. However, non-enzyme inducing AEDs (e.g. valproic acid) have also been associated with low vitamin levels and in turn with poor bone health.⁴ Therefore, although the newer AEDs (e.g. lamotrigine,

levetiracetam, oxcarbazepine) are less-potent enzyme inducers than carbamazepine or phenytoin, they are not necessarily inert in bone metabolism.

Studies have reported variable changes in bone mineral density and vitamin D levels in children taking antiepileptic drugs (AEDs).⁵ Studies have been done linking seizure frequency and vitamin D deficiency per se, in children.⁶

We aimed to describe the prevalence of, and risk factors for vitamin D insufficiency among children with epilepsy.

METHODS

Source of data

Children in age group of 2- 15 years in JSS hospital, Mysore with epilepsy were taken into study group after fulfilling the inclusion criteria from November 2012 to April 2013.

Study design

It is a prospective observational study.

Collection of data

All children 2 to 15 years of age with epilepsy were subjected for assessment of vitamin D status. 2ml of non-fasting peripheral venous blood without applying tourniquet was drawn after taking informed consent. This study was approved by the Ethics Committee of the University College of Medical Sciences. Samples were sent to laboratory and analysis was done for 25OH vitamin D by CLEA method. Chemiluminescent 25(OH) D assay is fully automated on the LIAISON analyzer. Under this format, a 25(OH) D-chemiluminescent tracer competes with 25(OH) D in the sample for binding to antiserum coated on paramagnetic beads. This antiserum has equal affinity for both the D2 and the D3 forms of the vitamin D metabolite, and the assay provides total 25(OH)D values.

Inclusion criteria

Children with epilepsy aged 2 to 15 years.

Exclusion criteria

- Children with metabolic bone disease
- Significant renal impairment, hepatic impairment, endocrine disorders
- Children with epilepsy who are seizure free and off medication for 3 or more years
- Children with first episode of seizure with fever
- Children on vitamin D supplementations

Statistical methods employed

Following statistical methods were employed in the present study; Descriptives; Crosstabs (contingency table analysis); Chi-square test.

RESULTS

The demographics of the 86 patients included in the analyses are presented in Figure 1.

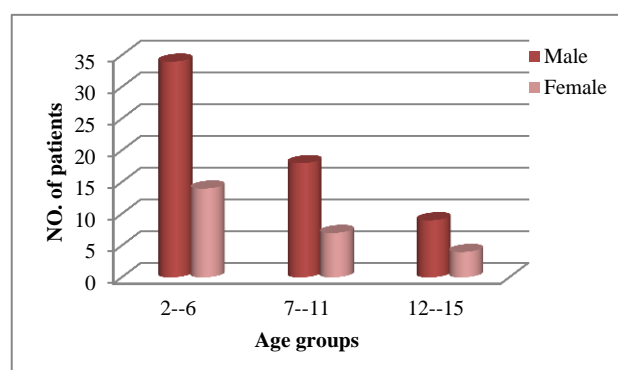


Figure 1: Age and sex distribution of cases.

Of the 86 patients studied, majority were in the age group of 2-6 years (48 patients accounting for 56%), and the least were in the age group of 12-15 years (13 patients accounting for 15%). Males accounted for 71% of the cases (61 patients) whereas females constituted 29% (25 patients).

Figure 2 shows percentage of children who were deficient in vitamin D. 65 children (75.5%) had vitamin D levels <20 ng/ml (deficient). 15 (17.4%) children had vitamin D levels between 21-29ng/ml (insufficiency) and only 6 (7.1%) children had vitamin D levels >30ng/ml (sufficiency).

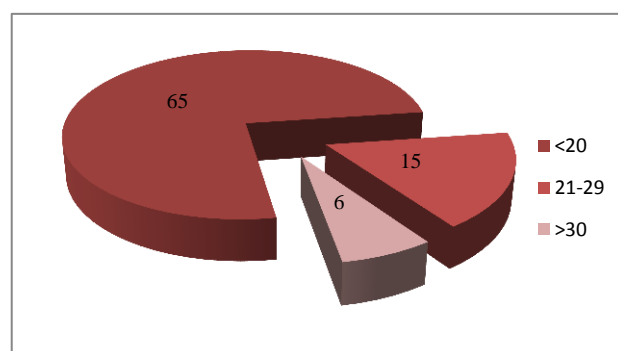


Figure 2: Levels of vitamin D in patients.

Figure 3 shows vitamin D levels in correlation to ambulatory status. It showed that vitamin D levels were significantly low in indoor patients (P value 0.004) as depicted in Figure 3.

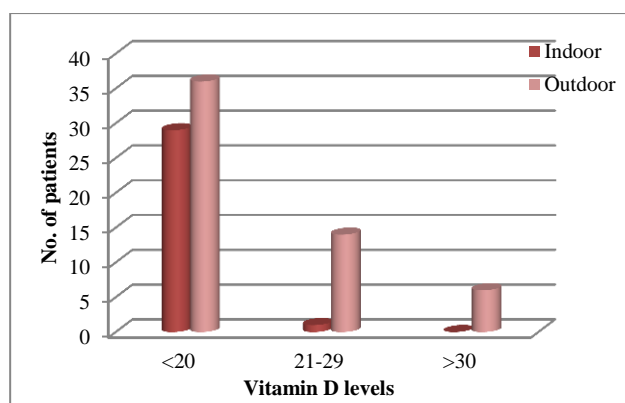


Figure 3: Vitamin D levels in correlation to ambulatory status.

Figure 4 shows that the levels of vitamin D decreased as the duration of anticonvulsant usage increased, which was statistically significant (P value 0.001).

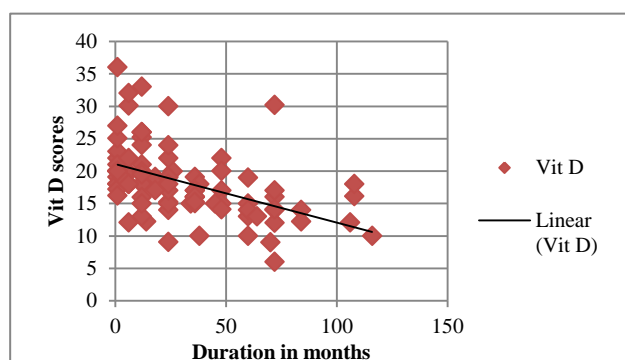


Figure 4: Linear relationship between vitamin D levels and duration of anticonvulsant usage.

Monotherapy versus polytherapy

There were a total of 44 patients in monotherapy category of which 35 patients had vitamin D levels less than 20ng/ml (79%), and 42 patients in polytherapy category of which 30 patients had vitamin D levels less than 20ng/ml (71.4%). There was no statistical significance of vitamin D levels with polytherapy or monotherapy with P value of 0.585.

DISCUSSION

Vitamin D deficiency was highly prevalent among the study group. Of the 86 patients studied, majority were in the age group of 2-6 years (48 patients accounting for 56%), and the least were in the age group of 12-15 years (13 patients accounting for 15%). Males accounted for 71% of the cases (61 patients) whereas females constituted 29% (25 patients). Vitamin D levels were significantly low in the study group with 75.6% (65 patients) was in the deficiency range, 17.4% (15 patients) in insufficiency range and 7% (6 patients) in normal range.

Study by Shellhaas RA⁷ showed vitamin D deficiency in 25% of children, and Choong Yi et al showed 22% children deficient in vitamin D.⁷ A study of Nettekoven et al showed 76% of children deficient in vitamin D which is comparable with the present study.

Study done by Baer et al showed that vitamin D levels were low in children who were non ambulatory irrespective of anticonvulsant use. Similar results were obtained in study done by Lamberg et al which showed low vitamin D levels in children who were non ambulatory and on anticonvulsants which was comparable with the present study.

Table 1: Comparison of vitamin D levels from different studies with the present study.

	Shellhaas RA et al (n=78)	Fong CY et al (n=111)	Nettekoven et al (n=38)	Present Study (n=86)
Vitamin D levels (ng/ml)				
<20	20 (25%)	24 (22%)	29 (76%)	65 (75.6%)
21-29	39 (50%)	45 (41%)	8 (21%)	15 (17.4%)
>30	19 (25%)	42 (37%)	1 (3%)	6 (7%)

Table 2: Comparing the effect of ambulation on vitamin D levels.

Vitamin D levels less than 20			
	BAER et al	Lamberg-allardt et al	Present study
Ambulatory			
Anticonvulsants (n=23)	2 (13%)		56 (64%)
No-anticonvulsants (n=226)	34 (23%)		
Non ambulatory			
Anticonvulsants (n=46)	11 (42%)	low levels	30 (96%)
No-anticonvulsants (n=43)	11 (42%)		

There was also linear relationship between vitamin D levels and duration of anticonvulsant use with decrease in vitamin D levels with prolonged use of anticonvulsants. Present study showed that 100% of children taking anticonvulsants for more than 100 months had vitamin D deficiency when compared to 93% in children with duration of 50-100 months and 70% with less than 50 months of duration.

Table 3: The effect of prolonged use of anticonvulsants on vitamin D levels.

Vitamin D levels (ng/ml) present study	<50 months	50-100 months	>100 months
<20	47	14	4
20-29	15	-	-
>30	5	1	-
Total number of children	67	15	4
	70% deficient	93% deficient	100% deficient

Study by Nicolaidou et al showed there was a significant decreasing trend of 25OH vitamin D ($p<0.03$) in relation to duration of use of anticonvulsant which is similar to the present study, where prolonged duration of anticonvulsant use resulted in lower vitamin D levels.⁵

Table 4: Decrease in vitamin D levels with prolonged usage of anticonvulsants.

Nicolaidou et al	Vitamin D levels	
Duration of anticonvulsants use	Cases	control
0 (n=51)	No difference	Same
1 st year (n=51)	Decreased	Same
2 nd year (n=25)	Decreased	Same
3 rd year (n=6)	Decreased	Same

No statistical significance was found between vitamin D levels and number of anticonvulsants used in the present study.

We view the high prevalence of inadequate vitamin D levels in pediatric epilepsy patients as significant, since these children are at additional risk for bone injury due to their seizures, comorbid neuromotor dysfunction, and long-term treatment with medications that affect bone health both through vitamin D metabolism and other mechanisms. Screening for and treating low vitamin D levels in pediatric epilepsy patients is inexpensive, lacks significant side effects, decreases the seizure frequency and may improve bone health in this vulnerable population.

Children on either type of AED regimen were at equal risk for low 25OHD levels. Virtually all children with epilepsy may be at risk for hypovitaminosis D. We do not

routinely screen children with epilepsy with dual energy X-ray absorptiometry scans to evaluate bone mineral density. Therefore, we cannot comment on the impact of our patients' low vitamin D levels on their bone mineralization. However, we postulate that low 25OHD levels should be associated with abnormal bone metabolism and likely places these patients at risk for poor bone health. We also lack systematic dietary assessments and so cannot comment on the impact of our patients' nutritional status on their vitamin D levels. Others have demonstrated that diet has an important effect on vitamin D levels and this should not be overlooked.⁸ However, since so many children do not have adequate vitamin D in their diets it should not be surprising that the prevalence of vitamin D insufficiency is high.^{9,10} This finding, in combination with the recent increase in the recommended daily vitamin D intake for children suggests that far more of our patients than previously recognized require vitamin D supplementation.

CONCLUSION

We found vitamin D insufficiency to be highly prevalent among our unselected cohort of children with epilepsy. Potential risk factors for low vitamin D were examined, and indoor ambulation and duration of anticonvulsant intake were found to be significant. For children with epilepsy, cerebral palsy and enzyme-inducing AEDs are often cited as risk factors for poor bone health. The high prevalence of hypovitaminosis D suggests that, almost all children with epilepsy are at risk. Increased attention on the part of both pediatric neurologists and primary care physicians to vitamin D status among children with epilepsy is warranted as vitamin D has a vast impact on health of children other than bone health such as reducing the frequency of seizures, immunity, autoimmune diseases, cancer protection to name a few.

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