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Research Article

Relationship between Benign Paroxysmal Positional Vertigo and 25 OH Vit D3

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Abstract

Objective: Several studies have reported the association between benign paroxysmal positional vertigo (BPPV) and vitamin D deficiency. The aim of this study was to evaluate serum 25-hydroxy vitamin D (25 (OH) D) levels in BPPV patients and to investigate the possible association between BPPV and low 25 (OH) D levels.

Material and Method: This retrospective study included 356 patients with BPPV and 159 healthy controls. Serum 25 (OH) D levels were recorded at the time of initial presentation in all patients, regardless of gender and age, and the results were compared with the healthy control group.

Results: The mean serum 25-OH vit D level (22,76 ± 7,2) of the participants in the control group was significantly higher than the 25-OH vit D level of the participants in the patient group (16,15 ± 7,7). According to the control and patient groups, there was a statistically significant difference between the mean vitamin D control values ($p < 0.05$).

Conclusion: In patients with BPPV, 25 OH Vit D levels were found to be significantly low. Our study shows that low 25 (OH) D may be a potential risk factor for BPPV.

Keywords: *Benign Paroxysmal Positional Vertigo; 25 OH Vit D Deficiency*

Introduction

Benign paroxysmal positional vertigo (BPPV), first described by Barany in 1921, is a peripheral vestibular disease characterized by onset of sudden short-term vertigoes appearing as the position of the head changes according to the direction of gravity [1,2]. BPPV is the most common peripheral vestibular system disease [3,4]. Idiopathic BPPV can be seen in all age groups, although it is frequent in 50 - 70 years of age. The incidence is 11 - 64 on 100.000. It is observed twice more in women than men [5]. In BPPV, which mostly affects posterior semicircular canal (PSSC), usually unilateral involvement is considered. However, it may also affect the lateral and superior canal as well as the bilateral posterior semicircular canal [4]. BPPV treatment consists of maneuver and exercises developed according to the underlying pathology. Knowing which canal is obstructed is important for the treatment to be applied. Dix-Hallpike test is applied to detect PSSC involvement. Epley's modified particle reposition maneuver and Semont-Liberatory maneuver are the most commonly used maneuvers in the treatment [3]. BPPV is explained by the theories of cupulolithiasis and canalithiasis. In the cupulolithiasis theory, vertigo attacks occur as a result of the obstruction of semicircular canal cupula by the calcium carbonate crystals resulting from utricle and saccule otoconia. In the canalithiasis theory, the calcium carbonate crystals fall into the canal and move freely, resulting in vertigo [6].

It is characterized by the positional vertigo and the positional nystagmus (PN) triggered by the modification of the position of the head in relation to gravity. Although BPPV is referred to as a benign disease, some BPPV patients have recurrence and approximately 20% of BPPV patients have 1-year recurrence rates and approximately 50% of the patients present 5-year recurrence rates [7]. In particular, some patients experience serious difficulties in their daily lives due to frequent recurrence of BPPV. The social impact of the disease is very important because it is common, and especially in elderly patients, falling, depression, and impairment of daily activity are more frequent [4]. In BPPV, clinical symptoms are thought to be caused by otoliths, which detach from the utricle or saccule with head movements and escape from the semicircular canals or adhere to the cupula and thus increase the sensitivity to gravity [4]. These crystal structures that are attached to hairy cells in the vestibule by protein bonds are active calcium metabolites of vestibular extremity organs (utricle and saccule). The calcium channel proteins involved in calcium metabolism in vestibular extremity organs have been shown to be vitamin D dependent. Some studies conducted on this subject have shown that vestibular dysfunction develop in vestibule cells which do not have vitamin receptors [8-10].

Vitamin D is more synthesized in the skin and changes in the liver to 25-hydroxyvitamin D (25-OH vitamin D) and 1,25-dihydroxyvitamin D [1,25 (OH) 2 vitamin D] in the kidneys. Among the metabolites, 25-OH vitamin D has the highest serum concentration, and the concentration level is a good indication of vitamin D maintained *in vivo*. Recently, there are case studies showing that vitamin D deficiency is present in patients with chronic relapse with results of studies showing that vitamin D levels of BPPV patients are lower compared to the controls [11-13]. Among these, the relationship between BPPV and both osteoporosis and vitamin D deficiency is of great interest, suggesting that abnormal calcium metabolism may be a pathogenic process of BPPV. Most studies have suggested that a low level of vitamin D leads to the occurrence and/or recurrence of BPPV [7,14,15]. In addition, studies have also shown a positive effect in the treatment of osteoporosis or vitamin D deficiency among BPPV patients [12-15]. However, in several studies, low vitamin D levels have been reported not to be associated with BPPV occurrence and/or recurrence [16-19].

Aim of the Study

The aim of our study was to compare the 25-OH vit D levels of the patients diagnosed as Benign Paroxysmal Position Vertigo (BPPV) after applying to our clinic for vertigo and the healthy control group without vertigo.

Patients and Methods

Our study is a retrospective study conducted on 356 patients diagnosed with BPPV after applying to Gazi Yasargil Training and Research Hospital Otorhinolaryngology clinic with a complaint of vertigo between February 2015 and February 2018 and on 159 healthy control persons (selected among the persons applying to our clinic for complaints other than vertigo, imbalance, or dizziness, who have been subject to serum vitamin D level measurement and who have not applied to physician during the last 1 year for vertigo, dizziness or imbalance). Patients and control group members who do not have any complementary vitamin D treatment (medical treatment or direct sunlight) who were residing in this region until one year before the application were included in the study.

For the definitive diagnosis of BPPV, we used the diagnostic criteria formulated by the Committee for the Classification of Vestibular Diseases [20]. All participants were subjected to audiometric examination after routine neuro-otological examination. The diagnosis of BPPV is based on a characteristic history and typical nystagmus observation during the Dix-Hallpike maneuver, supine roll or cephalic hyperextension tests. Detailed diagnostic methods have been defined in various studies [20]. After the affected side was determined considering the canal indicated by nystagmus, Epley maneuver was applied to the patients for posterior canal BPPV. Barbecue maneuver and reverse Epley maneuver were used respectively for Horizontal Canal BPPV and Posterior Canal BPPV. Patients affected on both sides were not included in the study. After two or three days, the patients were evaluated by the control and the maneuvers were repeated. The maneuvers applied to the patients who were called for control were pursued until the nystagmus was not observed in the tests.

The inclusion criteria were as follows: 1. BPPV, where typical positional nystagmus occurred, 2. Presence of follow-up examination results; 3. Presence of the actual value of 25 (OH) D in the serum in the first visit or in the follow-up examination; 4. Negative radiological results (MRG of the cerebrum); 5. Negative neurological condition.

Patients who had a history of head and ear trauma, and vestibular neuritis, Meniere's disease, migraine, ear surgery or sudden hearing loss, chronic hematological, renal, gastrointestinal, cardiovascular diseases, calcium supplements, drugs that affect vitamin D metabolism were not included in our study. Approval was obtained from our local ethics board. The principles of the Helsinki Declaration were applied.

Measurement of serum 25-hydroxyvitamin D

During the first application, venous blood samples were taken in the early morning (08:00am-10: 00am) and serum total 25-OH vit D was measured in Cobas e 602 device (RocheDiagnostics, Germany) by immunoassay method in the biochemistry laboratory. Serum 25-OH vit D levels were considered normal if above 20 ng/ml and as decreased if less than 20 ng/ml.

Statistical analysis

The data obtained in this study were analyzed with SPSS 17 package program. Kolmogorov-Smirnov and ShapiroWilk tests were used to investigate variables from normal distribution. When interpreting the results, 0.05 was used as the level of significance; in the case of $p < 0.05$, the variables were considered not conform to normal distribution, but in the case of $p > 0.05$, the variables were considered consistent with the normal distribution. Non-parametric Mann Whitney U test was used to compare the differences between the groups when the variables did not comply with normal distribution. When interpreting the results, 0.05 was used as the level of significance; there was a significant difference in the case of $p < 0.05$ and no significant difference in the case of $p > 0.05$.

Observations

	Group	Kolmogorov-Smirnova			Shapiro-Wilk		
		Statistical	sd.	p	Statistical	sd.	P
Vitamin D	Control	0.111	159	0.001	.950	159	0.001
	Patient	0.087	356	0.001	.963	356	0.001

Table 1: *Normality test.*

Prior to the analysis of the data set, it was tested whether the relevant variables were compatible with the normal distribution to determine the statistical method to be used. At this stage Kolmogorov-Smirnov and Shapiro-Wilk tests were used. The critical value was defined as $p = 0.05$. At the end of the test, if the p values obtained for the relevant variables were greater than 0.05, it was accepted that the data fit the normal distribution and if they were lower, the data were considered not conform to normal distribution. Since the data set did not conform to normal distribution, "Mann-Whitney U" test was used as nonparametric methods in comparison between groups.

	Group	N	Mean	sd.	Min	Max	Average	Z	P
Vitamin D	Control	159	22.76	7.25	7.00	34.00	341.27	-8.489	0.001*
	Patient	356	16.15	7.72	4.00	34.80	220.81		

Table 2: *Comparison of mean vitamin D values with Mann-Whitney U test according to the control and patient groups.*

According to the control and patient groups, there was a statistically significant difference between the mean "vitamin D" values between the control and patient groups ($p < 0.05$). The mean vitamin D value of the participants in the control group (22.76 ± 7.2) was significantly higher than the mean vitamin D value of the participants in the patient group (16.15 ± 7.7).

Discussion

Benign paroxysmal positional vertigo is the most common peripheral vestibular system disease and it is an easy to diagnose and treat disease despite the fact that the quality of life of the patient is quite impaired [8,9]. BPPV is characterized by short-term attacks of vertigo and occurs with changes in head position. Although the exact etiology is unknown, there is evidence that BPPV is caused by otoconia (calcium carbonate crystals), which is separated from the otoconial membrane in the utricle and that falls into one of the semicircular canals (most often the posterior canal). Theoretically, as with osteoporosis and osteopenia, deterioration in calcium metabolism may contribute to the development of BPPV. An increase in calcium absorption may produce a high concentration of free calcium in the endolymph and reduce the capacity to dissolve the displaced otoconia [4,8,9].

It may be very debilitating for an individual to quit, to stop driving, or to cause social isolation due to BPPV attacks. Understanding the factors leading to the development of BPPV may allow us to improve the initial management of affected individuals and reduce recurrence. A large number of studies have investigated the role of vitamin D in the pathogenesis of BPPV. Some studies have reported that low vitamin D levels are associated with BPPV occurrence and recurrence.

Vitamin D levels during BPPV episodes were significantly lower than those in BPPV remission [23]. Furthermore, normalization of serum vitamin D levels in BPPV patients may decrease the recurrence and intensity of BPPV [12,14,15]. In a study of Vibert., *et al.* [21] 332 women BPPV patients were compared with the control group and the authors reported that the rate of osteoporosis was higher in BPPV patients and that they considered that calcium metabolism disorders were associated with BPPV formation. The authors presented two mechanisms of the relationship between BPPV and osteoporosis or osteopenia. First, the reduction of estrogen in reducing the natural regulators of bone mass may disrupt the internal structure of otoconia and/or their binding to each another and their adhesion to the gelatinous matrix. Second, increased calcium absorption can produce a high concentration of free calcium in the endolymph and may reduce the capacity to dissolve the displaced otoconia [22]. In addition, a retrospective study from the USA confirmed that the treatment of osteoporosis in 260 women with calcitriol, bisphosphonates or vitamin D3 has a protective effect against BPPV [22]. In our study, clinical documentation was studied in patients who were admitted to our clinic for 3 years and were diagnosed with BPPV. Serum 25-OH vit D levels of BPPV patients and control group were compared and it was found that serum 25-OH vit D levels were significantly lower in BPPV patients compared to the control group. The mean vitamin D value of the participants of the control group was found to be (22.76 ± 7.2) while the mean vitamin D value of the participants of the patient group was found to be (16.15 ± 7.7). According to the control and patient groups, there was a statistically significant difference between the mean "Vitamin D" values ($p < 0.05$).

There are some controversies about the relationship between vitamin D and the occurrence or recurrence of BPPV. According to Jeong., *et al.* [13], while decreased vitamin D showed a significant relationship only with the formation of BPPV, the vitamin D level did not differ between de novo and recurrent groups. Büki., *et al.* [14] compared vitamin D levels in BPPV patients without recurrence of BPPV to patients with recurrent BPPV. They reported that serum levels of vitamin D in BPPV patients were similar to those of the general population, but the levels in patients with recurrent BPPV were significantly lower than in de novo BPPV patients. However, in a study conducted in Croatia, it was reported that there was no significant difference in vitamin D levels in BPPV patients with and without relapse [19]. Similar to this study, Karataş., *et al.* [17] found that the prevalence of osteoporosis and vitamin D deficiency was high in both BPPV patients and the general population. They proposed that osteoporosis and vitamin D deficiency were not risk factors for BPPV. Similarly, Cıkrıkcı., *et al.* [18] did not find that vitamin D deficiency was associated with the incidence or recurrence of BPPV. These paradoxical study results may be caused by different clinical settings such as the definition of BPPV recurrence, and the duration of follow-up. In addition, it was stated that vitamin D levels may be affected by season, skin color, lifestyle, additional use, geographical conditions, nutritional status and measurement methodologies. We suggest that there is a relationship between vitamin D and BPPV. Therefore, we recommend measuring 25 (OH) D in patients with BPPV and supplementing if there is a deficiency. The beneficial effect of Vitamin D on the reduction of attacks in BPPV can probably be helped by reducing the recurrence of chronic BPPV. The limiting factors of our study are

the lack of knowledge about the improvement of symptoms and attack frequencies in BPPV patients who have vitamin D deficiency and who have undergone replacement therapy.

Conclusion

We think that there is a connection between Benign Paroxysmal Positional Vertigo and serum 25 OH VIT D without any difference in age and gender, and we think that vitamin D supportive therapies may be helpful for treatment in order to reduce the recurrence and that it need to be supported by more comprehensive studies. Future studies are also needed to investigate the role of 25 (OH) D in the pathogenesis of BPPV.

Bibliography

1. Froehling DA., *et al*. "Benign positional vertigo: incidence and prognosis in a population-based study in Olmsted County, Minnesota". *Mayo Clinic Proceedings* 66.6 (1991): 596-601.
2. Casani AP., *et al*. "The treatment of horizontal canal positional vertigo: our experience in 66 cases". *Laryngoscope* 112.1 (2002): 172-178.
3. Ruckenstein MJ. "Therapeutic efficacy of the Epley canalith repositioning maneuver". *Laryngoscope* 111.6 (2001): 940-945.
4. Parnes LS., *et al*. "Diagnosis and management of benign paroxysmal positional vertigo (BPPV)". *Canadian Medical Association Journal* 169.7 (2003): 681-693.
5. Hilton M and Pinder D. "The Epley (canalith repositioning) manoeuvre for benign paroxysmal positional vertigo". *Cochrane Database of Systematic Reviews* 2 (2002): CD003162.
6. D Nuti., *et al*. Handbook of Clinical Neurology, Volume 137 (3rd series) Neuro-Otology Chapter 18 Benign paroxysmal positional vertigo and its variants.
7. Rhim GI. "Serum vitamin D and recurrent benign paroxysmal positional vertigo". *Laryngoscope Investigative Otolaryngology* 1.6 (2016): 150-153.
8. Hoenderop JG., *et al*. "Calcium absorption across epithelia". *Physiological Reviews* 85.1 (2005): 373-422.
9. Ross MD. "Calcium ion uptake and exchange in otoconia". *Advances in Oto-Rhino-Laryngology* 25 (1979): 26-33.
10. Yamauchi D., *et al*. "Vitamin D upregulates expression of ECaC1 mRNA in semicircular canal". *Biochemical and Biophysical Research Communications* 331.4 (2005): 1353-1357.
11. Wu YQ., *et al*. "Reduction of bone mineral density in native Chinese female idiopathic benign paroxysmal positional vertigo patients". *American Journal of Otolaryngology* 39.1 (2017).
12. Talaat HS., *et al*. "Low bone mineral density and vitamin D deficiency in patients with benign positional paroxysmal vertigo". *European Archives of Oto-Rhino-Laryngology* 272.9 (2015): 2249-2253.
13. Jeong SH., *et al*. "Decreased serum vitamin D in idiopathic benign paroxysmal positional vertigo". *Journal of Neurology* 260.3 (2013): 832-838.
14. Beuki B., *et al*. "Vitamin D deficiency and benign paroxysmal positioning vertigo". *Medical Hypotheses* 80.2 (2013): 201-204.

15. Sheikhzadeh M., *et al*. "Influence of supplemental vitamin D on intensity of benign paroxysmal positional vertigo: a longitudinal clinical study". *Caspian Journal of Internal Medicine* 7.2 (2016): 93-98.

16. Parham K., *et al*. "Prospective clinical investigation of the relationship between idiopathic benign paroxysmal positional vertigo and bone turnover: a pilot study". *Laryngoscope* 123.11 (2013): 2834-2839.

17. Karatas¸ A., *et al*. "Association of benign paroxysmal positional vertigo with osteoporosis and vitamin D deficiency: a case controlled study". *Journal of International Advanced Otology* 13.2 (2017): 259-265.

18. Cıkrıkcı Isık G., *et al*. "Analysis of vitamin D and calcium levels in benign paroxysmal positional vertigo". *Eurasian Journal of Emergency Medicine* 16 (2017): 128-132.

19. Maslovara S., *et al*. "25 (OH) D3 levels, incidence and recurrence of different clinical forms of BPPV". *Brazilian Journal of Otorhinolaryngology* 84.4 (2017).

20. Von Brevern M., *et al*. "Benign paroxysmal positional vertigo: diagnostic criteria". *Journal of Vestibular Research* 25.3-4 (2015): 105-117.

21. Vibert D., *et al*. "Benign paroxysmal positional vertigo in older women may be related to osteoporosis and osteopenia". *Annals of Otology, Rhinology and Laryngology* 112.10 (2003): 885-889.

22. Mikulec AA., *et al*. "Negative association between treated osteoporosis and benign paroxysmal positional vertigo in women". *Journal of Laryngology and Otology* 124.4 (2010): 374-376.

23. Kahraman SS., *et al*. "Calcium homeostasis during attack and remission in patients with idiopathic benign paroxysmal positional vertigo". *Otology and Neurotology* 37.9 (2016): 1388-1392.

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