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ORIGINAL ARTICLE

Evaluation of 25-Hydroxyvitamin D Levels in Patients with Tinnitus

Tinnituslu Hastalarda 25-Hidroksivitamin D Düzeylerinin Değerlendirilmesi

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Abstract

Introduction: This study was planned to investigate serum 25-hydroxyvitamin D levels of individuals who applied to Ear, Nose and Throat clinic with tinnitus complaint which is defined as a conscious awareness of an intracranial noise.

Methods: The study was performed in groups of 50 individuals (50 individuals with at least 6 months of tinnitus) with tinnitus complaint in unilateral or bilateral ears and 50 individuals (mean age of 50.67±14.63) without tinnitus. Serum levels of 25-hydroxyvitamin D were measured by chemiluminescent microparticle immunoassay.

Results: 25-hydroxyvitamin D levels were found to be significantly lower in both single and bilateral tinnitus groups than control group ($p<0.001$).

Discussion and Conclusion: It was concluded that the reasons for the lower levels of 25-hydroxyvitamin D in individuals with tinnitus were worth to be investigated in more detail in new studies.

Keywords: Intracranial noise; Tinnitus; 25-Hydroxyvitamin D

Tinnitus is defined as the conscious perception of an intracranial noise. Tinnitus, from the Latin tinnitus or ringing, is a situation characterized by ringing, swishing, or other noises that seem to be originating in the ear or head.[1,2] The frequency of prevalence increases characteristically with age. It is seen in 8%–15% of the general population and 33% of the elderly population, mostly at the age of 40–80 years.[1,3] In most cases, no specific organic cause is found, and the symptoms can only be subjectively reported.[4] Otologic, neurological, metabolic, pharmaco-

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logical, and psychological reasons are involved in the etiology of the disease. Despite all the advances in modern medicine, the etiopathology of tinnitus has not yet been fully clarified.[1,5–7] On the other hand, despite the high prevalence of tinnitus, there are no clinical standards or best practice guidelines for managing it.[8]

Vitamin D is synthetized in the skin upon exposure to ultraviolet B radiation by the action of the 7-dehydrocholesterol reductase, transferred to the liver, where it is hydroxylated to 25-hydroxyvitamin D (25-OH-D3, or calcidiol). In addition, it can be introduced to the diet from a few dietary sources. 25-(OH)-D3 is a major circulating and storage form of vitamin D. Serum 25-(OH)-D3 level is a valuable marker for the vitamin D status. The best known function of Vitamin D is the maintenance of calcium homeostasis by facilitating the calcium absorption of 1.25(OH)2D3 in the intestine, which is the active vitamin D metabolite and also called calcitriol.[9,10] Vitamin D is also very important for neurological and muscle functions to regulate more than 200 genes. Insomnia and depression may be due to Vitamin D deficiency.[11,12]

It has been known for many years that vitamin D plays a role in Ear, Nose, and Throat (E.N.T.) diseases. It has been reported that vitamin D deficiency should be considered in patients with unexplained bilateral cochlear hearing loss and vitamin D deficiency in 27 patients with bilateral deafness longer than 3 years and that hearing loss is caused by some otosclerosis, presbycusis, and chronic renal insufficiency.[13]

This study was planned for the detection of vitamin D levels in patients who clinically applied with tinnitus complaints.

Materials and Methods

Study Groups

The study was performed on a group of 100 individuals including 50 individuals with tinnitus complaints and 50 individuals without tinnitus (mean age of 50.67±14.63, min: 18, max: 85). The patient group was selected from individuals with similar physical characteristics (lighter skin color, living in the same city, without any diagnosis of osteoporosis, hypertension and diabetes, no thyroid surgery, no euthyroid, and otologic surgery) who had been admitted to the E.N.T. clinic with at least 6 months of tinnitus complaints. Patients with otitis media, craniofacial trauma (head and face trauma), or barotrauma (pressure trauma), those who underwent otologic surgery, used ototoxic drugs, had smoking history, those who were diagnosed with other systemic diseases (heart failure, hypertension, coronary artery disease, cor pulmonale, liver or kidney failure, diabetes, chronic obstructive pulmonary disease) in the last 4 weeks, those who were under 18 years of age, and pregnant women were excluded from the study. The patient group was divided into two subgroups as tinnitus in unilateral or bilateral ears. The study protocol was in line with the principles of the Declaration of Helsinki, and ethics approval was obtained from the Clinical Research Ethics Committee (2017/54).

The control group was formed from patients with similar age and gender characteristics and without otological findings to establish standardization.

Vitamin D Analysis

Serums were obtained by centrifuging blood samples (3000 rpm/10 min). Serum levels of 25-hydroxyvitamin D were measured by chemiluminescent microparticle immunoassay on the Architect-I 2000 system (Abbott Diagnostics, USA).

Blood samples from patients and control groups were taken during the summer season and after 12 h of fasting. Serum samples were obtained by centrifuging blood samples (3000 rpm/10 min). Serum levels of 25-hydroxyvitamin D were measured by chemiluminescent microparticle immunoassay on the Architect-I 2000 system (Abbott Diagnostics, USA).

Statistical Analysis

Results obtained for three groups, unilateral tinnitus, bilateral tinnitus, and control group, were evaluated statistically. The Kolmogorov–Smirnov test was used to test whether the data showed normal distribution, and the Levene variance analysis test for the homogeneity of group variances. One-way ANOVA test was used for group comparison in the groups with normal distribution. Tukey's test was used to determine different groups. In addition, gender distribution was assessed by the Chi-squared test (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.).

Results

Demographic characteristics of the study population are given in Table 1. 25-Hydroxyvitamin D levels obtained as a result of the evaluation of serum samples from the study groups are summarized in Table 2.

There was a significant difference between the control and tinnitus groups in terms of 25-hydroxyvitamin D levels ($p<0.000$). According to the control group, both unilateral and bilateral tinnitus groups were determined to have

Table 1. Demographic characteristics of the study population

Groups	Mean	Count	Minimum	Maximum	Median	SD
One-side						
Male (age)	51.25	8	18.00	72.00	53.00	16.29
Female (age)	48.60	10	30.00	75.00	48.50	12.28
Bi-side						
Male (age)	49.75	8	29.00	82.00	47.50	15.27
Female (age)	53.83	24	26.00	85.00	56.50	14.47
Control						
Male (age)	50.68	22	27.00	85.00	52.50	15.83
Female (age)	48.79	28	20.00	69.00	49.00	14.75

SD: Standard deviation.

Table 2. Serum vitamin D levels (ng/mL)

	Groups											
	One-side				Bi-side				Control			
	Mean	Min	Median	Max	Mean	Min	Median	Max	Mean	Min	Median	Max
Vitamin D	15.00	4.00	10.50	42.00	14.69	3.00	13.50	30.00	24.66	8.00	25.50	52.00
Age	49.78	18.00	51.00	75.00	52.81	26.00	53.50	85.00	49.62	20.00	50.50	85.00

Min: Minimum; Max: Maximum.

significantly lower 25-hydroxyvitamin D levels ($p<0.001$). However, there was no significant difference between one-side and both-side tinnitus groups ($p>0.5$).

Pearson's square test was performed to determine whether there was a difference between 25-hydroxyvitamin D levels in terms of the gender distribution of the female and male participants constituting the study groups ($p=0.185$).

Discussion

Reason-directed treatment is the first step of treatment in every branch of medicine. However, since the etiological cause of tinnitus can only be found in 5% of cases, symptomatic treatment methods which include different treatment options take an important place.

In this study, serum 25-hydroxyvitamin D levels of patients with one-side and both-side tinnitus were found to be significantly lower compared with the control group.

The risk of cancer, autoimmune, and infectious diseases increases in the absence of vitamin D.[14] It has been reported that vitamin D intake during pregnancy is beneficial[15] and that low serum vitamin D levels during pregnancy can lead to much congenital hearing loss in the baby.[12]

Many factors could be the reason for decreasing vitamin D levels in the organism, such as lack of certain foods, inadequate sunlight exposure, dark skin, wearing thick clothing, cloudy weather and environmental pollution, and limiting the penetration of ultraviolet light. It has been reported that a decrease in the concentration of 7-dehydrocholesterol in the skin can be among the causes of age-related hearing loss. Likewise, it is suggested that insufficient vitamin D in winter leads to more frequent upper respiratory tract infections.[12]

Blood vitamin D [25(OH)D] levels were measured in patients who were admitted to the E.N.T. clinic with various complaints and did not respond to conventional treatments and were subject to various physiological and environmental conditions, and vitamin D levels were found to be normal in only 3 of 86 patients. In the remaining 83 patients, vitamin D concentrations were assessed as deficient or inadequate.[12]

Patients become more susceptible to infections due to increased mucus production in upper respiratory tract infections that cause a significant portion of E.N.T. diseases. The reduction of pancreatic secretions leads to fat malabsorption, and blood vitamin D levels decrease with decreased vitamin D absorption.[12]

Inactivated vitamin D is converted to active 1.25(OH)D3 in the respiratory epithelium, and its absence increases the incidence of upper respiratory tract infections that cause otitis media, retraction pockets, and cholesteatoma. Vitamin D deficiency leads to cholesteatoma osteoclastic activity, leading to low bone density and osteoporosis.[16,17]

Hearing loss, tinnitus, and vertigo are common in patients with type-2 diabetes. There were statistically significant differences between hearing impairment versus normal hearing for vitamin D, calcium, and phosphorous levels. Diabetic patients with hearing loss were likely to have high blood glucose and other risk factors such as hypertension, retinopathy, nephropathy, and neuropathy, and low levels of vitamin D, calcium, and phosphorous.[18]

Tinnitus is often a side effect of cases of noise-induced or ototoxic damage. The generation of damaging reactive oxygen species in inner ear tissues results from a variety of sources: aminoglycoside antibiotics, chemotherapeutic agents, industrial solvents, and, of course, traumatizing noise levels.[19]

Antioxidants have been suggested for use as prophylactic or rescue agents in cases of noise-induced or ototoxic damage. Using vitamin D, which reduces or repairs associated inner ear damage, could have benefits that influence tinnitus severity.[19]

Several vitamins have been shown to provide inner ear protection or to reverse damage; however, these agents have not consistently reduced tinnitus severity. Indeed, it is likely that the most benefit from antioxidants will be related to the prevention of damage that leads to tinnitus rather than reducing tinnitus severity per se.[19] Supplementation of vitamin D in all E.N.T. patients not responding to conventional treatment was informed to be hopeful and worth trying.[12]

Hypophosphatemic osteomalacia patients had subjective hearing loss, episodic tinnitus, deafness, and vertigo similar to that in Ménière's disease (MD).[20] MD is a disorder of the inner ear characterized by an insidious onset and specific symptoms, such as dizziness, vertigo, tinnitus, and hearing loss. Vitamin D binding protein and apolipoprotein-1 are significantly decreased in the plasma of MD-affected individuals.[21]

The biological actions of vitamin D are largely mediated through binding to the vitamin D receptor (VDR). VDR signaling plays an important role in ear development in the zebrafish model system. Mutations in VDR gene have been implicated in ear disorders (hearing loss and balance disorder).[22]

The calcium and phosphorus content of the woven bone of the otic capsule is much higher than that of other bones. The calcium and phosphorus content of these bones may be more affected by vitamin D levels, especially low levels.[12]

Although it is known that vitamin D levels in the organism are affected by several factors such as age, gender, menstruation, nutrition, calcium, and its metabolism, and may be important in the prevention and treatment of ear diseases, according to the results obtained in this study, it was seen that the serum 25-hydroxyvitamin D levels of patients with unilateral and bilateral tinnitus decreased significantly compared with the control group, and gender did not affect this situation. The lower level of 25-hydroxyvitamin D in patients with tinnitus and its role in the physiology and etiology of the disease were thought to be worth investigating. To be considered as a parameter in the etiology of tinnitus and in the diagnosis, treatment, and follow-up of the disease, further studies investigating vitamin D metabolism and related parameters are suggested to reveal the reasons for the low levels of vitamin D.

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