Measurement of vitamin-D in sera of children with epilepsy and its relation with anticonvulsants administration

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Abstract
The study had conducted in Tikrit city for the period from January to June 2018 on 33 children with epilepsy and under treatment with anticonvulant with age group 1-12 years for measurement of Vitamin-D in sera of children with epilepsy. Based on the clinical signs of patients and diagnostic tests, the number of these children had assigned to the present study. The study also included 40 healthy children as a control group. The study included the collection of 3 ml of venous blood at the beginning of the study and 3 months after anticonvulant administration for identification and measurement of vitamin-D by using ELISA technique (Koma-Biotech, Co, USA). The study also included the taking of full information from cases like living situations, age. The study showed that 90.91% of children with epilepsy have vit D deficiency compared with 12.5% of healthy control (P: 0.001). The study showed that the lowest mean of vit D had recorded in children with epilepsy as compared with healthy control. The study showed no significant relation of the age of children with the frequency of epilepsy and showed that the lowest mean of vitamin-D was recorded in children with epilepsy whose ages were below 3 years (7.33±0.9 ng/ml) (P<0.05). The study showed that the lowest mean of vit D had recorded in children with epilepsy after the administration of treatment (anticonvulant) for three months as compared with children before treatment (7.19±1.1) versus (11.12 ±1.4 ng/ml). The study showed the strong negative correlation of vitamin D level of children under epilepsy with the duration of treatment of epilepsy (r: -0.74) which is mean that vitamin D level will decrease whenever the duration of treatment will increase and vice versa. In conclusion, Vitamin D levels had reduced significantly in epileptic children especially whom under long-term anticonvulant therapy.

Keyword: Epilepsy, Children, Vitamin D, anti-conversant


Introduction
Vitamin D is a member of a group of fat-soluble secosteroids, which are mainly important for the homeostasis of calcium, phosphate and magnesium. In this group, the most important compounds are vitamin D2 [ergocalciderol] and vitamin D3 [cholecalciferol] (1). The association between vitamin D, antiepileptic drugs, and poor bone health in individuals with epilepsy had first recognized in 1979 and had thought to be particularly relevant in childhood as this is the time of maximum bone mineralization (2). Children and adolescents treated with antiepileptic drugs had known to have problems with bone metabolism, bone mineral density loss, and 2–3 times the fracture risk of healthy controls (3, 18). The major cause of vitamin D deficiency may be insufficient exposure to sunlight. Obesity and antiepileptic drugs have considered associated with vitamin D deficiency as well (3). Many scientific societies had recommended vitamin D maintenance supplementations with 400 IU daily for all children. Yet, because of insufficient evidence to recommend a specific maintenance dose for children with epilepsy, the American Academy of Pediatrics had recommended 400 IU daily similar to healthy children, 400 and 1000 IU for children who had treated recently for vitamin-D deficiency. The Endocrine Society recommended a higher dose ranging from (600 to 1000 IU) daily for children at risk of developing vitamin-D deficiency (5, 19). However, the importance of vitamin D is most essential in bone metabolism through the intestinal...
absorption of calcium and phosphate, an increase of osteoclast number and promotion of normal functioning of parathyroid hormone [PTH] to maintain serum calcium levels. Insufficient serum levels of calcium and vitamin D may lead to rickets and osteomalacia due to disturbance of bone mineralization \((6,7)\). Therefore, the aim of the study was to measure of Vitamin-D in sera of children with epilepsy.

**Material and method**

The study was conducted in Tikrit city for the period from January to June 2018 on 33 children with epilepsy and under treatment with anticonvulsants with age group 1-12 years. Based on the clinical signs of patients and diagnostic tests, the number of these children have assigned to the present study. The study also included 40 healthy children as a control group. The study included the collection of 3 ml of venous blood at the beginning of the study and 3 months after anticonvulsant administration for identification and measurement of vitamin D by using ELISA technique (Koma-Biotech, Co, USA). The study also included the taking of full information from cases like living situations, age.

**Statistical analysis**

Computerized statistically analysis had performed using Mintab ver 18.0 statistic program for determination of the \(P\) value \((P<0.05: \text{significant})\).

**Findings**

The study showed that 90.91\% of children with epilepsy have vitamin D deficiency compared with 12.5\% of healthy control \((P: 0.001)\), (Table 1).

<table>
<thead>
<tr>
<th>Vitamin D level (ng/ml)</th>
<th>Children with epilepsy</th>
<th>Healthy control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Normal</td>
<td>3</td>
<td>9.09</td>
</tr>
<tr>
<td>Deficient</td>
<td>30</td>
<td>90.91</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>100</td>
</tr>
</tbody>
</table>

\(P<0\)

The study showed that the lowest meant of vitamin D was recorded in children with epilepsy as compared with healthy control, (Table 2).

<table>
<thead>
<tr>
<th>Vitamin D level (ng/ml)</th>
<th>Children with epilepsy</th>
<th>Healthy control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Mean</td>
</tr>
<tr>
<td></td>
<td>33</td>
<td>11.31</td>
</tr>
</tbody>
</table>

\(P<0.05\)

The study showed no significant relation of age of children with frequency of epilepsy and showed that the lowest mean of vitamin D was recorded in children with epilepsy whose age were below 3 years \((7.33\pm0.9\ ng/ml)\) \((P<0.05)\) (Table 3).

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Children with epilepsy</th>
<th>Vitamin D (Mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>1-3</td>
<td>10</td>
<td>30.3</td>
</tr>
<tr>
<td>4-6</td>
<td>12</td>
<td>36.37</td>
</tr>
<tr>
<td>7-10</td>
<td>11</td>
<td>33.33</td>
</tr>
</tbody>
</table>
The study showed that the lowest mean of vitamin D was recorded in children with epilepsy after administration of treatment (anticonvulsant) for three months as compared with children before treatment (7.19±1.1 versus 11.12 ±1.4 ng/ml) (P :0.001), (Table 4).

**Table 4: Results of vitamin D in children with epilepsy according to duration of medication**

<table>
<thead>
<tr>
<th>Vitamin D level (ng/ml)</th>
<th>Before treatment</th>
<th>After 3 months of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Mean</td>
<td>11.12</td>
<td>7.19</td>
</tr>
<tr>
<td>Sd.</td>
<td>1.4</td>
<td>1.1</td>
</tr>
</tbody>
</table>

P<0.05

The study showed strong negative correlation of vitamin D level of children under epilepsy with the duration of treatment of epilepsy (r: -0.74) which is mean that vitamin D level will decrease whenever the duration of treatment will increase and vice versa (Figure 1).

**Figure 1: Correlation of vitamin D level of children under epilepsy with the duration of treatment of epilepsy**

**Discussion**

There is still controversy in the scientific literature about normal levels of vitamin D, partly because of the differences in serum levels between ethnic groups (8). A recent review suggested that optimal levels of vitamin D for all outcomes are approximately 30 ng/ml (9). The latest guidelines supported by Royal College of Pediatrics and Child Health [RCPCM] indicates that deficiency exists when blood levels of 25-OH-vitamin D is below 25 nmol/L, insufficiency when blood levels of 25-OH-vitamin D ranges between 25 to 50 nmol/L, and sufficiency when blood levels of 25-OH-vitamin D is more than 50 nmol/L. The World Health Organization defines vitamin D deficiency when 25-OH-vitamin D level is less than 20 ng/ml and insufficiency when 25-OH-vitamin D levels are 21 – 29 ng/ml (10). Most of the studies of bone mineral density markers in children with epilepsy have found a significant difference in bone mineral density markers and vitamin D in children with epilepsy as compared with healthy ones (11-14). However, these studies could be biased as most included a small sample and did not include large enough numbers to
enable comparison between specific antiepileptic drugs or therapies, or between different epileptic syndromes. Previous studies showed a prevalence of vitamin D deficiency in a pediatric epilepsy population of about 22% (13) and 25%, respectively (14). The reason why the previous two studies showed different prevalence compared to this study might be attributable to the difference in target ethnic group, environmental difference such as the amount of sunshine, and the number of patients included in this study. A higher prevalence of vitamin D deficiency in the Korean population compared to that of the United States population suggests that ethnic or environmental differences have a significant influence on the prevalence of vitamin D deficiency. Several previous studies showed the risk factors for vitamin D deficiency in a pediatric epilepsy population on antiepileptic drugs. In 2008, Nettekoven et al (15) reported that the prevalence of vitamin D deficiency in pediatric epilepsy patients on antiepileptic drugs is high, especially in the group receiving polytherapy. A recent study on vitamin D status in adult patients with epilepsy documented that patients taking enzyme-inducing antiepileptic drugs (e.g., carbamazepine, phenobarbital, phenytoin, primidone) had a higher prevalence of vitamin D deficiency compared to the patients who were not taking enzyme-inducing antiepileptic drugs (16). Another longitudinal cohort study in children on antiepileptic drugs reported a significant decline in vitamin D level among patients during follow-up and showed that longer duration of antiepileptic drugs was associated with a significant decrease in the 25(OH) D level (17).

Conflict of interest: None
Source of findings: self.
Ethical clearance: This research had carried out with the patient's verbal and analytical approval before the sample was taken
Conclusion: Vitamin D levels was reduced significantly in epileptic children especially in whom under long-term anticonvulsant therapy.

Reference