

Hypovitaminosis D, Low Bone Mineral Density, and Diabetes Mellitus as Probable Risk Factors for Benign Paroxysmal Positional Vertigo in the Elderly

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Abstract

Introduction Studies have found that elderly patients with benign paroxysmal positional vertigo (BPPV) may present low levels of vitamin D (25 (OH) D), changes in bone mineral density, and diabetes mellitus (DM).

Objective: To investigate the possible association between BPPV, bone mineral density, hypovitaminosis D, 25 (OH) D and DM.

Methods The sample consisted of 109 elderly subjects. The BPPV was verified by a standardized questionnaire and the Dix-Hallpike maneuver. Blood samples were collected for the investigation of 25 (OH) D serum levels. The bone mineral density was evaluated by means of a densitometer. Diabetes mellitus verification was performed using a self-reported questionnaire.

Results Of the 109 participants, 17 had BPPV. There was a statistically significant difference between BPPV and gender ($p = 0.027$, $\phi = 0.222$), with female representing 88.2% of those with BPPV. In the group with BPPV, there was a statistically significant difference for the amount of vitamin D found ($p = 0.001$) and for age ($p = 0.001$). In the elderly group with DM and BPPV, a difference was found for the standard deviation of the femur ($p = 0.022$) with posthoc Dunn, identifying the difference between diabetics with and without BPPV ($p = 0.047$).

Conclusion Although no association was found (25 (OH) D levels) with BPPV in the general population of this study, it was observed that there was an association with bone mineral density in the elderly group with DM and BPPV, and, in the group with BPPV, there was an association between the amount of vitamin D and age.

Keywords

- ▶ vitamin D
- ▶ bone mineral density
- ▶ benign paroxysmal positional vertigo
- ▶ elderly

Introduction

Benign paroxysmal positional vertigo (BPPV) is defined as a vestibular dysfunction of peripheral origin and unilateral predominance, characterized by episodes of vertigo that are usually intense, short in duration, and typically triggered by certain postural changes in the head.^{1–3} Benign paroxysmal positional vertigo represents ~ 20 to 30% of dizziness diag-

noses in specialized clinics, with an incidence of 0.6% per year, and its prevalence rate increases to 3.4% in individuals over 60.2 years of age. It is the most common cause of vertigo in adults, affecting women twice as much and constituting in most cases of the idiopathic BPPV.^{4–6}

Low levels of vitamin D have been associated with the development and recurrence of BPPV, with a possible level of disturbance attributed to vestibular endolymph Ca^{2+} , which

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results in the formation of abnormal otoconia. Calcium is the main component of these otoconia that are generated by the same mechanism of calcium absorption that occurs in bones, which, in turn, has many important biological functions, including the regulation of homeostasis of calcium.⁷⁻⁹

All people have several free otoconia in the semicircular canals; however, the body is able to absorb calcium usually within hours or days without triggering symptoms.⁹ Epidemiological studies have found that a significant portion of the world population, regardless of age, ethnicity, and geographic location, has a prevalence of osteoporosis and low serum vitamin D levels in patients with BPPV.^{8,10-13} Bone mineral density (BMD) and serum 25-hydroxyvitamin D (25 (OH) D) levels may be affected by several factors, such as age; gender; preexisting metabolic disorders, such as diabetes mellitus (DM), and lifestyle.^{14,15}

Since there is a scarcity of studies that provide evidence of such associations, which may lead to better prevention and treatment options for BPPV in the elderly, this research aimed to investigate a possible association between BPPV, bone mineral density, hypovitaminosis D, levels of 25 (OH) D, and DM in this population.

Methods

Study Design

The present study is a cross-sectional analysis. The sample consisted of a population of 43,610 elderly enrolled in the 38 Basic Health Units of the urban area of the municipality of Londrina, Parana, Brazil. The sample selection of individuals was randomly stratified, taking into consideration the five regions of the city; They are 15% of the central region, 27% of the northern region, 23% in the southern region, 19% in the eastern region, and 16% in the western region. This study is part of the ELLO Project (Study on Aging and Longevity).

Part of this sample was selected to perform the bone densitometry test. The selection criteria for bone densitometry were: to be physically independent according to the functional classification proposed by Spirduso: 3 (physically independent) and 4 (physically active).¹⁶ Of the 323 elderly individuals who were invited to perform bone densitometry, 42 were not found, 28 refused to participate, 135 were excluded because they had one of more of the exclusion criteria, and 9 died. The final sample consisted of 109 elderly subjects. For this part of the study, the following inclusion criteria were used: age ≥ 60 years; both genders; voluntarily agree to participate in the study. The exclusion criteria were: present unilateral and/or bilateral conductive or mixed hearing loss; present otorrhea, surgery in the vestibular system, and not agreeing to perform one of the study evaluations. The study was approved by the ethics committee of the institution, and all subjects participated voluntarily after signing the free and informed consent term to comply with resolution 466/12.¹⁷

Clinical Evaluation

Benign paroxysmal positional vertigo diagnosis was verified by vertigo complaint, an audiological anamnesis,¹⁸ and the Dix-Hallpike diagnostic maneuver.¹⁹ The diagnosis of BPPV

includes a greater caution regarding the history of dizziness associated with changes in head position, confirmed by the Dix-Hallpike maneuver, and the patient who presented nystagmus was considered with BPPV.

The 25-OH-vitamin D dosages were performed in serum samples by fully automated chemiluminescent method (Architect iSR2000-Abbott). They were adopted according to 25-OH vitamin D serum with the following criteria: Vitamin D deficiency was defined as a 25(OH)D below 20 ng/ml (50 nmol/liter), vitamin insufficiency D as a 25(OH)D of 21 to 29 ng/ml, normal or sufficient as a 25(OH)D ≥ 30 ng/ml and hypovitaminosis D as a 25(OH)D ≤ 29 ng / ml.^{20,21}

The BMD was evaluated with the QDR 4500 duo-energy densitometer (Hologic Inc., Bedford, MA, USA) in the lumbar spine (L1-L4), femoral neck and total femur regions. For the analysis, we used the criteria of the World Health Organization,²² normal BMD with T-score up to $-1.0 \pm$ standard deviation (SD), osteopenia with T-score between -1.0 to $-2.4 \pm$ SD, and osteoporosis with T-score $\leq -2.5 \pm$ SD at any bone site.

Specific data on vertigo complaint and comorbidities²³ were also verified with self-reported responses.

The Statistical Package of Social Science (SPSS) 20.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. The normality of the data was verified with the Kolmogorov-Smirnov test, but as the assumption was not met, the Mann-Whitney and Kruskal-Wallis test with Dunn posthoc were selected to analyze the quantitative variables in the comparison between the groups. For analysis of subgroups, normality was also verified. The *t*-test for a sample selected for the BPPV subgroup. The Kolmogorov-Smirnov test for a sample was selected for the control group. The Chi-square test was selected to verify the association between BPPV and other categorical variables. A 95% confidence interval and a significance level of 5% ($p < 0.05$) were established for all tests.

Results

The variables analyzed were: serum levels of vitamin D, vitamin D classification (deficiency, insufficiency, normal), hypovitaminosis, BMD, diabetes (DM). In addition to the covariates related to personal data (sex and age), symptoms (tinnitus and headache), lifestyle (physical activity), and comorbidity (hypertension and diabetes mellitus). Of the 109 participants, 17 had BPPV confirmed by the Dix-Hallpike maneuver. The general characteristics of the sample are presented in ►Table 1. (view ►Table 1).

There was a significant association between BPPV and gender ($p = 0.027$; $\phi = 0.222$), as shown in ►Table 2. The female gender represented 88.2% of those with BPPV. There was also an association between hypovitaminosis and gender ($p = 0.038$; $\phi = 0.199$); of the female group, 68.7% were classified as hypovitaminosis D.

Although no statistical difference was found between BPPV and bone mineral density ($p = 0.125$), lumbar spine densitometry was the variable that most approached a significant value. Only 23.5% of the elderly with BPPV diagnosed with normal densitometry, 47.1% with osteopenia,

Table 1 Descriptive data of the sample (N = 109)

GENERAL CHARACTERISTICS	N (%)
GROUPS	
With BPPV	N = 17 (15.6%)
Without BPPV	N = 92 (84.4%)
GENDER	
Female	N = 69 (63.3%)
Male	N = 40 (36.7%)
AGE RANGE	
60–64 years	N = 32 (29.4%)
65–74 years	N = 58 (53.2%)
75 years and over	N = 19 (17.4%)
Mean ± standard deviation	68.7 ± 6.1 ^a
VITAMIN D	
Normal (≥ 30 ng/ml)	N = 26 (23.9%)
Insufficiency (21–29 ng/ml)	N = 49 (45.0%)
Deficiency (≤ 29 ng/ml)	N = 34 (31.2%)
HYPOVITAMINOSIS D	
Normal (≥ 30 ng/ml)	N = 26 (23.9%)
Hypovitaminosis D (≤ 29 ng/ml)	N = 83 (71.6%)
BMD	
Normal	N = 21 (19.3%)
Osteopenia	N = 56 (51.4%)
Osteoporosis	N = 32 (29.4%)

Abbreviations: BMD, bone mineral density; BPPV, benign paroxysmal positional vertigo.

^a(mean and standard deviation).

and 29.4% with osteoporosis. That is, the elderly with BPPV presented worse results than their healthy controls.

Subgroup analysis showed that, in the group with BPPV, there was a statistically significant difference for the amount of vitamin D found ($p = 0.001$) and for age ($p = 0.001$) when compared with its healthy controls, as shown in **Table 3**. Adjusted analyzes for BPPV and comorbidities, such as arterial hypertension and DM, were also performed. The Kruskal-Wallis test identified a difference for the elderly group with DM and BPPV for the femur SD ($p = 0.022$) with Dunn posthoc identifying the difference between the groups with BPPV and with DM, and the group without BPPV and with DM ($p = 0.047$). The other analyzed variables presented $p > 0.05$.

Discussion

In this study, no association was found between low levels of BMD, hypovitaminosis D and levels of 25 (OH) D and DM with BPPV in the general population. However, it was observed that in the elderly group with DM and BPPV, a statistically significant difference was found for BMD with the SD of the femur. In the group with BPPV, there was a statistically

significant difference for the variables amount of 25 (OH) D found and age. These findings contribute to group information on this controversial aspect of human health.

The effect of low levels of BMD, hypovitaminosis D and levels of 25 (OH) D, and DM on the health of the older population has been largely studied; however, their effects on BPPV is less known. Previous studies have found an association between changes in BPPV hypovitaminosis D.^{8,24}

Regarding the prospective relation between low levels of BMD, hypovitaminosis D and levels of 25 (OH) D, and DM with BPPV, other studies diverge on the associations found.

For instance, in a study to investigate the relationship between BMD and 25-hydroxyvitamin D with the occurrence and recurrence of BPPV, evaluated the records of 130 idiopathic BPPV. The records of 130 idiopathic BPPV patients (55 ± 12 years old, 30 men and 100 women) and 130 age- and gender-matched controls who underwent bone mineral densitometry. Was compared the BMD and serum 25-hydroxyvitamin D between the patients and controls, and also compared the BMD between recurrent and non-recurrent BPPV groups. Among the female subjects, the BPPV group showed significantly decreased BMD compared with the controls ($p < 0.05$). The men in the control group had significantly higher 25-hydroxyvitamin D levels than the men with BPPV ($p < 0.05$). Sixty-three patients (48%) reported recurrent attacks of BPPV. The women with recurrent BPPV were significantly older and showed a significantly lower BMD than non-recurrent women ($p < 0.001$). However, multiple regression analysis revealed that age alone was significantly associated with the recurrence of BPPV in women. Bone mineral density in women and serum 25-hydroxyvitamin D levels in men are associated with the occurrence of BPPV. Only age is an independent predictor of recurrence, although a low BMD and age correlate with the recurrence of BPPV.²⁵ Similar findings regarding gender and age were observed in our study, since there was a statistically significant difference in the amount of vitamin D, age, and gender in the BPPV group.

We also found that in the elderly group with DM and BPPV, there was a significant difference in relation to BMD for femoral SD, although we found no association between BMD and 25 (OH) D levels in women; this association only occurred in BPPV in the total population. The exact pathophysiology of diabetic damage to the peripheral vestibular organ is not yet fully understood. However, a loss of sacculate type I hair cells has been described in human subjects with DM.^{26,27} Glucose uptake is regulated in most tissues by the expression of glucose transporters on cell surfaces.²⁸ In DM, the saccule represents the main structure of the maze affected by pathological damage due to endolymphatic hydrops. Cohen et al²⁹ analyzed a cohort of 112 patients with BPPV, of whom 24 (14%) had DM. The authors pointed out that this prevalence is higher than the 4% rate of diabetics in the United States population. A recent literature review suggests that a large number of peripheral vestibular changes such as BPPV and DM may be strongly influenced by blood insulin and blood glucose levels.³⁰

Recently a meta-analysis did not support the lower vitamin D level relationship with BPPV occurrence. However, it

Table 2 Comparative analyses between groups (n = 109)

		BPPV	Controls (without BPPV)	P (Mann-Whitney test)
Quantitative Variables				
Age (years)		67 [10] ^b	68 [7.75]	p = 0.728 U = 823.500
Vitamin D (ng/ml)		27.8 [10.10]	23.8 [11.28]	p = 0.260 U = 917.000
Categorical variables				
P (Chi-square test)				
Sex	Female	15 (88.2%)	54 (58.7%)	p = 0.020* X ² = 5.390
	Male	2 (11.8%)	38 (41.3%)	
Physical activity	No-active	10 (17.9%)	46 (82.1%)	p = 0.504 X ² = 0.447
	Active	7 (13.2%)	46 (86.8%)	
Vitamin D classification	Normal	6 (35.3%)	20 (21.7%)	p = 0.304 X ² = 2.317
	Insufficiency	8 (47.1%)	41 (44.6%)	
	Deficiency	3 (17.6%)	31 (33.7%)	
D hypovitaminosis	Normal	6 (35.3%)	20 (21.7%)	p = 0.371 X ² = 0.801
	Hypovitaminosis	11 (64.7%)	72 (78.3%)	
Spine BMD	Normal	4 (23.5%)	45 (48.9%)	p = 0.125 X ² = 4.019
	Insufficiency	8 (47.1%)	30 (32.6%)	
	Deficiency	5 (29.4%)	17 (18.5%)	
Tinnitus	Yes	9 (52.9%)	35 (38%)	p = 0.250 X ² = 1.323
	No	8 (47.1%)	57 (62%)	
Hypertension	Yes	12 (70.6%)	52 (56.5%)	p = 0.279 X ² = 1.171
	No	5 (29.4%)	40 (43.5%)	
DM	Yes	5 (29.4%)	20 (21.7%)	p = 0.706 X ² = 0.142
	No	12 (70.6%)	72 (78.3%)	
Headache	Yes	9 (52.9%)	28 (30.4%)	p = 0.072 X ² = 3.241
	No	8 (47.1%)	64 (69.6%)	

Abbreviations: BMD, bone mineral density; BPPV, benign paroxysmal positional vertigo; DM, diabetes mellitus.

^bMedian and interquartile range

*Statistically significant difference.

Table 3 Comparative analyses subgroups

Variables	BPPV (cases) N = 17	P (BPPV group)	Without BPPV (controls) N = 92	P (control group)
Vitamin D (ng/ml)	27.8 [10.1]	p = 0.001*	23.8 [11.28]	p = 0.704
Age (years)	67.0 [10.0]	p = 0.001*	68 [7.75]	p = 0.273

Abbreviation: BPPV, benign paroxysmal positional vertigo.

*Statistically significant difference.

supports, with normal heterogeneity, the fact that recurrent episodes of BPPV are associated with low vitamin D.³⁰

Although in our study we found a significant difference within the subgroup, in the BPPV-adjusted analysis with a higher amount of vitamin D in its group, we did not find this difference in the general study population, constituting serum 25 (OH) D levels in the BPPV group (27.8 ng/ml) and in the

control group decreased serum levels (23.8 ng/ml). One explanation for the non-association found between low BMD levels, hypovitaminosis D, 25 (OH) D levels, and DM in relation to BPPV in the general population may be related to the fact that the serum 25 (OH) D level in the population was not sufficiently low in our study as compared with the study by Talaat et al,¹⁰ which indicates that the vitamin D concentration in the

control group (19.5 ng/ml) is higher than in the BPPV group (16.0 ng/ml). Another explanation concerns latitude differences involving hours of sun exposure. This could explain the variation in serum levels in different studies,^{20,21,31,32} since vitamin D is acquired in humans through the production of 7 dehydrocholesterol, provitamin D3 in the skin, absorption of UVB radiation and ingestion.^{31,33–37}

Mean serum vitamin D concentrations may differ between institutions in the study country.^{8,10,38,39} Therefore, direct comparison of values in the study results requires close attention. These differences in serum levels may be one of the factors for the divergence of research findings regarding the relationship between vitamin D and BPPV.

The strengths of the present study include the bone densitometry test, the application of Dix-Hallpike diagnostic maneuver, and the 25 (OH) D dosages. The limitations include the of self-reported vertigo complaint. However, the use of self-reported measures of vertigo complaint is habitual in prospective studies due to its simplicity and low-costs.⁴⁰ In addition, the vertigo complaint was supported by the application of Dix-Hallpike maneuver.

From the specific literature and the results of the present research, it is shown the need to verify the comorbidities involved in the BPPV for good targeting of the better treatment selection.

Conclusion

Although there was no association between low levels of BMD, hypovitaminosis D, and levels of vitamin D (25 (OH) D with BPPV in the general population of this study, in the elderly group with DM and BPPV, it was found significant difference for SD of the femur, and, in the group with BPPV, there was a statistically significant difference for the amount of vitamin D found and for the age.

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Conflicts of Interest

The authors have no conflicts of interest to declare.

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