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Relationship between suicidal patients and vitamin D: A prospective case-control study

İntihar girişim olan hastalar ile D vitamini arasındaki ilişki: Prospektif vaka-kontrol çalışma

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Ethics Committee Approval: The approval of Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee was obtained by the protocol numbered 2018/11/47. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
Etik Kurul Onayı: Bu çalışma Kanuni Sultan Süleyman Eğitim ve Araştırma Hastanesi Etik Kurulu tarafından, 2018/11/47 sayılı protokol ile onaylandı. İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

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Abstract

Aim: When a person ends their life consciously and intentionally, it is called suicide. One of the most investigated issues related to suicide is mental disorders. It has been reported that vitamin D has a prominent role in the treatment of many chronic diseases in recent years. Growing evidence implicates sunlight, or vitamin D, is a key environmental factor in the etiology of neuropsychiatric diseases. The aim of this study was to investigate the vitamin D levels in patients admitted to our emergency department due to suicide intervention and contribute to the treatment of clinical applications according to the results.

Methods: This study included 59 individuals with suicidal attempt and 42 control group subjects. The gender, age, educational level, marital status, and economic status of the patients, whether they had previously received psychiatric treatment, or attempted suicide were recorded in a separate Sociodemographic Information Form (SBF) for each patient. Mann Whitney U test was used for statistical evaluations based on categorical (nominal or ordinal) and binary variables.

Results: The minimum and maximum Vitamin D laboratory parameters of the study group were 4.4 ng/ml and 33 ng/ml, respectively. The mean vitamin D levels in the suicide and control groups were 9.6 ng/ml and 13.8 ng/ml, respectively. There were statistically significant relationships between vitamin D levels, the presence of psychiatric disease (P<0.001) and previous suicide attempts (P=0.02).

Conclusion: Suicidal tendency increases in depression, which is a psychiatric illness. We believe that suicide attempts may be reduced by adding vitamin D to treatment protocols, especially in depression, and that it may direct future studies in this direction.

Keywords: Vitamin D, Suicide, Depression

Öz

Amaç: Kişinin bilinçli olarak ve isteyerek yaşamına son vermesine intihar denir. İntihar ile ilgili en çok araştırılan konulardan biri de zihinsel bozukluklardır. Son yıllarda birçok kronik hastalığın tedavisinde D vitamininin önemli bir rol oynadığı bildirilmiştir. Artan kanıtlarda güneş ışığının veya D vitaminin, nöropsikiyatrik hastalıkların etiyolojisinde önemli bir çevresel faktör olduğu bildirilmektedir. Bu çalışmanın amacı acil servisimize intihar girişimi nedeniyle başvuran D vitamini düzeylerini araştırmak ve sonuçlara göre klinik uygulamaların tedavisine katkıda bulunmaktı.

Yöntemler: Çalışmaya intihar girişimi olan 59 kişi ve kontrol grubu olan 42 kişi dahil edildi. Sosyodemografik Bilgi Formu (SBF) Hastaların cinsiyeti, yaşı, eğitim düzeyi, medeni durumu ve ekonomik durumu, daha önce psikiyatrik tedavi almış veya intihar girişiminde bulunmuş olması her hasta için ayrı bir forma kaydedildi. Kategorik (nominal veya sıralı) ve ikili değişkenlere dayalı istatistiksel değerlendirmeler için Mann Whitney U testleri kullanıldı.

Bulgular: Çalışma grubunun laboratuvar D vitamini düzeyleri minimum 4,4 ng/ml maksimum 33 ng/ml değerleri bulundu. İntihar girişiminde bulunanların D vitamin ortalaması 9,6 ng/ml, kontrol grubunun D vitamin ortalaması 13,8 ng/ml idi. D vitamini düzeyleri ile psikiyatrik hastalık varlığı arasındaki ilişki istatistiksel olarak anlamlı bulundu (P<0,001).D vitamini düzeyleri ile önceki intihar girişimleri arasındaki ilişki anlamlı bulundu (P=0,02).

Sonuç: Psikiyatrik bir hastalık olan depresyonda intihar eğilimi artmaktadır. Özellikle depresyon hastalığında tedavi protokollerine D vitamini eklenerek intihar girişimlerinin azaltılabileceğini ve bu doğrultuda gelecekteki çalışmalara yön verebileceği kanaatindeyiz.

Anahtar kelimeler: Vitamin D, İntihar, Depresyon

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Introduction

When a person and their life consciously and intentionally, it is called suicide. Although suicide is a way out of an overwhelming crisis or problem, it is not a random and purposeless act. The person who committed suicide carries out this action with the thoughts of despair and the lack of people around to help. Suicide attempt is related to the decrease in solutions with the continuation of stress factors [1,2]. The most common method used for suicide is the use of multiple drugs. It has been reported that the possibility of suicide is high in family members of people who have attempted to commit suicide repeatedly [3,4]. In the studies in the literature, it was reported that mental disorders are high in individuals who have attempted suicide or died due to suicide [5-9]. According to past reviews, most persons who die by suicide have an identifiable psychiatric condition at the time of death [10]. In a study involving 100 people in the literature, 70% had depression, 15% had alcoholism, 3% had schizophrenia and 5% had other disorders [11]. The psychiatric diseases which have resulted in suicide are related to many organic pathologies [12], one of them being vitamin D deficiency. The vitamin D molecule plays a key role in the treatment of vitamin D deficiency [13].

Vitamin D and its metabolism

Vitamin D was originally classified as a nutrient when cod liver oil (a source of vitamin D) was found to have antirachitic effect in infants. However, after the discovery of the vitamin D receptor in 1969, it was considered a more complex molecule of the endocrine system [14]. There are two types of vitamin D: Cholecalciferol (vitamin D3) and ergocalciferol (vitamin D2). The most important of the sterols belonging to the vitamin D family is cholecalciferol (vitamin D3), which is produced from 7- dehydrocholesterol (7-DHC, provitamin D3) in the skin with ultraviolet rays [15]. Cholecalciferol is also obtained from dietary sources (oily fish, such as salmon and mackerel, animal liver, fish liver oils, eggs). During exposure to light, 7-DHC absorbs solar radiation (ultraviolet B rays or UVB, wavelengths 290-315 nm), which causes its transformation to previtamin D3. It undergoes a temperature dependent isomerization within a few hours and is then transported from the skin to the circulation, where it is bound by the vitamin D-binding protein [16]. Ergocalciferol is created from viosterol, which in turn is created when ultraviolet light activates ergosterol. Ergosterol, is a component that functions like cholesterol in animal cells. Ergocalciferol is therefore a synthetic molecule, which can be found in fortified foods (milk, cereals, bread products) in some countries or administered as a supplement, orally or parenterally. Recently, Armas et al. [17] demonstrated that ergocalciferol is much less effective than cholecalciferol in humans. Evidence that vitamin D regulates nerve growth factor and glial cell line-derived neurotrophic factor suggests that it may be neuroprotective [18]. Vitamin D can protect the brain against reactive oxygen species via upregulation of antioxidant molecules, such as glutathione, in non-neuronal cells [19]. It has been reported that vitamin D3 receptors and 1α-hydroxylase, the enzyme responsible for active vitamin D in the human brain, were found in both neurons and glial cells in the human brain. The strongest immunohistochemical staining for both the receptor and enzyme was in the hypothalamus and in the large (presumably dopaminergic) neurons within the substantia nigra. This report suggests that vitamin D may have autocrine/paracrine properties in the human brain [20]. Today, vitamin D deficiency is known affect primarily the bones, such as in the case of osteoporosis, and poses a risk for autoimmune diseases, cardiovascular system diseases, type 2 diabetes, some cancer diseases, and infectious diseases [21-24].

Vitamin D has previously been studied in many chronic diseases, but the study of vitamin D levels in suicidal patients has not been adequately studied yet. The aim of this study was to investigate the vitamin D levels in patients admitted to our emergency department due to suicide intervention and contribute to the treatment, according to the results.

Materials and methods

Patient Group

This study was conducted prospectively in patients presenting with suicide in Istanbul Health Sciences University Kanuni Sultan Suleyman Training and Research Hospital Emergency Medicine Clinic between 01.12.2018-01.02.2019 with the approval of Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee by the protocol numbered 2018/11/47. The patients were informed about the study and a separate interview was performed with the volunteers to obtain the necessary information and for clinical evaluations. Our study involved two groups. Power analysis was performed to determine the appropriate sample size. Accordingly, the minimum sample size of this study was calculated as at least 41 individuals for each group, with 0.50 effect, 85% power and 0.05 α error. The study included 59 individuals with suicidal attempt and 42 subjects in the control group. All patients in the study group were evaluated by a psychiatrist when they were able to meet after the completion of their emergency medical treatment. Patients with psychiatric diseases were divided into two groups based on their diagnosis.

Gender, age, educational level, marital status, and economic status of the patients, whether they had previously received psychiatric treatment, or attempted suicide were recorded in a separate Sociodemographic Information Form (SIF) for each patient. The families of the patients were also interviewed to complete the possible deficiencies in sociodemographic information.

For vitamin D measurement, blood samples were collected in disposable, 10 ml, vacuumed, anticoagulant-containing, biochemical tubes. About 5-7 ml of blood was drawn from the patients and the control group, which were centrifuged at 2500 rpm for 10 minutes to separate the serum. Separated serums were stored at -80°C until examined. Each serum was only dissolved once on the day of the study. Values under 20 ng/ml, between 20-29 ng/ml, >30 ng/ml and > 150 ng/ml were considered as deficiency, insufficiency, normal (normal value 40-60 ng/ml), and intoxication, respectively [25].

Statistical analysis

Statistical Package for the Social Sciences (SPSS) 20.0 was used for the analysis. All variables were tested for conformity to normal distribution, and compliance with

parametric test criteria with the Kolmogorov Smirnov test. In addition, the normality of distribution of the data was evaluated by histogram, one of the graphical methods. Descriptive statistics were used in the demographic evaluation of the patients. Within the scope of clinical research, Chi-Square (χ^2) was used to evaluate independent, categorical variables. In the study data, numerical values are expressed as mean (SD). The data obtained from the study conducted within the scope of clinical research were used in student t test for variables that were statistically parametric. For the non-statistical data obtained by the study, Mann Whitney U test was used for statistical evaluations based on categorical (nominal or ordered) and binary variables. The results were evaluated for a significance level of $P<0.05$.

Results

A total of 59 patients and 42 individuals were included in our study. Among all, 65% (n=38) of the patients were female and 35% (n=21) were male. Of those in the control group, 63.4% (n=27) were female and 36.6% (n=15) were male. There was no statistically significant difference in terms of gender between the two groups (x^2:4.768; $P=0.078$). The mean age of the patients was 30.9 (10.7) years, and the mean age of the healthy control group was 30.5 (7.84) years, which were also similar ($P=0.082$).

Among the patients, 50.8% (n=30) were discharged healthily, 29.5% (n=17) were hospitalized and 20.4% (n=12) were admitted to the intensive care unit. When the time zone of the patients was evaluated by suicide intervention, 16.4% (n=10) of the patients had attempted suicide between 08:00-16: 00, 41% (n=24), between 16:00-24: 00 and 42.6%, between 24:00-08:00 (n=25) (Table 1). All patients with suicide attempts were evaluated by the consultant psychiatrist. Of the patients, 57.6% (n=34) had psychiatric diseases and 42.3% (n=25) were not diagnosed with one. 69% (n=23) of the patients who had attempted suicide with psychiatric diseases before were diagnosed with depression, 31% (n=11) with anxiety, panic attack, and post-traumatic stress disorder. 22% (n=13) of the patients had previously attempted suicide, while 78% (n=46) had not. Laboratory values of vitamin D ranged between 4.4 ng/ml and 33 ng/ml. The mean vitamin D levels in the suicide and control groups were 9.6 ng/ml and 13.8 ng/ml, respectively (Figure 1) (Table 1). A significantly negative relationship was found between vitamin D and suicidal attempt (z:-3.630, $P<0.001$) (Table 2). The mean vitamin D values of those with and without prior suicide attempts were 7.6 (5.08) and 10.04 (4.05), respectively. There was a significant relationship between vitamin D levels and previous suicide attempts (z: -2.260, $P=0.02$) (Table 2). Mean vitamin D levels of the patients with and without previous psychiatric diseases was 8.15 (3.23) ng/ml and 11.3 (3.45) ng/ml, respectively (Figure 2), the difference between which was statistically significant (z: -2.494, $P=0.013$) (Table 2). The mean vitamin D levels of patients who attempted suicide and who were diagnosed with depression and other psychiatric diseases were 7.1 (2.1), and 13.2 (3.2), respectively. This difference in vitamin D levels between suicidal patients with other psychiatric diseases and those with depression was statistically significant (z: -3.589, $P<0.001$).

Table 1: Demographic characteristics of participants

Independent variables		Number	Percent (%)	Mean (SD)	*P*-value
Patients groups' gender	Female	38	65		0.078[b]
	Male	21	35		
Control groups' gender	Female	27	63.4		
	Male	15	36.6		
Patients groups' age				30.9(10.7)	0.082[b]
Control groups' age				30.5(7.84)	
Presence of psychiatric disease		34	57.6		
No psychiatric diseases present		25	42.3		
Previously attempted suicide		13	22		
Did not previously attempt suicide		46	78		
Attempt hours of the patients	08:00-16:00	10	16.4		
	16:00-24:00	24	41		
	24:00-08:00	25	42.6		
Vitamin D level average (ng/ml)	Suicide group			9.59(4.37)	0.001[a]
	Control group			13.80(6.59)	
Clinical outcomes of the patients	Discharged With health	30	50.8		
	Hospitalized	17	28.8		
	Intensive care unit	12	20.4		

a: Significant at the 0.05 level ($P<0.05$), b: Not significant

Table 2: Statistical results of vitamin D levels of patients with suicide attempt

Groups	Vitamin D Mean (SD)	Z	*P*-value
Previously attempted suicide	7.6 (5.08)	-2.260	0.02
Did not previously attempt suicide	10.04 (4.05)		
Previous psychiatric diseases	8.15 (3.23)	-2.494	0.013*
No previous psychiatric disease	11.3 (3.45)		
Patients diagnosed with depression	7.1 (2.1)	-3.589	0.001*
Patients with other psychiatric diseases	13.2 (3.2)		

*: Significant at the 0.05 level ($P<0.05$)

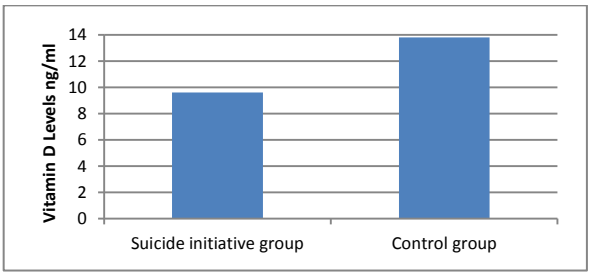

Figure 1: Vitamin D averages of suicide initiative group and control group

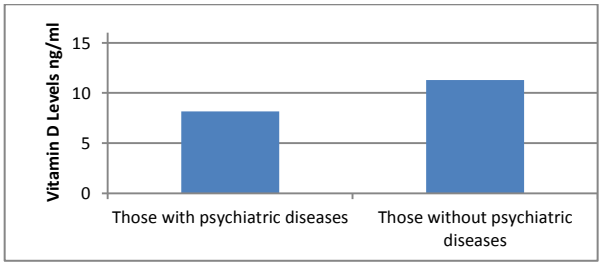

Figure 2: Vitamin D averages of those with and without psychiatric diseases

Discussion

The phenomenon of ending life is an increasing trend in societies. To decrease its incidence, studies regarding the risk factors of individuals are conducted among patients who attempted suicide. The results of our study indicate low vitamin D levels in both the control and suicide attempt groups, which shows that people in Turkey cannot adequately benefit from the sunlight and supplements. We concluded that vitamin D levels were lower in patients who attempted suicide compared to the healthy control group, especially in patients with suicidal ideation and history of depression.

Until recently, little was known about the role of vitamin D in brain function. Growing evidence implicates sunlight, or vitamin D, is a key environmental factor in the etiology of neuropsychiatric diseases [26]. The risk of suicide is different in every psychiatric disorder. Various psychiatric

disorders are more commonly associated with increased risk of suicide, such as major depression [27-29]. Like these studies, suicidal attempt was present in our study, and previous diagnoses of depression was found in the majority of patients with a prior psychiatric diagnosis. In some studies related to depression, depressive symptoms were reported to increase with low vitamin D [30-32], while in others, no relationship was found between low vitamin D and depressive symptoms [33,34]. Unlike our study, Park et al. [35] reported that low vitamin D was not a risk factor in their study on depression and suicidal ideation. The difference may be due to the fact that it was performed in the general population and on individuals who had not finalized suicide. The study of Umhau et al. [36] was conducted on patients who had attempted suicide, and its results regarding vitamin D levels resemble ours. The identification of vitamin D receptors in brain regions affecting depression has strengthened the relationship between vitamin D and depression. In human and animal studies, vitamin D receptors and 1-α-hydroxylase enzyme are found in the brain and the role of vitamin D in central nervous system functions have been shown [37,38]. In another laboratory study, brain development was assessed in neonatal rats whose mothers were rendered vitamin D deficient by eliminating vitamin D from the diet and UVB radiation from the lighting in the animal holding room [39]. The effects on the brain of the offspring were dramatic. Vitamin D deficiency changed the size and shape of the neonatal brain, altered growth factor expression, and cell proliferation. These data confirm that vitamin D deficiency can have effects on the structure of brain, like enlarged ventricles and cortical thinning [40,41]. There is increasing evidence that there is a relationship between depressive symptoms and low serum/plasma 25 (OH) D levels. Cross-sectional studies and prospective data also support that low vitamin D levels are associated with an increased risk of depression [42,43]. In a study showing that vitamin D deficiency and mood disorders were very common among the elderly, the quality of life of the elderly women with low vitamin D (<400 IU/day) was lower than those with higher vitamin D levels. To improve the quality of life in the elderly, it was emphasized that the recommended daily intake of vitamin D (≥400 IU/day) is important [43]. According to the results of our study, the level of vitamin D of the patients with psychiatric diseases was lower in the patient group than those without psychiatric disease. In addition, the vitamin D levels of the group diagnosed with depression in our study were lower than that of the other group. Studies in the literature emphasize low vitamin D in depressive symptoms, especially in psychiatric disorders. Motsingera's previous study on mood disorders and quality of life also yielded similar results [44]. This suggests that vitamin D level is low in suicidal patients and it may be important to measure vitamin D level in patients with suicide ideation. Nutrition plays an important role in the treatment of mental disorders [45]. Recent epidemiologic investigations have reported interesting and consistent associations between dietary patterns and symptoms of anxiety and depression [46,47]. In our study, low levels of vitamin D were found in suicidal patients who were associated with depressive mood.

Limitations

The participants in our study could not be further grouped due to the low number of patients.

Conclusion

Suicide attempts are reduced when the underlying risk factors are eliminated. In especially depression, suicide attempts increase. In addition to the current treatments in depression, we believe that suicide attempt can be indirectly reduced with vitamin D supplements.

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