Research Article

Level of Vitamin D in Children with Newly Diagnosed Idiopathic Epilepsy

Samir T. Abdallah, Doaa M. Mahrous, and Somaya F. Folly Mohammed
Department of Pediatrics, El-Minia Faculty of Medicine

Introduction

Epilepsy is a disease of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition, it is one of the most common neurological illnesses that affect individuals of any age and ethnicity[(1)]. Epilepsy is the most frequent chronic neurologic condition in childhood that affects 0.5 : 1.0 % of children globally[(2)]. About 30% of childhood epilepsy is idiopathic[(3)].

Vitamin D3 (25-hydroxy vitamin D3) have an important role in human health, it plays a pivotal role in calcium and bone metabolism (by increasing the absorption of calcium and phosphorus in the intestine and inhibiting the secretion of parathyroid hormone), therefore, its deficiency may cause rickets, osteopenia, and osteoporosis[(4)]. In addition, vitamin D plays an important role in brain development and behavior as well (it is involved in neuroprotection, brain cell proliferation and differentiation)[(5)]. It is also has been reported that vitamin D deficiency has been associated with increased risk of many diseases such as cancers, autoimmune diseases, hypertension, and infectious diseases[(6)].

Epileptic children need long-term anticonvulsant therapy, therefore, they have a higher risk of adverse effects[(6)]. A large body of evidence since 1960 indicates that antiepileptic drugs (AEDs) impact bone metabolism negatively leading to impaired bone quality and increased risk of fractures[(7)].

Recently, it has been reported that children with epilepsy who were treated with AEDs are at increased risk of poor bone health and they often have additional risk factors for vitamin D deficiency[(8)]. This observation lead to extensive research on the interaction between antiepileptic drugs and vitamin D[(9)]

Aim of the Work

The aim of this work is:

To assess level of 25-OH vitamin D3 in children with newly diagnosed idiopathic epilepsy who are treated with different anti-epileptic drugs and correlate its level with other parameters.

Patients and Methods

This is a prospective comparative study included a total of 80 children (51 males and 29 females) with age range of 3-12 years. All of these children were recruited from neurologic pediatric out-patient clinic and inpatient department of Minia Pediatric University hospital during the period from March 2015 to May 2016. The objective of this study is to assess level of 25-OH vitamin D3 in children with newly diagnosed idiopathic epilepsy who are treated with different anti-epileptic drugs. All the included children were classified to two groups:

❖ ***Group (I): Cases:*** included 50 newly diagnosed (if there is evidence of ongoing seizures for 1 year) idiopathic epilepsy patients (epilepsy without evidence cause).

❖ ***Group (II): Control:*** included 30 healthy control subjects.

Patients were chosen according to the following:

- ***Inclusion criteria:***

1) Children with age range of 3-12 years.
2) Children with idiopathic epilepsy.

- ***Exclusion criteria:***

1) Children with congenital anomalies or mentally retarded children.
2) Children with any abnormalities during clinical examination or with history of head trauma.

Results

The present study included a total of 80 children with age range 3-12 years who were classified to two groups:

❖ ***Group (I): Cases:*** included 50 newly diagnosed idiopathic epilepsy patients.

❖ ***Group (II): Control:*** included 30 healthy age and sex matched Children .

The objective of this study was to assess the level of 25-OH Vitamin D_3 level in children with newly diagnosed idiopathic epilepsy who were treated with anti-epileptic drugs. The results will be presented in tables from (1:6) and figures (1:4).

Table (1) shows the comparison between patients and control groups regarding the demographic data.

Table (1): Comparison between patients and controls regarding the demographic data.

Variable		Groups		P. value (Sig.)
		Group (I) Cases (n=50)	**Group (II) Control (n=30)**	
Age (year), mean ± SD (range)		4.9 ± 3.5 (3-11)	7.1 ± 4.1 (3-12)	**<0.01****
Sex	**Male**	33 (66.0 %)	18 (60.0 %)	0.588
	Female	17 (34.0%)	12 (40.0 %)	
Family history	**-ve**	39 (78.0%)	30 (100.0 %)	**<0.01****
	+ve	11 (22.0%)	0 (0.0%)	
Consanguinity	**-ve**	37 (74.0 %)	29 (96.7 %)	**<0.01****
	+ve	13 (26.0 %)	1 (3.3 %)	
	No	42 (84.0 %)	30 (100.0 %)	**0.020***
	Yes	8 (16.0 %)	0 (0.0%)	

T- test and Chi-square were used.
**** Significant (P≤ 0.01)**
*** Significant (P≤ 0.05)**

Table (1) shows demographic data of studded groups where are aged from 3-12 years, in the epileptic children with 33 females and 17 males, also shows the comparison between patients and control groups in family history consanguinity and other affected sibling.

Table (2): Characteristics of epileptic patients group.

Variable		Descriptive (n=50) N (%)
Type of convulsion	**Idiopathic generalized seizure**	43 (86.0%)
	Simple Partial seizure	2 (4.0%)
	Partial seizure with secondary generalization	5 (10.0%)
Duration of antiepileptic drugs (month)	**< 6 months**	40(86%)
	> 6 months	10 (14%)
Treatment	**Valproic acid (old AED)**	36 (72.0%)
	Levetiracetam (New AED)	12 (24.0%)
	Combined	2 (4.0%)
Supplementation with Multi-vitamin	**No**	19 (38.0%)
	Yes	31 (62.0%)
Controlled fits	**Yes**	48 (96.0%)
	No	2 (4.0%)
EEG study*	**Normal**	2 (4.0%)
	Epileptiform discharge	39 (78.0%)
	Diffuse background slowing	9 (18.0%)
CT, MRI*****	**Normal**	48 (96.0%)
	Abnormal	2 (4.0%)

*** Electroencephalography** **** Computed Tomography**
***** Magnetic response imaging (MRI).**

Table (2) showed that of the 50 epileptic patient in our study, there were 43 patient with idiopathic generalized seizure (86.0%), 2 patients with partial seizure (4.0%), 5 patients with secondary generalized tonic clonic (10.0%) (fig. 5). A total of 48 patients of them were controlled while 2 cases were not controlled on the antiepileptic drugs (one of them was post-traumatic epilepsy and the other was epilepsy with hydrocephalus).

Table (4): Correlations between vitamin D and various demographic, clinical and laboratory data.

Parameter		(* vitamin D) Correlation coefficient *(r)*	P. value (Sig.)
Age	**Early childhood**	0.21	0.14
	Late childhood	0.25	0.08
Sex	**Male**	0.28	0.07
	Female	0.19	0.34
Type of convulsion		0.01	0.96
Duration of convulsion treatment		0.21	0.14
Lab. investigations	**Alkaline P.**	0.03	0.834
	Phosphorus	-0.17	0.234
	Calcium	0.18	0.201
Control of fits		0.13	0.35

Grades of correlation (r):
0.00-0.24 (no or week association)
0.25-0.49 (fair)
0.50-0.74 (moderate)
≥ 0.75(strong)

Table (4) presented the correlations between vitamin D level and various demographic and laboratory data in epileptic patients. The results showed that there was insignificant weak positive correlation between vitamin D level and age of child, ALP and calcium levels. However, insignificant weak negative correlation was found between vitamin D level and Phosphorus level.

Discussion

Epilepsy is the most frequent chronic neurologic condition in childhood, it affects 0.5: 1.0% of children globally[(1)]. Idiopathic epilepsy is common, about 30% of childhood epilepsy is idiopathic[(5)]. Reduction of bone mass density [BMD] has been observed in most epileptic patients and about 25% of patients with epilepsy suffer from osteoporosis[(6)]. Children with epilepsy are at increased risk of poor bone health and they often have additional risk factors for vitamin D deficiency[(6)]. Globally, vitamin D deficiency is estimated to be present in more than 1 billion people[(8)].

Vitamin D plays an important role in brain development and behaviour as well ***(Li9)***. Vitamin D has shown to have a neuroactive property in the brain, it is also involved in neuroprotection, brain cell proliferation and differentiation that influences brain development[(10)]. Also, vitamin D deficiency may cause rickets and osteomalacia, resulting in a higher fracture risk and an increased incidence of osteoporosis in adult life[(2)].

The present study is a prospective case control study included a total of 80 children with age range 3-12 years and were classified to two groups: ***Group (I): Cases:*** included 50 newly diagnosed idiopathic epilepsy patients and ***group (II): Control:*** included 30 healthy subjects. The objective of this study was to assess the level of 25-OH Vitamin D_3 level in children with newly diagnosed idiopathic epilepsy who were treated with anti-epileptic drugs and correlate it with other parameters.

The present results showed that epileptic group of children had significantly higher positive family history of epilepsy and consanguinity ($P \leq 0.01$) and also, other affected sibling ($P \leq 0.01$).

The present results agreed with the results of a most recent study conducted in Saudi Arabia by Alanazi et al., (2018) who studied the consanguinity between parents and risk of epilepsy among children. They found that consanguinity between parents was significantly associated with the development of epilepsy where 59.1% of epilepsy patients who participated in the current study had parents who were cousins and 13.6% were non-relatives of the same family (p=0.000). Also, they added that family history of epilepsy was significantly associated with the development of it where 68.2% of epilepsy patients who participated in the study had

Conclusion And Recommendations

- Epileptic children who took anticonvulsant therapy had significantly lower vitamin D level and higher prevalence of vitamin D insufficiency than the non-epileptic control group. The mechanism and effect of vitamin D deficiency in seizure is still unknown.
- Also, epileptic children had obviously lower calcium level compared to control ones (number of cases with low Ca level was significantly higher in epileptic group compared to control).
- No obvious correlation was found between vitamin D level and other clinical of laboratory variables, this may be attributed to the relatively small sample size which did not aid to reach statistical significance.
- Screening and monitoring of vitamin D levels "regularly" should be strongly considered in all children with epilepsy, as vitamin D has a vast impact on health of children other than bone health such as reducing the frequency of seizures.
- We also suggest that further studies including a larger sample of patients are needed to draw a firm conclusion regarding an association between vitamin D deficiency and epilepsy with the evaluation of neurotransmitters, signal pathways, and also lifestyle habits including diet, exercise, and others.
- Finally, future studies are needed to evaluate the effects of vitamin D supplementation on epileptic children.

References

1. Aaberg KM, Gunnes N, Bakken IJ, et al.,. (2017): Incidence and Prevalence of

Childhood Epilepsy: A Nationwide Cohort Study. Pediatrics.;139(5):e20163908

2. Benarroch, E.E. (2011). Na+, K+-ATPase functions in the nervous system and involvement in neurologic disease. Neurology 76, 287–293.
3. Bergey GK (2013): Neurostimulation in the treatment of epilepsy. Experimental neurology; (244): 87–95.
4. Bartels, L.E., Jorgensen, S.P., Agnholt, J., Kelsen, J., Hvas, C.L., and Dahlerup, J.F. (2007). 1, 25-Dihydroxyvitamin D3 and dexamethasone increase interleukin-10 production in CD4+ T cells from patients with Crohn’s disease. Int. Immuno-pharmacol. 7, 1755–1764.
5. Engel Jr J, Wiebe S, French J, et al., (2003): Practice parameter: temporal lobe and localized neocortical resections for epilepsy. Report of the Quality Standards Subcommittee of the American Academy of Neurology, in Association with the American Epilepsy Society and the American Association of Neurological Surgeons. Neurology;60:538–47.
6. Donner, E.J.; Camfield, P.; Brooks, L.; Buchhalter, J.; Camfield, C (2017).; Loddenkemper, T.; Wirrell, E. Under-standing Death in ChildrenWith Epilepsy. Pediatr. Neurol., 70, 7–15.
7. Giussani, G.; Cricelli, C.; Mazzoleni, F.; Cricelli, I.; Pasqua, A.; Pecchioli, S.; Lapi, F.; Beghi, E(2014). Prevalence and incidence of epilepsy in Italy based on a nationwide database. Neuroepidemiology, 43, 228–232.
8. Holick, M.F. and Garabedian, M. (2006): Vitamin D: Photobiology, Metabolism, Mechanism of Action, and Clinical Applications. Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 6th ed. (Washington, DC: American Society for Bone and Mineral Research), pp. 106–114.
9. Jancic, J., Djuric, V., Hencic, B., van den Anker, J. N., & Samardzic, J. (2018). Comorbidity of Migraine and Epilepsy in Pediatrics: A Review. Journal of Child Neurology, 088307381878894.
10. Kesby, J.P., O’Loan, J.C., Alexander, S., Deng, C., Huang, X.-F., McGrath, J.J., Eyles, D.W., and Burne, T.H. (2012). Developmental vitamin D deficiency alters MK-801-induced behaviours in adult offspring. Psychopharmacology (Berl.). 220, 455–463.
11. Klar, N., Cohen, B. & Lin, D. D. M(2016): Neurocutaneous syndromes. Handb. Clin. Neurol. 135, 565–589.