Association of Benign Paroxysmal Positional Vertigo with Osteoporosis and Vitamin D Deficiency: A Case Controlled Study

Abdullah Karataş, Gülşah Acar Yüceant, Turgut Yüce, Cemal Hacı, Işıl Taylan Cebi, Mehti Salviz

Clinic of Otorhinolaryngology, Haseki Training and Research Hospital, Istanbul, Turkey (AK, GAY, CH, ITC)
Clinic of Otorhinolaryngology, Derince Training and Research Hospital, Kocaeli, Turkey (TY)
Department of Otorhinolaryngology, Yenyüzüyl University School of Medicine, Istanbul, Turkey (MS)

OBJECTIVE: Benign paroxysmal positional vertigo (BPPV) is a common type of vertigo caused by the peripheral vestibular system. The majority of cases are accepted as idiopathic. Calcium metabolism also plays a primary role in the synthesis/absorption of otoconia made of calcium carbonate and thus might be an etiological factor in the onset of BPPV. In this study, we aimed to investigate the role of osteoporosis and vitamin D in the etiology of BPPV by comparing BPPV patients with hospital-based controls.

MATERIALS and METHODS: This is a case-control study comparing the prevalence of osteoporosis and vitamin D deficiency in 78 BPPV patients and 78 hospital-based controls. The mean T-scores and serum vitamin D levels were compared. The risk factors of osteoporosis, physical activity, diabetes mellitus, body mass index, and blood pressure were all compared between the groups. To avoid selection bias, the groups were stratified as subgroups according to age, sex, and menopausal status.

RESULTS: In this study, the rates of osteoporosis and vitamin D deficiency detected in BPPV patients were reasonably high. But there was no significant difference in mean T-scores and vitamin D levels, osteoporosis, and vitamin D deficiency prevalence between the BPPV group and controls.

CONCLUSION: The prevalence of osteoporosis and vitamin D deficiency is reasonably high in the general population. Unlike the general tendencies in the literature, our study suggests that osteoporosis and vitamin D deficiency are not risk factors for BPPV; we conclude that the coexistence of BPPV with osteoporosis and vitamin D deficiency is coincidental.

KEYWORDS: Vitamin D, osteoporosis, positional vertigo

INTRODUCTION
Benign paroxysmal positional vertigo (BPPV) is defined as brief vertigo spells triggered by the act of moving the head to a new position [1]. It typically leads to positional vertigo but occasionally patients may complain of positional dizziness [1]. BPPV is a common type of vertigo caused by the peripheral vestibular system. The 1-year prevalence rate of BPPV is 0.5% in subjects of age 18–39 years and increases to 3.4% in individuals of age >60.2 years. Women are two times more likely to have BPPV. Postmenopausal women are more likely to have BPPV than premenopausal women [2].

There is no consensus on the factors causing BPPV. As the etiological factors are uncertain, most cases are accepted as idiopathic. The suggested predisposing factors are old age, female sex, hormonal factors, whiplash injuries, and viral origin [3-7]. Additionally, a familial tendency for the occurrence of BPPV was identified as a factor [8].

Otoconia are composed of calcium carbonate in the form of calcite crystals and an organic core predominantly consisting of glycoproteins [9-16]. Calcium metabolism also plays a primary role in the synthesis/absorption of otoconia made of calcium carbonate and thus might be an etiological factor in the onset of BPPV [11-18].

Over the last 15 years, several studies investigated the role of calcium metabolism in the pathogenesis of BPPV. In 2003, Vibert et al. [14] observed that osteoporosis, osteopenia, and disorders of calcium metabolism presented more often in female BPPV patients.
over 50 years of age and concluded that osteopenia and osteoporosis could be potential etiological factors in BPPV. In consequent years, studies conducted in several regions reported a prevalence of osteoporosis and vitamin D (vit D) deficiency in BPPV patients [3, 14-17]. However, these studies all had major selection bias in that the control group did not represent the population [3, 6, 14, 15]. Bone mineral density (BMD) and serum 25-hydroxy vitamin D (25-OH vit D) levels might be affected by various factors such as age, hormonal factors, sex, nutrition and lifestyle habits, and pre-existing metabolic disorders [18-20]. Previous studies did not take such factors into account, and most of them pooled healthy subjects into the control group. Furthermore, quite high prevalence values concerning overall osteoporosis and vit D deficiency levels are given by numerous epidemiological studies [16, 17]. The condition is defined as a pandemic of osteoporosis and vit D deficiency by several sources [20, 25].

Considering these assessments, the relationship between BPPV and osteoporosis and vit D deficiency is debatable.

In this study, we aimed to investigate the role of osteoporosis and vit D in the etiology of BPPV by comparing BPPV patients with hospital-based controls.

MATERIALS and METHODS
Our study was designed as a hospital-based case control study and was conducted between July 2014 and November 2015. Seventy-eight idiopathic BPPV patients and 78 controls without histories of dizziness were included. The study design was reviewed and approved by the local ethics committee (protocol: 57/2014). In accordance with the Declaration of Helsinki, oral and written informed consent about the design, aim, and clinical implication of our study was obtained from all participants.

Subjects
All participants (BPPV patients and controls) underwent neuro-otological examination, audiologic and bithermal caloric tests, and were reviewed for a history of head trauma to avoid including those with otolith organ disorders secondary to previous vestibular disease. Subjects who had neuro-otological diseases detected by history-taking or physical examination, unexpected hearing loss defined by audiologic tests, canal paralysis detected by bithermal caloric test, a history of head trauma, or previous treatment for osteoporosis or osteopenia were excluded from the study.

Case Group
Patients diagnosed with BPPV were enrolled in this study. The diagnosis of BPPV was established based on patient history and characteristic nystagmus observed with video nystagmography during Dix-Hallpike and head-roller tests. Seventy-three posterior canal and five lateral canal BPPV cases were detected. Repositioning maneuvers (Epley, Barbecue, Forced Prolonged Positional Procedure, and Head Shake) concerning the involved canal were performed. Two days later, all patients were examined, and repositioning maneuvers were reperformed by those showing no improvement. Control examination and maneuvers were continued until the nystagmus had disappeared.

Control Group
All subjects in the control group were recruited from individuals admitted to our hospital with acute upper airway tract infection. The control group was stratified as subgroups based on age, menopausal status, and sex and was matched to BPPV patients to avoid selection bias.

Regular physical activity habits (walking at a brisk pace for ≥30 min or more three times a week), blood pressure measurements, body mass index (BMI), and the presence of diabetes mellitus (DM), all of which might affect BMD, were all recorded in both groups.

Measurement of BMD
All subjects in the study were examined with dual-energy X-ray absorptiometry to assess BMD. Measurements were taken using the NORLAND XR-46 (Norland Co., Fort Atkinson, WI, USA) device. The lowest T-score obtained from the lumbar vertebrae and femur levels were accepted as the valid T-score. T-scores of <−2.5 were regarded as osteoporosis.

Data Analysis
Our study compared mean T-scores, osteoporosis prevalence, mean serum vit D levels, and the prevalence of vit D deficiency between BPPV patients and the control group. These two groups were also divided into subgroups according to age (below 45 and over 45 years), sex, and menopausal status (pre and postmenopause).

Our study sample size was determined based on power analysis (power:0.80/α:0.05/β:0.2).

Mean, standard deviation, median, minimum, maximum, frequency, and ratio values were used for descriptive statistics of the data. Distribution of variables was measured using Kolmogorov–Smirnov test. The Mann–Whitney U test and independent samples T-test were used for the analysis of quantitative data. Qualitative data was analyzed using Fisher’s or Chi-square test. The SPSS 22.0 (SPSS Inc.; Chicago, IL, USA) program was used for statistical analysis.

RESULTS
No significant difference was found regarding mean age and sex distribution between the BPPV and control groups (p=0.278 and p=0.624, respectively). Dispersion properties of participants below and above 45 years of age, as well as menopausal status, did not differ between the two groups (p=0.611 and p=0.671 respectively). The demographic characteristics of participants are shown in Table 1.

The mean BMI of the BPPV group was 26.2±3.0 kg/m²; eight patients (10%) had DM, and 12 (16%) had hypertension. Six patients (7%) claimed to exercise regularly. The mean BMI of the control group was 26.0±2.3 kg/m²; 10 volunteers (13%) had DM, and 15 (19%) had hypertension; eight volunteers (10%) claimed a regular physical exercise habit. No significant difference in mean BMI, DM, hypertension frequency, and/or regular physical exercise habits were found between the two groups (p=0.845, p=0.803, p=0.673, and p=0.781, respectively) (Table 1).
The mean T-scores of the BPPV and control groups were −1.5±1.3 and −1.7±1.0, respectively. Osteoporosis prevalence in the BPPV and control groups were 23% (18 individuals) and 26% (20 individuals), respectively. There was no significant difference in mean T-scores and osteoporosis prevalence between the two groups (p=0.210 and p=0.852, respectively) (Table 2).

The mean T-scores of those aged <45 years in the BPPV group and those aged <45 years in the control group were −1.3±1.0 and −1.2±1.0, respectively. Osteoporosis prevalence in those aged <45 years in the BPPV and control groups was 8% (two individuals) and 11% (three individuals), respectively. There was no significant difference in mean T-scores and osteoporosis prevalence between these two groups (p=0.527 and p=1.0, respectively).

The mean T-scores of those aged ≥45 years in the BPPV group and those aged ≥45 years in the control group were −1.6±1.3 and −2.1±1.0, respectively. Osteoporosis prevalence in those aged ≥45 years in the BPPV and control groups was 30% (16 individuals) and 34% (17 individuals), respectively. There was no significant difference in mean T-scores and osteoporosis prevalence between these two groups (p=0.063 and p=0.677, respectively) (Table 3).

The mean T-scores among female BPPV patients and female members of the control group were −1.4±1.3 and −1.6±1.2, respectively. Osteoporosis prevalence among female BPPV patients and female members of the control group was 22% (11 individuals) and 24% (11 individuals), respectively. Mean T-scores in male BPPV patients and the male control group were −1.8±1.1 and −1.9±0.8, respectively. Osteoporosis prevalence among male BPPV patients and male members of the control group was 24% (seven individuals) and 27% (nine individuals), respectively. There was no significant difference in mean T-scores and osteoporosis prevalence between the females from both groups (p=0.333, p=1.0 respectively) and between the males from both groups (p=0.813, and p=1.0, respectively) (Table 4).

The mean T-scores in premenopausal BPPV patients and premenopausal members of the control group were −0.7±1.2 and −0.8±1.0, respectively. Osteoporosis prevalence in premenopausal BPPV patients and premenopausal members of the control group were 6% (one person) and 5% (one person), respectively. Mean T-scores in postmenopausal BPPV patients and controls were −1.7±1.3 and −2.2±1.0, respectively. Osteoporosis prevalence in postmenopausal BPPV patients and controls was 22% (10 individuals) and 37% (10 individuals), respectively. There was no significant difference in
mean T-scores and osteoporosis prevalence between the premenopausal and postmenopausal groups (p=0.987, p=1.0, p=0.115, and p=0.784, respectively) (Table 5).

**Serum vit D Levels**

The mean serum 25-OH vit D levels in BPPV patients and controls were 23.0±14.4 ng/mL and 17.0±12.3 ng/mL, respectively. Vit D deficiency prevalence in these two groups was 28% (22 individuals) and 40% (31 individuals), respectively. There was no significant difference in mean serum vit D and vit D deficiency prevalence between these two groups (p=0.066, p=0.176, respectively) (Table 2).

The mean serum 25-OH vit D in BPPV patients and controls aged <45 years was 22.6±14.8 ng/mL and 14.4±9.6 ng/mL, respectively. Vit D deficiency prevalence in these two groups was 22% (10 individuals) and 30% (14 individuals), respectively. There was no significant difference for mean serum vit D and vit D deficiency prevalence between individuals aged <45 years and those aged ≥45 years (p=0.087, p=0.588, p=0.074, and p=0.197, respectively) (Table 3).

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**Table 3.** Bone mineral density and serum vitamin D in BPPV patients and controls aged <45 and ≥45 years

<table>
<thead>
<tr>
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<th>BPPV group</th>
<th>Control group</th>
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<tbody>
<tr>
<td></td>
<td>Mean±SD/ n-%</td>
<td>Med (min–max)</td>
</tr>
<tr>
<td>Age&lt;45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T score</td>
<td>−1.3 ± 1.0</td>
<td>−1.3 (−2.5–1.1)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>yes</td>
<td>2 (8%)</td>
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<td></td>
<td></td>
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<tr>
<td>vit D</td>
<td>22.6±14.8</td>
<td>19.1 (5.8–44.8)</td>
</tr>
<tr>
<td>Deficiency</td>
<td>yes</td>
<td>10 (41%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Age≥45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T score</td>
<td>−1.6±1.3</td>
<td>−1.8 (−4.4–1.2)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>yes</td>
<td>16 (30%)</td>
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<td></td>
<td></td>
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<tr>
<td>vit D</td>
<td>23.1±14.5</td>
<td>18.0 (5.4–77.8)</td>
</tr>
<tr>
<td>Deficiency</td>
<td>yes</td>
<td>12 (22%)</td>
</tr>
</tbody>
</table>

Mann–Whitney U test, Fisher’s, and Chi-square test

**Table 4.** Bone mineral density and serum vitamin D in females and males in BPPV and control groups

<table>
<thead>
<tr>
<th></th>
<th>BPPV group</th>
<th>Control group</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD/ n-%</td>
<td>Med (min–max)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T score</td>
<td>−1.4±1.3</td>
<td>−1.5 (−4.4–1.2)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>yes</td>
<td>11 (22%)</td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>vit D</td>
<td>23.4±14.6</td>
<td>19.2 (5.4–77.8)</td>
</tr>
<tr>
<td>Deficiency</td>
<td>yes</td>
<td>14 (29%)</td>
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<td></td>
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<tr>
<td>Male</td>
<td></td>
<td></td>
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<tr>
<td>T score</td>
<td>−1.8±1.1</td>
<td>−2.0 (−3.7–0.0)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>yes</td>
<td>7 (24%)</td>
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<tr>
<td>vit D</td>
<td>21.7±14.2</td>
<td>16.1 (6.8–48.3)</td>
</tr>
<tr>
<td>Deficiency</td>
<td>yes</td>
<td>8 (28%)</td>
</tr>
</tbody>
</table>

Mann–Whitney U test, Fisher’s, and Chi-square test

SD: standard deviation; min: minimum; max: maximum; BPPV: benign paroxysmal positional vertigo.
The mean serum 25-OH vit D in female BPPV patients and female controls was 23.4±14.6 ng/mL and 15.9±10.9 ng/mL, respectively. Vit D deficiency prevalence in these two groups was 29% (14 individuals) and 53% (24 individuals) respectively. There was a significant difference in mean serum vit D levels and vit D insufficiency prevalence between the two groups (p=0.003 and p=0.021, respectively). The female controls had lower serum 25-OH vit D levels and higher vit D deficiency prevalence than the female BPPV group. The mean serum 25-OH vit D level in male BPPV patients and male controls was 21.7±14.2 ng/mL and 18.5±14.1 ng/mL, respectively. Vit D deficiency prevalence in these two groups was 28% (eight individuals) and 21% (seven individuals), respectively. There was no significant difference in serum vit D levels and vit D deficiency prevalence between these two groups (p=0.767 and p=0.769, respectively) (Table 4).

The mean serum 25-OH vit D level in premenopausal BPPV patients and premenopausal controls was 22.0±13.4 ng/mL and 19.2±10.2 ng/mL, respectively. Vit D deficiency prevalence in these two groups was 29% (five individuals) and 78% (14 individuals), respectively. There was a significant difference in mean serum vit D levels and vit D deficiency prevalence between the two groups (p=0.016 and p=0.007, respectively). The control group had lower serum 25-OH vit D levels and higher vit D deficiency prevalence than the premenopausal BPPV group. The mean serum 25-OH vit D in postmenopausal BPPV patients and the postmenopausal control group was 24.1±15.4 ng/mL and 18.0±10.2 ng/mL, respectively. Vit D deficiency prevalence in these two groups was 28% (nine people) and 37% (10 people), respectively. There was no significant difference in serum vit D levels and vit D deficiency prevalence between these two groups (p=0.091 and p=0.578, respectively) (Table 5).

**DISCUSSION**

The present study showed that BPPV patients and controls had a similar prevalence of osteoporosis and vit D deficiency. These results showed that low serum vit D levels and osteoporosis are not risk factors for BPPV.

In our study, the prevalence rates of osteoporosis and vit D deficiency detected in BPPV patients were reasonably high, as reported in previous studies. Interestingly, unlike in other studies, we found that osteoporosis and vit D deficiency occurred at a higher rate in our control group. We believe that control group selection criteria are responsible for the different results obtained by other studies. In addition, ethnic differences or latitude (involving hours of sun exposure) could explain the variation of vit D levels across different studies. In this aspect, the results of several studies investigating the relationship between BPPV and osteoporosis and/or vit D deficiency are controversial.

The studies conducted by Vibert and Hausler [6] and Mikulec et al. [15] did not state inclusion criteria for their control groups. Moreover, they simply stated that their control groups were drawn from healthy subjects, which could not represent the general population. They also reported very low osteoporosis prevalence rate in their control groups that seems impossible considering the expected rate in the population. Vibert and Hausler [6] stated that both control and patient groups were chosen from the same geographic region; however, none of the 83 female control subjects over 50 years of age had osteoporosis. In this study, osteoporosis prevalence rate of the control group was 0%. Additionally, Vibert and Hausler [6] and Mikulec et al. [15] investigated the prevalence rate of osteoporosis in a restricted group of subjects (only females over 50 years of age) that could carry a potential risk for confounding factors such as menopausal state.

Jeong et al. [3] and Talaat et al. [14] evaluated both male and female BPPV patients with wider age ranges. Talaat et al. [11] chose healthy volunteers as controls, and no data were given on the prevalence of osteoporosis and vit D deficiency in the geographic region in which the study was performed. In the study of Jeong et al. [3], osteoporosis frequency in the control group (9.4%) was quite low compared with the overall osteoporosis prevalence in Korea (males, 7.3%; females, 38%) [21].
By the assessment of all these studies, we can assume that the significant relationship between osteoporosis and/or vit D deficiency in BPPV patients and control groups found by other researchers may be controversial.

Quite high prevalence values concerning overall osteoporosis and vit D deficiency levels are reported by epidemiological studies. The condition is defined as a pandemic of osteoporosis and vit D deficiency by several sources [26-25].

Some European studies reported osteoporosis prevalence of 6.6%–9.7% in men and 22.1%–39% in women over 50 years old [26-28]. Studies from the USA report osteoporosis prevalence of 4.3%–13% and 15.4%–51% in men and women over 50 years of age, respectively [29, 30]. The prevalence of osteoporosis in Korea is 7.3% in men and 38% in women over 50 years of age [29]. The prevalence of osteoporosis in Turkey is 22.2% in men and 27.2% in women over 50 years of age [18].

European studies report vit D deficiency prevalence of approximately 36% in men and 47% in women [19]. Percentages of 25%–57% have been reported by various studies from the USA [32]. The prevalence of vit D deficiency in Turkey was reported as 33.7% [19].

We assume that the prevalence values of the control group being concordant with those of the general population increases the reliability of the studies evaluating the relationship of osteoporosis and vit D deficiency to BPPV, as these diseases have high overall prevalence values.

Although BPPV is common in women and older population, it may also occur in men and the younger population. Unlike most of the other studies, the BPPV patient group in our study has a wider age range (22–85 years) and consists of both sexes (49 females, 29 males). We believe that our population sample is much more valuable than other study samples that consist only of female and older BPPV patients.

The osteoporosis and vit D deficiency prevalences of our control group were parallel with the data obtained from overall prevalence studies in our geographic region, and these prevalence values are within reliable limits. Furthermore, factors (age, sex, menopausal status, DM, hypertension, and physical activity habits) affecting BMD and serum 25-OH vit D levels were similar in both patient and control groups. The two groups had similar demographic characteristics and comorbidities. These features increase the reliability of our study.

Our findings suggest that the coexistence of BPPV with osteoporosis and vit D deficiency, which are very common in the general population, is coincidental.

The prevalence of osteoporosis and vit D deficiency is reasonably high in the general population. Unlike the general tendencies in the literature, our study suggests that osteoporosis and vit D deficiency are not risk factors for BPPV and that the coexistence of BPPV with osteoporosis and vit D deficiency is coincidental. We think more multicenter studies with larger sample sizes and wider age ranges, including both sexes, different ethnicity, and latitude are needed for a more accurate and reliable assumption of the relationship of these diseases with BPPV. We believe that other factors that are capable of causing macular degeneration and otoconial fragmentation (such as autoimmune pathology, vasculitis, trauma, and systemic illness) should be investigated for BPPV etiology.

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