RESEARCH ARTICLE

Vitamin D Influence on the Clinical Course of Benign Paroxysmal Positional Vertigo: A Retrospective Cohort Study

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Abstract

Aim and objective: This retrospective cohort study was designed to investigate the possible relationship between vitamin D and the clinical course of benign paroxysmal positional vertigo (BPPV).

Materials and methods: The medical records of patients admitted to a tertiary health center between January 2017 and December 2018 were retrospectively reviewed. Ninety idiopathic BPPV and one hundred healthy subjects without vertigo were included in the study.

Results: The serum vitamin D concentration and BPPV occurrence were not correlated ($p = 0.601$). BPPV recurrence was significantly affected by age ($p = 0.028$) and serum vitamin D concentrations ($p = 0.02$).

Conclusion: This study indicated that there is no causal relationship between low vitamin D levels and BPPV. Another result of the study is that low vitamin D concentrations and older age increase BPPV recurrences. This increase in recurrence due to vitamin D deficiency does not eliminate oral vitamin D treatment.

Clinical significance: The relationship between vitamin D and BPPV is still controversial and the effect of vitamin D administration on the BPPV treatment process is unknown.

Keywords: Logistic regression, Recurrence of BPPV, The effect of age, Vitamin D administration.

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Introduction

Benign paroxysmal positional vertigo (BPPV) is a disease of the peripheral vestibular system characterized by short vertigo attacks that are triggered by head movements.[1] It is the most common vestibular disorder with a lifetime cumulative incidence of up to 10% in the community.[2] Although BPPV can be seen at any age, its incidence rate increases with aging. For example, the 1-year prevalence of BPPV among individuals aged between 18 and 39 years old is 0.5% while the prevalence increases to 3.4% over the age of 60 years.[2,3] Though the management of BPPV has been well established, the factors leading to otoconial degeneration and dislodgement have not been fully understood yet.[4] Vitamin D plays a critical role in maintaining normal otolith functions through maintaining vestibular endolymph calcium at a certain level that allows the otoconia to properly mineralize.[5] Unlike many previous clinical studies put forward that low vitamin D levels lead to BPPV formation and its recurrence[5–7], more recent studies have reported that vitamin D is not related to either BPPV occurrence or its recurrence.[8–11] Therefore, the relationship between vitamin D and BPPV has been still controversial. Moreover, it is not known the effect of vitamin D treatment in the clinical course of BPPV.

Accordingly, this study was designed to investigate the possible relationship between vitamin D and BPPV.

Materials and Methods

Between January 2017 and December 2018, the medical history record of 217 patients, who were admitted to the tertiary health center and whose vitamin D level was measured, were retrospectively reviewed. Initially, the local ethics committee approval was obtained (protocol: 01/2019). Ninety-seven patients with idiopathic BPPV and one hundred patients with no history of vertigo were included in the study. Twenty subjects were excluded for not meeting the study criteria.

Study Group

One hundred and seven patients who presented to the clinic with the complaint of dizziness triggered by head movements were evaluated. The patients with diagnostic nystagmus were initially included in the study following the Dix–Hallpike test and Head Supine Roll test. Later, the patients who underwent ear surgery, who had head trauma up to 1 month before the diagnosis of BPPV, who had vestibular neuronitis, patients with Meniere's disease, patients with tinnitus, patients with migraine, patients with sudden hearing loss, patients with vitamin D treatment, patients with chronic illnesses that may affect vitamin D levels, patients whose information is missing were excluded from research. Among the patients with BPPV, patients who had dizziness in the same way as

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in the previous year and were treated with canalith repositioning maneuver in other clinics or the patients who admitted to our clinic with the same complaints after 1 month period following the canalith repositioning maneuver treatment were considered as a recurrent case. Oral vitamin D was prescribed to all patients whose vitamin level was below 30 ng/mL.

Control Group

Between January 2017 and December 2018, patients who presented to the ENT (ear, nose, and throat) clinic due to non-vertigo reasons, who had no dizziness in their history, and whose vitamin D levels were measured at the outpatient clinic of other departments or ENT clinic were included in the control subjects. The patients with chronic illnesses that may affect vitamin D levels and patients with vitamin D treatment were excluded from the study.

Vitamin D Measurement

Serum vitamin D level was measured using the CMIA (chemiluminescence microparticle immunoassay) (Abbott Laboratories, Chicago, IL, USA) device. Values below 10ng/mL were considered vitamin D deficiency.

Statistical Method

SPSS Windows version 24.0 package program was used for all statistical analyses. Shapiro–Wilk test was used to test the normal distribution of the data. Student's t-test was used to compare the two independent groups if the data were normally distributed. If not, the Mann–Whitney U test was used to compare the groups. The relationships of two independent variables at the categorical measurement level were tested by Fisher's exact test. Also, logistic regression was used to model the binary dependent variable with independent variables. Mean ± standard deviation for numerical variables and number and percentage for categorical variables were reported as descriptive statistics. $p < 0.05$ was considered a statistically significant level.

Results

The mean age of the patients in the study (BPPV) group (57.29 ± 12.45) was statistically significantly higher than the controls (48.02 ± 13.68) ($p = 0.001$). While the percentage of postmenopausal women was 51% in the study population, it was 30% in the control subjects, and BPPV and control group were significantly different in terms of menopausal status ($p = 0.001$). Similarly, the two groups were significantly different in terms of the number of patients over the age of 45 ($p = 0.001$).

The mean BMI was 30.02 ± 4.90 and 29.05 ± 6.58 in the BPPV and control groups, respectively. BMI was not significantly different in the two groups ($p = 0.265$). There were 16 hypertension (HT) patients (16.5%) and 14 diabetes mellitus (DM) patients (14.4%) in the BPPV group while there were 15 HT patients (15%) and 10 DM patients (10.0%) in the control group. However, the two groups were not significantly different in terms of DM and HT ($p = 0.342$ and $p = 0.773$, respectively) (Table 1).

Serum Vitamin D Levels

Among ninety-seven BPPV patients, ninety-five patients had posterior and two had lateral canal. The average vitamin D concentrations were 15.87 ± 8.61 and 15.82 ± 10.23 ng/mL in the BPPV and control groups, respectively. There was no statistically significant difference between the control and BPPV group vitamin D concentrations ($p = 0.971$). The frequency of vitamin D deficiency was 33% in the total of both groups.

Over the age of 45, the vitamin D concentrations and the prevalence of vitamin D deficiency were not statistically different in BPPV and healthies ($p = 0.977$ and $p = 0.900$, respectively). Similarly, the serum vitamin D level and vitamin D deficiency prevalence were not significantly different in patients under the age of 45 in vertigo and healthy subjects ($p = 0.658$ and $p = 0.932$, respectively) (Table 2).

Vitamin D concentration and prevalence of vitamin D deficiency were not statistically different in females in both groups ($p = 0.438$

Table 1: Clinical characteristics of patients and controls

		Group				
		Control		*BPPV*		
		N	*%*	*N*	*%*	*P*
Age	*Mean ± SD*	48.02 ± 13.68		57.07 ± 12.57		0.001
BMI	*Mean ± SD*	29.05 ± 6.58		30.02 ± 4.90		0.265
Year	<45	42	42.0	19	19.6	0.001
	≥45	58	58.0	78	80.4	
Sex	Male	48	48.0	34	35.0	0.056
	Female	52	52.0	63	65.0	
Premnp.		22	42.3	13	21.0	0.001
Postmnp.		30	57.7	50	79.0	
HT	No	15	15.0	16	16.5	0.773
	Yes	85	85.0	81	83.5	
DM	Yes	10	10.0	14	14.4	0.342
	No	90	90.0	83	85.6	
Vit D	Normal (≥30 ng/dL)	7	7.0	6	6.2	0.973
	İnsufficient (10–30 ng/dL)	60	60.0	59	60.8	
	Deficient (<10 ng/dL)	33	33.0	32	33.0	

Independent samples T-test, Fisher's, and Chi-square test; Premnp, premenopausal; Postmnp, postmenopausal; BMI, body mass index; DM, diabetes mellitus; HT, hypertension; max, maximum; BPPV, benign paroxysmal positional vertigo; SD, standard deviation

Table 2: Serum vitamin D in BPPV patients and controls aged <45 and ≥45 years

	Group						
	Control			*BPPV*			
	Mean ± SD/	*n (%)*	*Median (min–max)*	*Mean ± SD/*	*n (%)*	*Median (min–max)*	*p*
Age <45							
Vit D (ng/dL)	15.40 ± 7.98		14.60 (3.60–34.90)	14.44 ± 7.42		13.00 (3.00–67.80)	0.658
Deficiency	Yes	15 (35.7)		Yes	7 (36.8)		0.932
	No	27 (64.3)		No	12 (63.2)		
Age ≥45							
Vit D (ng/dL)	16.21 ± 9.09		14.75 (3.50–38.70)	16.16 ± 10.8		12.85 (3.00–67.80)	0.977
Deficiency	Yes	18 (31.0)		Yes	25 (32.1)		0.900
	No	40 (69.0)		No	53 (67.9)		

Independent samples T-test, Fisher's, and Chi-square test; BPPV, benign paroxysmal positional vertigo; SD, standard deviation; min–max, minimum–maximum

Table 3: Serum vitamin D in females and males in BPPV and control groups

	Group						
	Control			*BPPV*			
	Mean ± SD/	*n (%)*	*Median (min–max)*	*Mean ± SD/*	*n (%)*	*Median (min–max)*	*p*
Male							
Vit D	17.90 ± 7.11		18.20 (6.20–37.90)	16.41 ± 7.94		12.90 (6.00-42,70)	0.377
Deficiency	Yes	7 (14.60)		Yes	6 (18.20)		0.665
	No	41 (85.40)		No	27 (81.80)		
Female							
Vit D	13.99 ± 9.48		10.30 (3.50–38.70)	15.52 ± 11.28		12.70 (3.00–67.80)	0.438
Deficiency	Yes	26 (50.00)		Yes	26 (40.60)		0.313
	No	26 (50.00)		No	38 (59.40)		

Independent samples T-test, Fisher's, and Chi-square test; BPPV, benign paroxysmal positional vertigo; SD, standard deviation; min–max, minimum–maximum

Table 4: Independent predictors of BPPV occurrence using multiple logistic regression analysis

				95% CI odds ratio	
	B	*P*	*Odds ratio*	*Lower*	*Upper*
BMI	0.001	0.992	1.000	0.944	1.058
Age	0.057	**0.001**	1.058	1.031	1.086
DM	0.234	0.636	1.264	0.479	3.335
HT	–0.342	0.440	0.710	0.298	1.693
Dvit	–0.009	0.601	0.991	0.959	1.025
Constant	–2.772	0.007	0.063		

Wald test $p < 0.05$; B coefficients obtained from logistic regression; CI, confidence interval; BMI, body mass index; DM, diabetes mellitus; HT, hypertension

Table 5: Independent predictors of BPPV recurrences using multiple logistic regression analysis

				95% CI odds ratio	
	B	*p*	*Odds ratio*	*Lower*	*Upper*
BMI	0.030	0.528	1.030	0.939	1.130
Age	0.052	**0.028**	1.053	1.006	1.103
DM	–0.862	0.220	0.423	0.107	1.676
HT	–0.711	0.412	0.491	0.090	2.685
Vitamin D	–0.116	**0.020**	0.891	0.808	0.982
Constant	–2.343	0.398	0.096		

Wald test $p < 0.05$; B coefficients obtained from logistic regression; CI, confidence interval; BMI, body mass index; DM, diabetes mellitus; HT, hypertension

and $p = 0.313$, respectively). Male patients were also not statistically different ($p = 0.377$ and $p = 0.666$, respectively) (Table 3).

Female patients were subdivided into pre and postmenopausal subgroups and analyzed each sub-group individually. Premenopausal vertigo and the control subjects were not significantly different in terms of vitamin D concentration and vitamin D deficiency prevalence ($p = 0.704$ and $p = 0.568$, respectively). Similarly, there was no statistical difference in postmenopausal subjects ($p = 0.971$ and $p = 0.880$, respectively) (Table 4).

In regression analysis, age was found to be an independent variable on BPPV ($p = 0.001$) while other variables in the model were not statistically significant (Table 5). Moreover, age was found to be a significant variable on the recurrence ($p = 0.028$) and high vitamin D levels had a protective effect on the recurrence ($p = 0.028$).

The average follow-up time was 426 days in non-recurrent cases and 411 days in patients with recurrence. Follow-up time was not statistically different ($p = 0.718$).

Considering the seasonally measured period, the number of patients in the summer period (April–September) of BPPV groups was 55 (57%) and the number was 49 (49%) in the control group.

Discussion

Because vitamin D regulates some Ca^2+ binding protein expression through its receptors located in inner ear epithelial cells.[12] The

possible causative effect of vitamin D deficiency on the occurrence of BPPV has been emphasized due to abnormalities in calcium metabolism in the inner ear. However, there is no consensus on this notion because of the contradictory results of the clinical studies.[13] The results of our study do not support a causal relationship between vitamin D levels and BPPV. Furthermore, we did not find any associations between vitamin D levels and BPPV formation in patients, even divided them into the subgroups considering menopausal status, gender, and under or above 45 years of age. In contradiction of our results, Han et al.[14] reported that postmenopausal women with BPPV had significantly lower vitamin D concentration than healthy postmenopausal women. The possible explanation of this result could be the fact that control subjects in their study were selected among the healthy individuals admitted to the check-up center. Karataş et al.[9] also reported that serum vitamin D levels of postmenopausal controls were not different from patients with postmenopausal BPPV when the participant of control groups was selected among the patients who applied to the ENT department because of upper respiratory tract infection. In the study conducted by Parham et al.,[8] they compared postmenopausal women with BPPV and women without postmenopausal osteoporosis and dizziness in terms of vitamin D levels, and they reported no significant difference in vitamin D levels.

Although the currently available clinical studies in the literature reported contradictory results on the relationship between the formation of BPPV and vitamin D levels, most studies in the literature suggest that low serum vitamin D concentrations increase BPPV recurrences. For example, Buki et al.[6] reported that the vitamin D concentration was low in patients with recurrent BPPV and that BPPV relapse could be prevented by vitamin D supplementation. Moreover, Talaat et al.[15] found that low serum vitamin D levels lead to the development of BPPV and critically low serum vitamin D levels increase BPPV recurrences. In another study by Talaat et al.,[16] they also reported a decrease in the recurrence of BPPV through improving vitamin D levels. Furthermore, Rhim[7] analyzed 232 patients with idiopathic BPPV retrospectively and the results suggested that serum vitamin D levels are another risk factor of BPPV recurrence independently from age, sex, follow-up period, and BPPV types. Yang et al.[4] also reported that bone mineral density and age influence the recurrence; however, only age was an independent predictor of the recurrence. Similarly, we also found that the low serum vitamin D levels along with an increase in age elevate the recurrence.

Based on the available data in the literature, the recurrence rates in idiopathic BPPV generally range from 10 to 20% although it has been reported up to 44% in some studies.[17] On the other hand, the recurrence rates were reported between 16% and 45% in the studies investigating the relationship between vitamin D concentration and BPPV recurrence, and vitamin D levels in patients with recurrence ranged from 11.93 to 19.3 ng/mL.[13] The recurrence rate of 16.5% found in our study and the mean vitamin D level of 10.01 ng/mL in recurring patients were consistent with the available literature data. We cannot say with certainty whether oral vitamin D treatment prevents recurrence in patients with low vitamin D levels. However, the vitamin D treatment can not eliminate the difference in the frequency of recurrence between BPPV patients with normal vitamin D levels and low vitamin D levels at the onset of the disease.

Although conditions, such as DM and HT have been previously reported to increase the recurrence in BPPV,[18,19] our results do not support such a relationship. However, it does not mean that there is no such relationship exists between DM or/and HT and the recurrence due to the limited number of patients analyzed in the present study.

Serum vitamin D levels depend on several factors, including gender, stage of life, ethnicity, and seasons.[20,21] When the values less than 10 ng/mL in our study were accepted as vitamin D deficiency, we observed that the vitamin D deficiency rate was 33% in all subjects. The exact incidence rate of vitamin D deficiency in the Turkish population is not known. The reported prevalence of vitamin D deficiency in Europe is lower than the values reported in our study. For instance, in a study consisting of 55,844 European individuals, vitamin D deficiency was found to be 13% in the population when vitamin D deficiency was considered as the value is less than 12 ng/mL.[22] Furthermore, this value was found to be 17.7% in the winter period while 8.3% in the summer period in the same study.

The main difference in our study comparing to other similar studies on this topic is the selection procedure of the control group. In our study, the records of the subjects who presented to the ENT outpatient clinic were examined retrospectively. Among the patients whose vitamin D levels were measured, the patients who were admitted to the outpatient clinic during the past two years due to non-dizziness reasons were included in the control group. No exclusion criteria were applied except for the lack of dizziness, chronic disease affecting vitamin D concentrations, and usage of vitamin D supplements. The possible differences between BPPV and the control population were evaluated by multiple logistic regression analysis. Moreover, the subgroups, which were created with the consideration of age, gender, BMI, and comorbidities (HT, DM), were compared to eliminate other variables that may affect possibly vitamin D concentrations and the occurrence of BPPV. In this way, a more suitable control group was created. Because the groups selected from healthy individuals may not reflect the general population. Furthermore, a comparison of patients who apply to different outpatient clinics may influence the results. For example, the general profiles of the patients who applied to the Physical Therapy or Geriatrics Outpatient Clinic or Check-up Center may be different than the profile of patients presenting to the ENT or neurology outpatient clinic. On the other hand, selecting the control group among the patients with a specific disease (e.g., osteoporosis, upper respiratory tract infection, etc.) leads to the possible risk that vitamin D levels of such patients could be different than that of the general population. A good example of this situation is that vitamin D concentration was reported to be lower in subjects with upper respiratory tract infections.[23,24]

This study is also not without limitations due to the inherent limitations associated with a retrospective study. Vitamin D levels were not measured in the patients at a certain time interval and fasting period. Because, depending on seasonal differences, vitamin D levels may differ. In our study, the two groups were incidentally displaying similar seasonal distribution.

Conclusion

Our cumulative findings suggest that low vitamin D levels are not a risk factor for BPPV occurrence. The incidence of vitamin D deficiency does not increase in BPPV patients. However, the low vitamin D and older age might be risk factors for BPPV recurrences. Vitamin D replacement does not seem to alter the course of BPPV. Future prospective studies including large series of well-selected control groups are still needed to shed light on the exact relationship between vitamin D and BPPV.

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