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Klinik Araştırma

Evaluation of vitamin D status in children with refractory epilepsy

Çocukluk çağı dirençli epilepsi olgularında D vitamini düzeyinin değerlendirilmesi

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ABSTRACT

Objective: Vitamin D deficiency has been reported in children using antiepileptic drugs. Multiple antiepileptic drugs may conceivably increase the risk of vitamin D deficiency. The aim of this study is to determine vitamin D status and risk factors for vitamin D deficiency in children with refractory epilepsy.
Methods: Forty children with refractory epilepsy evaluated in our tertiary pediatric neurology outpatient clinic were included in the study, and serum 25-hydroxy vitamin D, parathyroid hormone, calcium, phosphate and alkaline phosphatase levels were assessedd. Vitamin D deficiency was defined as 25-hydroxy vitamin D levels <20 ng/mL, and insufficiency between 21 and 29 ng/mL. Correlations between vitamin D levels and type of epilepsy (generalized or localized), etiology of epilepsy (symptomatic vs idiopathic), body mass index, frequency of seizures, number, and type (old or new; enzyme inducing or not) of antiepileptic drugs, presence of intellectual disability, ambulatory status and gross motor function classification scores were evaluated.
Results: The study group consisted of 17 boys and 23 girls with a mean age of 6.65±5.29 years. Vitamin D deficiency was identified in 25 (62.5%) and insufficiency in 6 (15%) the patients. There was no correlation between vitamin D levels and type of epilepsy, etiology of epilepsy, body mass index, seizure frequency, number of antiepileptic drugs, type of antiepileptic drugs, presence of intellectual disability, ambulatory status and gross motor function classification scores.
Conclusion: We found that vitamin D deficiency was increased in this cohort of children with refractory epilepsy. Vitamin D level should be monitored in patients with refractory epilepsy irrespective of the potential risk factors.

Key words: Children, refractory epilepsy, vitamin D

ÖZET

Amaç: Antiepileptik ilaç kullanan çocuklarda D vitamini eksikliği görülebileceği bildirilmiştir. Çoklu antiepileptik ilaç kullanımının D vitamini eksikliği riskini arttırabileceği düşünülmektedir. Bu çalışmanın amacı dirençli epilepsisi olan olgularda D vitamini düzeyinin ve D vitamini eksikliği ile ilişkili olabilecek risk faktörlerinin belirlenmesidir.
Yöntemler: Çocuk nöroloji polikliniğinde dirençli epilepsi olarak değerlendirilen 40 olgu çalışmaya dâhil edildi. Hastaların 25-OH D vitamini, kalsiyum, fosfor, alkalen fosfataz ve paratiroid hormon düzeyleri değerlendirildi. D vitamini eksikliği 25-OH D vitamin düzeyinin <20 ng/mL; D vitamin yetmezliği 25-OH D vitamin düzeyini 21 ve 29 ng/mL arasında olması olarak tanımlandı. D vitamin düzeyi ile birlikte epilepsi tipi, epilepsi etiyolojisi, vücut kitle indeksi, nöbet sıklığı, antiepileptik ilaç sayısı, antiepileptik ilaçların türü, eşlik eden mental retardasyon, ambulatuvar durum ve kaba motor fonksiyon klasifikasyon skorları değerlendirildi.
Bulgular: Olguların 17'si erkek, 23'ü kızdı. Ortalama yaş: 6,65±5,29 idi. D vitamini eksikliği 25 olguda (%62,5) ve D vitamini yetmezliği 6 olguda (%15) saptandı. D vitamin düzeyi ile epilepsinin tipi ve etiyolojisi, vücut kitle indeksi, nöbet sıklığı, antiepileptik ilaçların türü, eşlik eden mental retardasyon, ambulatuvar durum ve kaba motor fonksiyon klasifikasyon skoru arasında anlamlı ilişki saptanmadı.
Sonuç: Dirençli epilepsili olguların değerlendirildiği çalışmamızda D vitamini eksikliği ve yetmezliği yüksek oranda saptanmış olup, tüm dirençli epilepsili hastalarında risk faktörlerinden bağımsız D vitamini düzeyi kontrol edilmelidir.

Anahtar kelimeler: Çocukluk çağı, dirençli epilepsi, D vitamini

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INTRODUCTION

The association between vitamin D, antiepileptic drugs (AEDs) and poor bone health in epileptic patients is known [1-3]. In children this issue is particularly important because they use AEDs during the time of maximum bone mineralization [4]. Seizures, neuromotor dysfunction, long term treatment with medications affect bone health of epileptic children and vitamin D deficiency creates additional risk for poor bone health [5]. Vitamin D is also essential for organ systems other than skeletal system and deficiency has been associated with an increased risk of infections, autoimmune diseases, diabetes, metabolic syndrome, obesity, asthma and certain neurological diseases [6].

Studies about bone mineral density and/or bone biochemistry in children treated with AEDs have found a prevalence of 25-OH vitamin D levels less than 20 of between 25% and 75% [4]. AEDs increase the catabolism of vitamin D via the induction of cytochrome P450 system [7]. Non-enzyme inducing AEDs (e.g., valproic acid) have also been associated with poor bone health [8]. Polypharmacotherapy in epileptic patients is a risk factor for vitamin D deficiency [9]. In addition to polypharmacotherapy, children with refractory epilepsy might have additional risk factors like cognitive impairment and psychiatric disturbances due to frequent seizures, motor dysfunction related immobility and frequent respiratory infections in which vitamin D may be beneficial [9]. In this study we aimed to determinate the vitamin D status and risk factors for vitamin D deficiency in children with refractory epilepsy.

MATERIAL and METHODS

In this cross sectional study, we collected data from March 2013 to June 2013, in Dokuz Eylül University Pediatric Neurology outpatient clinic in Izmir, Turkey. Children with refractory epilepsy were included in study. Refractory epilepsy was defined as at least one seizure in a month in the past six months despite treatment with at least two AEDs. Data obtained included the following: (1) demographic data (2) features of epilepsy (generalised or partial, symptomatic or idiopathic, duration of epilepsy) (3) seizure types and frequency (4) AEDs (number of AEDs, type of medication used, using enzyme inducing AEDs or not, using old or new group AEDs) (5) ambulatory or nonambulatory (6) intellectual disability (7) body mass index (8) gross motor function classification system (GMFCS) scores. Patients were not taking any multivitamin or vitamin D supplementation during the course of the study. Bone health blood tests were performed during spring of 2013. Serum 25-hydroxy vitamin D (25-OHD), parathyroid hormone (PTH), calcium (Ca), phosphate (P) and alkaline phosphatase (ALP) were measured. Vitamin D deficiency was defined as 25-hydroxy vitamin D levels <20 ng/mL, and insufficiency between 21 and 29 ng/mL. AEDs were classified as new (lamotrigine, levetiracetam, oxcarbazepine, topiramate, vigabatrin, and zonisamide) or old (carbamazepine, clonazepam, ethosuximide, phenobarbital, phenytoin and valproate). Carbamazepine, phenobarbital, and phenytoin were enzyme-inducing AEDs and the others were not. Patients were classified as taking old or enzyme-inducing AEDs if at least one of their medications were belonged to these categories. The study was approved by the ethics committee, and patients and parents gave written informed consent to participate in the study. SPSS, version 15 (SPSS Inc, Chicago, IL), was used for statistical analysis. Mean 25-OHD concentration was defined (Mean±SD). Potential differences in study population characteristics and risk factors about vitamin D status were performed by chi-square test. P-value less than 0.05 was considered statistically significant.

RESULTS

The study consisted of 40 children (17 boys and 23 girls; mean age of 6.65±5.29 years) with refractory epilepsy. Patient characteristics are presented in Table 1. Mean 25-hydroxy vitamin D level of the

population was 20.68±16.09. Vitamin D deficiency was identified in 25 (62.5%) and insufficiency in 6 (15%) of the patients. Among patients with vitamin D deficiency, only two had high PTH levels with hypocalcemia and hypophosphatemia. There was no correlation between 25-OH vitamin D levels and epilepsy type (generalized or localization related), epilepsy etiology (symptomatic vs idiopathic), body mass index, seizure frequency, number of AEDs, type of AEDs (old or new; enzyme inducing or not), presence of intellectual disability, ambulatory status, GMFCS scores (all P>0.05).

DISCUSSION

In our study vitamin D deficiency was identified in 25 (62.5%) and insufficiency in 6 (15%) of the patients. A study from Turkey reported vitamin D deficiency in 8% and vitamin D insufficiency in 25.5% of 849 healthy children and adolescents [10]. Another study with 440 healthy children showed that 40% of the subjects had 25 hydroxy vitamin D less than 20 ng/mL [11]. Our study showed lower levels of vitamin D in epileptic patients on polytherapy then these studies with healthy subjects. We did not compare the levels of our patients with healthy controls and this is a limitation of our study. But the prevalence in our patients is comparable to the reported data. Our patients live in mediterranean climate, which may place them at lower risk for vitamin D insufficiency than the general population.

Our findings are consistent with other studies reporting that epileptic children on polytherapy frequently have vitamin D deficiency [12]. It has been reported that patients under polytherapy have significantly lower 25-OHD levels than patients with monotherapy [9].

One study reported vitamin D deficiency in 12 of 13 children with pharmacoresistant epilepsy [13]. Another study revealed vitamin D insufficiency in 51% of children with intractable epilepsy [14]. The authors found higher levels of 25-OHD in patients with adequate vitamin D intake. They also showed negative association between number of AEDs and 25-OHD levels and no association between vitamin D status and age, gender, ambulatory status, cerebral palsy, and mental retardation [14]. In this study vitamin D status was not correlated with type of epilepsy, etiology of epilepsy, body mass index, seizure fre-

Tablo 1. Patient Characteristics.

Sample size	n=40
Sex (number, %)	
Female	23 (57.5)
Male	17 (42.5)
Mean age, yr, ± SD	6.65±5.29
Mean duration of epilepsy, yr, ± SD	4.50±4.23
Seizure type (number, %)	
Generalized	32 (80)
Partial	8 (20)
Etiology (number, %)	
Idiopathic	15 (37.5)
Symptomatic	25 (67.5)
Seizure types (number, %)	
Generalized (tonic, clonic or tonic clonic)	25 (62.5)
Partial	5 (12.5)
Complex partial	5 (12.5)
Myoclonic	3 (7.5)
Spasms	1 (2.5)
Atonic	1 (2.5)
Seizure frequency (number, %)	
Daily seizures	23 (57.5)
Less than daily seizures	17 (42.5)
Number of antiepileptic drug (number, %)	
2	21 (52.5)
3	15 (37.5)
4	4 (10)
Type of AEDs (enzyme inducing or not; number, %)	
Enzyme inducing drugs	11 (27.5)
Not enzyme inducing drugs	29 (72.5)
Type of AEDs (old, new or both; number, %)	
Old	3 (7.5)
New	5 (12.5)
Both	32 (80)
Intellectual disability (number, %)	
Yes	31 (77.5)
No	9 (22.5)
Ambulatory status (number, %)	
Ambulatory	24 (60)
Nonambulatory	16 (40)
Body mass index (number, %)	
Underweight (BMI <5th percentile)	6 (15)
Normal	30 (75)
Obese (BMI ≥95th percentile	4 (10)
Gross Motor Function Scale (GMFCS) scores (number, %)	
1-2	24 (60)
≥3 (need an assistive mobility device)	16 (40)
Vitamin D status (number, %)	
Normal	9 (22.5)
Deficient (<20 ng/mL)	25 (62.5)
Insufficient (20-29 ng/mL)	6 (15)

quency, number of antiepileptic drugs, type of antiepileptic drugs, presence of intellectual disability, ambulatory status and gross motor function classification scores. Many potential risk factors such seizures, comorbid neuromotor dysfunction, and long-term treatment with medications may cause vitamin D deficiency in this population. This is a relatively small study, so that we could not find a potential risk factor contributing to low vitamin D levels.

In our study we could not find a correlation between bone markers and 25-OHD levels. Among patients with vitamin D deficiency only two had high PTH levels with hypocalcemia and hypophosphatemia. It is not exactly known whether low 25-OHD levels are associated with an increased bone turnover in children using AEDs or not [15].

Children with intractable epilepsy might need recurrent hospitalizations because of frequent infections related with their motor dysfunction and immobility. Vitamin D levels in children with refractory epilepsy might be particularly important because of its regulatory effects on immune functions [6]. There is also data about seizure control with vitamin D supplementation in children with refractory epilepsy [13]. The mechanism of this action is not exactly known but thought to be due to the changes in gene expression via vitamin D receptor [13].

CONCLUSION

In conclusion, we found that vitamin D deficiency was high in this cohort of epileptic children using polytherapy. A study with control group and a larger sample size is necessary to further validate this observation.

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