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Investigation of Serum Calcium and Vitamin D Levels in Patients with Refractory Benign Paroxysmal Positional Vertigo

Original Investigation

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Abstract

Objective: It is not known exactly what causes recurrence in benign paroxysmal positional vertigo (BPPV) patients. We aimed to investigate the relationship between the number of maneuvers and serum vitamin D and calcium levels in BPPV cases treated with appropriate maneuvers after correct diagnosis.

Methods: A total of 86 BPPV patients, 68 (79.9%) female and 18 (20.1%) male were included in the study. Of these, 16.3% (n=14) were aged under 45 years, 29.1% (n=25) between 45-60 years, and 54.7% (n=47) over 60 years. All were evaluated with videonystagmography. Patients who underwent maneuvers for BPPV treatment were examined. Serum 25-hydroxyvitamin D and calcium levels were measured.

Results: Repeated maneuvers were performed in 43% of the patients (n=37). Serum calcium measurements did not differ significantly between the groups. Serum vitamin D levels were not significantly different between the groups in terms of sex (p=0.387) and age (p=0.323). However, vitamin D levels were significantly lower in the group that resisted the maneuvers than in the group that did not resist [resistance: 22.9, interquartile range (IQR): 12.9-27.0; non-resistance: 28.6, IQR: 18-35, p=0.009].

Conclusion: Vitamin D measurements were observed to be significantly lower in patients requiring repeat maneuvers for BPPV treatment. We recommend that vitamin D levels be evaluated in resistant cases.

Keywords: Benign paroxysmal positional vertigo, vitamin D deficiency, calcium, repositioning maneuvers, recurrence, nystagmography, therapeutic resistance

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Introduction

Benign paroxysmal positional vertigo (BPPV) is characterized by nystagmus and recurrent vertigo that occur depending on the position of the head. The periodic recurrence of symptoms significantly reduces quality of life, decreases daily activity performance, and causes loss of work productivity. BPPV results from the unintended migration of otoconia into the semicircular canals. However, the causes of otoconia degeneration and separation from the utricle, which are thought to result from macular degeneration, are not fully known (1).

Most patients with BPPV are successfully treated with canalith repositioning maneuvers (CRPs), but some patients require repeated maneuvers. Success rates with one or more CRPs vary among authors and have been reported to range from 50% to 70% (2). It has also been reported in the literature that BPPV recurs at varying rates, up to 50% (3). Therefore, it is important to clarify the factors that have been reported to predispose to the recurrence of BPPV, such as female sex, older age, hypertension, head trauma, other inner ear disorders, and vitamin D deficiency (4-8). Some studies indicate an association between vitamin D deficiency and recurrent BPPV, while others do not. Vitamin D is associated with vestibular pathology through its effects on skeletal mineral homeostasis, which in turn affects the temporal bone. The crucial calcium concentration in the vestibular endolymph required for otolithic organ function is maintained by normal serum vitamin D levels (9,10). Another hypothesis suggests that the immunomodulatory functions protect against autoimmune or inflammatory pathologies in the inner ear (11,12).

Although CRP is generally effective in improving BPPV, some patients may require more than one maneuver. In our study, we aimed to determine whether there is an association between the number of maneuvers performed and vitamin D and calcium levels in patients with BPPV treated with appropriate maneuvers after correct diagnosis.

Methods

The study was approved by the İzmir Katip Çelebi University Health Research Ethics Committee (approval no: 0297, date: 19.12.2024). All patients were informed and consent was obtained. Eighty-six BPPV patients, 68 (79.9%) women and 18 (20.1%) men, diagnosed with BPPV by videonystagmography (VNG) in the vertigo laboratory in January-December 2024 were included in the study. Those with other causes of vertigo, migraine history, and chronic ear disease were excluded. Patients with a history of head trauma or alcohol abuse that could cause refractory BPPV, and those using any calcium or vitamin D supplements were also excluded.

Demographic and clinical data such as patients' age, sex, and recurrence status were recorded. Patients were divided into three age categories: <45 years, 45-60 years, and >60 years. All patients' serum 25-hydroxyvitamin D and serum calcium levels were measured by standard biochemical analysis methods. A vitamin D level ≤20 ng/mL was considered deficiency, between 21-29 ng/mL was considered insufficiency, and ≥30 ng/mL was considered sufficiency (13,14).

In patients diagnosed with BPPV and positional nystagmus on VNG, the affected canal, type of maneuver performed, and number of maneuvers were recorded. Maneuvers were performed only by the authors participating in the study. We performed the Epley maneuver for canalithiasis and the Semont maneuver for cupulolithiasis in posterior canal involvement; the Barbecue maneuver for canalithiasis and the Appiani maneuver for cupulolithiasis in lateral canal involvement; and the Yacovino maneuver for anterior canal involvement. Patients were called for weekly follow-ups, and maneuvers were repeated if symptoms persisted and VNG findings continued. Patients who underwent at least one and at most five maneuvers were included in the study. Patients who underwent more than one maneuver were considered refractory.

Statistical Analysis

An a priori power analysis was conducted using G*Power 3.1 (t-tests, difference between two independent means, two-tailed). Assuming a standardized mean difference of $d=0.61$, a type I error rate of $\alpha=0.05$, and a desired statistical power of 0.80 with an equal allocation ratio between groups ($N_2/N_1=1$), the required total sample size was estimated as 88 participants (44 per group). Under these assumptions, the non-centrality parameter (δ) was 2.86, the critical t-value was 1.99 (df=86), and the corresponding actual power was approximately 0.8. Due to practical constraints in recruitment, the final sample size slightly deviated from this target (15). Differences in calcium levels according to sex, age group, and recurrence status were analyzed using the independent samples t-test and one-way analysis of variance. For vitamin D levels, the Mann-Whitney U test and the Kruskal-Wallis test were applied. All statistical analyses were performed using IBM SPSS Statistics version 30, and a p-value <0.05 was considered statistically significant.

Results

Of the total 86 patients, 79.9% (n=68) were female; and 16.3% (n=14) were aged under 45 years, 29.1% (n=25) were between 45-60 years, and 54.7% (n=47) were over 60 years. Thirty-two underwent the Epley maneuver (posterior canalolithiasis), nine the Semont maneuver (posterior cupulolithiasis), 18 the Barbecue maneuver (lateral canalolithiasis), 16 the Appiani maneuver (lateral cupulolithiasis), and 11 underwent the Yacovino maneuver (anterior canal).

Of the 86 patients, 49 received one maneuver, 31 received two maneuvers, two received three maneuvers, two received four maneuvers, and two received five maneuvers. Patients requiring more than one maneuver (43%; n=37) were considered to have refractory BPPV. Of these 37 patients, 8 were aged <45 years, 13 between 45-60 years, and 16 >60 years. No significant differences were identified in calcium levels between the sexes (females: 9.8±0.4, males: 9.6±0.4, p=0.133), between age groups (<45 years: 9.7±0.4; 45-60 years: 9.7±0.4; >60 years: 9.8±0.5, p=0.688) and between

refractory and non-refractory groups (refractory: 9.8±0.5, non-refractory: 9.7±0.4, p=0.815) (Table 1).

Vitamin D levels were evaluated, and no significant association was observed between sexes (p=0.387) or age groups (p=0.323). However, vitamin D levels were significantly lower in the refractory group than in the non-refractory group [refractory: 22.9, interquartile range (IQR): 12.9-27.0; non-refractory: 28.6, IQR: 18-35; p=0.009] (Table 2). Vitamin D findings across sex, refractory status, and age categories are presented in Figure 1.

Discussion

It is important that serum vitamin D and calcium levels are normal for the otoconia, which are composed of calcium carbonate, to maintain their function. Imbalance in serum calcium levels, and thereby calcium levels in the vestibular endolymph, can alter the otoconia, leading to abnormal mineralization and degeneration. In the inner ear, these critical calcium levels are maintained by the transepithelial Ca_2+ channel transport system (16,17). Disturbance of the calcium metabolism in patients with osteoporosis may represent a pathogenesis resulting in BPPV because of the disruption of otoconia associated with calcium deficiency (10). Besides these classical effects of vitamin D, its immunomodulatory function, and its effect in suppressing the autoimmune and inflammatory processes have been confirmed by genome-wide analyses *in vivo* and *in vitro* studies (18).

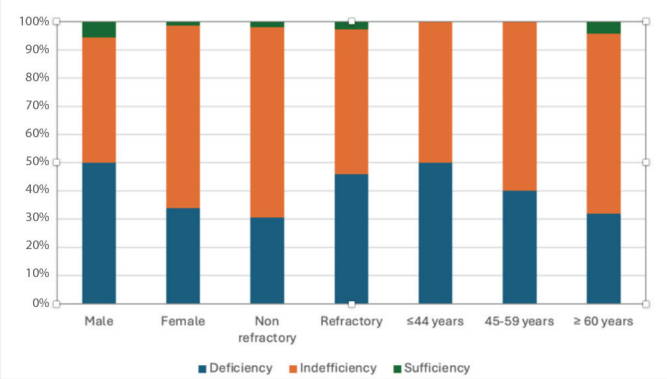

Figure 1. Vitamin D status in sex, refractory, and age categories

Table 1. Calcium levels in BPPV patients

Groups	n	Calcium levels (mg/dL)	p
Sex			0.133
Male	18	9.8±0.4	
Female	68	9.6±0.4	
Refractory categories			0.815
Non-refractory	49	9.7±0.4	
Refractory	37	9.8±0.5	
Age range			0.688
≤44 years	14	9.7±0.4	
45-59 years	25	9.7±0.4	
≥60 years	47	9.8±0.5	

BPPV: Benign paroxysmal positional vertigo

A review investigating the relationship between temporal bone diseases and vitamin D reported evidence regarding diseases such as vestibular neuritis, endolymphatic hydrops, idiopathic sudden hearing loss, idiopathic facial paralysis, and BPPV (11). Although all these diseases have various etiological factors, it has been reported that autoimmune or autoinflammatory reactions could be involved after viral infection. It has been explained that vitamin D could affect the suppression of this postviral autoimmune reaction with its immunomodulatory effect and antioxidant activity and its endothelial cell stabilizing effect. Experimental studies have shown degenerative changes in the inner ear ganglion cells, the otoconia, and hair cells in mice with vitamin D receptor deficiency (11). Gibson et al. (19) have shown that dietary vitamin D, at physiological concentrations, maintains calcium homeostasis and supports bone health, as well as having a stabilizing effect on endothelial stability and an anti-inflammatory response. While these provide a plausible link to the diseases mentioned above, further studies on the association between temporal bone diseases and vitamin D deficiency are recommended.

Vitamin D deficiency has been found to be associated with longer duration of BPPV symptoms, lower success rates of repositioning maneuvers, and higher recurrence rates (14,20-24). A study in postmenopausal women found an association between osteoporosis and idiopathic BPPV, with approximately half of these patients having vitamin

Table 2. Vitamin D levels in BPPV patients

	Vitamin D levels (n)			p
	Deficiency (≤20 ng/mL)	Insufficiency (21-29 ng/mL)	Sufficiency (≥30 ng/mL)	
Groups (n)	32	52	2	
Sex				0.387
Male	9	8	1	
Female	23	44	1	
Refractory categories				0.009
Non-refractory	15	33	1	
Refractory	17	19	1	
Age range				0.323
≤44 years	7	7	0	
45-59 years	10	15	0	
≥60 years	15	30	2	

BPPV: Benign paroxysmal positional vertigo

D deficiency and impaired local Ca_2+ homeostasis (10). Yamanaka et al. (6) stated that the recurrence of BPPV was higher in osteoporosis patients. We did not find a significant difference in serum calcium levels in the refractory BPPV group in which we performed more than one maneuver. This may be due to the fact that serum calcium levels are affected by various factors.

CRPs are mostly successful in treating BPPV, but some patients require repeated CRPs. Prolonged vertigo symptoms before application, bilateral or multiple canal involvement, and age over 50 years have been associated with the need for multiple CRP. Korkmaz and Korkmaz (25) found that hypertension was an influential factor for repetitive maneuvers in the treatment of BPPV. Response to treatment with a single maneuver varies between 37% and 87% (26). In our study, 57% of patients improved with a single maneuver, and 43% required more than one maneuver. Yoon et al. (2) found that 69.5% of their patients had improved with only one CRP and the overall success with repeat CRPs was 96.4%. In a similar study, 68% of patients improved with only one maneuver while 87.6% needed more than one maneuver for improvement (25).

Although CRPs are commonly used to reposition displaced otoconia in the inner ear, these treatments are practitioner-dependent, and it is difficult to standardize diagnostic and therapeutic tests (27). In our study, maneuvers were performed only by researchers according to nystagmus findings detected with VNG, and those requiring more than one maneuver were considered refractory. However, we did not evaluate patients with canalolithiasis or cupulolithiasis separately. Most recent meta-analyses and studies in literature have focused on recurrent BPPV. We specifically focused on refractory BPPV cases and those that required multiple maneuvers. In our study, significant decrease in serum vitamin D levels in the refractory group requiring multiple maneuvers suggests that vitamin D levels could be related to the resistance to maneuvers in disease prognosis. Therefore, measuring vitamin D levels and providing replacement to maintain adequate levels should be considered in patients with refractory BPPV. In our study, only two of the 86 patients (2.33%) had sufficient serum vitamin D levels.

In a recent study, contrary to our results, no significant association was found between persistent BPPV and vitamin D deficiency, and factors such as male sex and the presence of concomitant diseases were indicated as predictors of resistance to CRP (28).

Vitamin D deficiency has been reported to possibly be affected by seasonal conditions and that more research is needed on this subject (12,29). Our study was conducted throughout the year, and vitamin D levels, which may vary seasonally, were not considered. This is one of the limitations of our study. Another limitation is our small sample size and the non-homogeneous distribution across sex and age groups which limits the strength of subgroup analyses. Additionally, potential confounders factors such as diabetes, hypertension, and osteoporosis were not taken into consideration.

The findings of this study suggest that the evaluated predictors show a meaningful association with the clinical outcomes; however, these results should be interpreted with caution due to several methodological considerations. First, the sample size did not fully meet the a priori target determined by the power analysis, particularly in the refractory group, which remained below the anticipated 44 participants. Although the total sample was deemed acceptable based on the GPower estimation parameters (effect size, α level, and power), this shortfall represents a limitation that may have reduced statistical precision. Additionally, the imbalance between groups (37 vs. 49 participants) may have influenced the robustness of the comparisons, potentially contributing to reduced power. Furthermore, while the observed relationships were consistent with the existing literature, the cross-sectional/observational nature of the design precludes any inference of causality; therefore, the results should be understood as demonstrating associations rather than definitive causal effects.

Study Limitations

Although our study has some limitations, such as not evaluating seasonal changes and working with a small and non-homogeneous group, our findings suggest that vitamin D levels could be predictive of resistance to maneuvers in the prognosis of the disease. We can hypothesize that extremely low vitamin D levels may impair the body's local repair capacity in the inner ear, potentially leading to permanent adhesion (cupulolithiasis) or delayed otoconia mobilization, thus contributing directly to the cases refractory to the maneuver rather than predisposing to recurrence. Nevertheless, it should be noted that many patient-related, environmental, and clinician-related factors can also have an impact on patients who show resistance to maneuvers, and the necessity of studies with larger series should be considered.

Conclusion

In our study evaluating serum vitamin D and calcium levels in patients with BPPV undergoing repositioning maneuvers, we found that vitamin D levels were significantly lower in those who were refractory to the maneuvers.

Ethics

Ethic Committee Approval: The study was approved by the İzmir Katip Çelebi University Health Research Ethics Committee (approval no: 0297, date: 19.12.2024).

Informed Consent: All patients were informed and consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.F.B., B.Ç., Concept: A.F.B., Design: A.F.B., Data Collection and/or Processing: B.Ç., M.D., Analysis or Interpretation: A.F.B., B.Ç., M.D., Literature Search: A.F.B., B.Ç., Writing: A.F.B., B.Ç.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Main Points

- Although benign paroxysmal positional vertigo (BPPV) is a disease that is treated with high efficacy using canalith repositioning maneuvers, resistant patients are encountered.
- Comorbid diseases and risk factors should be investigated in refractory patients.
- Vitamin D deficiency may be a predisposing factor for the occurrence and recurrence of BPPV.
- Vitamin D levels should be investigated in cases of BPPV resistant to maneuvers.

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