The Egyptian Journal of Otolaryngology

ORIGINAL ARTICLE Open Access

Evaluation of serum vitamin D3 and total serum calcium in patients with posterior canal benign paroxysmal positional vertigo

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Abstract

Background Benign paroxysmal positional vertigo is the most common neurootologic disorder, characterized by brief attacks of vertigo aggravated by certain head positions. During the last two decades, several studies were performed in different countries trying to find a relationship between benign paroxysmal positional vertigo and vitamin D3 (25 hydroxyvitamin D) deficiency.

Objectives This study aimed to find the relationship between vitamin D3 deficiency and total serum calcium with benign paroxysmal positional vertigo.

Patients and methods A case–control study conducted from January 2021 to December 2021, consisted of 62 participants; 30 patients with posterior canal benign paroxysmal positional vertigo and 32 healthy persons considered as a control group. The age and sex of both groups were matched, and diagnosis was made by history and examination (Dix-Hallpike's maneuver). A blood sample was taken to evaluate serum vitamin D level and total serum calcium. The results were compared between both groups.

Results The mean levels of vitamin D3 in patients and control groups were 18.57 ± 9.88 ng/ml and 64.12 ± 24.64 ng/ml, respectively, with a statistically significant difference at $p \leq 0.0001$. Moreover, regarding vitamin D3 deficiency below 20 ng/ml between patients and control groups, there was a statistically significant difference $p = 0.001$. Furthermore, there was no significant difference regarding total serum calcium between the two groups, the mean of both groups was 8.57 ± 0.68 mg/dl and 8.93 ± 0.92 mg/dl for patients and control, respectively, at $p = 0.084$.

Conclusion There might be an association between benign paroxysmal positional vertigo and vitamin D3 deficiency. Moreover, there was no significant difference concerning total serum calcium levels between the patient and control groups.

Keywords Benign paroxysmal positional vertigo, Vitamin D3 deficiency, Vertigo, Osteoporosis

Introduction

Benign paroxysmal positional vertigo (BPPV) is the most common ear-related neurootological disorder [1, 2] and one of the most common vestibular disorders [3] accounting for approximately 20–30% of diagnoses in specialized dizziness clinics [1]. Benign paroxysmal positional vertigo (BPPV) is characterized by brief attacks of vertigo that are induced by a change in head position with respect to gravity [4]. Recently, the mechanism of BPPV has been clearly established as free-floating otolith debris (canalolithiasis)

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or debris attached to the cupula (cupulolithiasis) [3]. The otoconia are composed of calcium carbonate as calcite crystals and an organic core consisting predominantly of glycoproteins [3, 5]. There are many predisposing factors for BPPV like old age, female gender, hormonal factors, head injuries, and viral infection. Also, the familial tendency for the occurrence of BPPV was reported as a predisposing factor [6]. Over the last 15 years, several studies investigated the role of calcium metabolism in the pathogenesis of BPPV. Studies conducted in several regions reported a prevalence of osteoporosis and vitamin D3 (vit. D3) deficiency in BPPV patients [3, 7, 8].

Vitamin D3, 1alpha, 25-dihydroxyvitamin D3 [1,25(OH)2D3] is a pleiotropic hormone that regulates the calcium homeostasis of the organism. Vitamin D3 is mostly synthesized in the skin and is changed into 25-hydroxyvitamin D (25-OH vitamin D) in the liver and into 1,25-dihydroxyvitamin D [1,25 (OH) vitamin D] in the kidney to act on various parts of the human body. It induces differentiation and inhibits the proliferation of various normal and cancer cells [9]. Evidence suggests different roles of vitamin D3 and its active metabolites in a large number of tissues, and nearly every tissue in the body has receptors for the active form of vitamin D3 [10]. In the nose, vitamin D3 was found to have a role in allergic rhinitis [11].

Calcium plays a key role in physiological situations such as bone formation, muscle contraction, cellular cell membrane potential stabilization, and blood clotting. The bone is constantly subjected to turnover through bone remodeling. The calcium (Ca) and phosphorus (P) ions in and out of the bone mineral phase are under the control of three main hormones: estrogens, parathyroid hormone, and vitamin D3 metabolites. Vitamin D3 plays an important role in the homeostasis of calcium and phosphate [12].

The aim of this study is to investigate serum vitamin D3 levels and serum calcium in patients with BPPV and compare the results with healthy participants to find a possible correlation between vitamin D3 deficiency and low serum calcium with BPPV.

Patients and methods

A case–control study was performed in the outpatient clinic at the Al-jumhoory Teaching Hospital in Mosul for the period from January 2021 to December 2021.

The study included two groups: the patient group consisted of 30 patients with a clinical diagnosis of posterior canal BPPV and 32 healthy persons as a control group.

Inclusion criteria were:

1. Males and females over 18 years.
2. Clinical diagnosis of posterior canal BPPV proved by Dix-Hallpik maneuver.
3. Normal hearing threshholds by PTA.

Exclusion criteria were:

1. Any central cause of vertigo.
2. Renal failure.
3. Liver diseases.
4. Head trauma
5. History of ear surgery

Analysis of the patient group reveals that all our patients were cases of primary benign paroxysmal positional vertigo affecting the posterior semicircular canal only.

Informed consent was taken from the patients prior to participation in the study after a complete understanding of the purpose and nature of the study. This study was approved by the Medical Research Ethics Committee (MREC) ref.no.UOM/COM/MREC/21–22(26) at 5/1/2021.

Patients with BPPV usually present with brief and severe attacks of vertigo which are usually aggravated by head position and the most common movements are rolling in bed, extending the neck to look up, and bending forward. The patient can identify the affected ear by stating the direction of movement that aggrevates the attacks. Usually, the attack lasts for a few seconds to minutes and may be associated with nausea and vomiting.

History was taken from the patient regarding the number of episodes, duration of attack, aggravating factors, and associated symptoms like nausea, vomiting, tinnitus, aural fullness, or headache.

Dix-Hallpik maneuver was done to all patients with BPPV, all included patient experience characteristic vertigo with nystagmus torsional and beating toward the affected ear. The history and eye movement during positional testing is the gold standard for the diagnosis of BPPV.

A blood sample was taken to investigate vitamin D3 level with a VIDAS automated benchtop immune analyzer based on enzyme-linked fluorescent assay (ELFA) technology, made in France.

Vitamin D3 deficiency was classified according to concentration, less than 20 ng/ml deficient; from 21 ng/ml to 30 ng/ml insufficient; 30 and above sufficient [9]. Moreover, serum calcium level was measured with a biochemistry analyzer smart 150 device from GENOTEK, made in the USA. Total serum calcium normal range is considered from 8.5 to 10.5 mg/dl, according to WHO guidelines.

The data collected during the study were summarized in sheets of Microsoft Excel 2007. The statistical analysis was performed by using IBM-SPSS 26. Means and

standard deviations were calculated for numerical data. The nominal data were described by number and proportions. The *t*-test for numerical and chi-square for nominal data were performed. The p value ≤ 0.05 was considered significant.

Results

The study sample consists of 62 persons; namely, 30 patients and 32 persons as a control group. Of the patient group, 21 subjects (70%) have vit. D > 20 mg/dl, 8 subjects (26.6%) their vit. D were 20–30 mg/dl, and 1 subject (3.4%) has vit. D level was < 30. Concerning the control group, only one subject (3.2%) had vit. D level below 20 mg/dl, and other subjects (96.8%) were above 30 mg/dl.

Table 1 shows the comparison between patients and controls in relation to age in years, vitamin D3, and total serum calcium. The data reveals that the mean age of patients was 45.80 ± 14.45 years, whereas it was 39.16 ± 13.19 for the control group. There was no statistical difference between the two groups.

Vitamin D3 level was 18.57 ± 9.88 ng/ml in the patient group which is significantly lower than that of controls 64.12 ± 24.64 ng/ml at $p \leq 0.0001$.

Total serum calcium was 8.57 ± 0.68 mg/dl in the patient group and 8.93 ± 0.92 mg/dl in the control group; the difference is statistically non-significant at $p = 0.084$.

Table 2 demonstrates the comparison between patients and controls in relation to gender and depicts that males were 40% of patients and 28% of controls. On the contrary, females constitute 60.0% and 71.9% of patients and controls respectively; the difference was statistically non-significant.

The scatter diagram for the study sample in Fig. 1 shows the correlation of vitamin D3 level with age and depicts that the level of vitamin D3 decreases by getting older, although the correlation is weak but statistically significant.

Table 3 demonstrates the comparison between levels of vitamin D3 of patients and controls in relation to gender. The results reveal statistically significant differences between levels in males 20.33 ± 6.16 ng/ml among patients and the level among controls 59.07 ± 19.51 ng/ml at $p = 0.001$. Moreover, vitamin D3 level in females was 17.39 ± 11.77 ng/ml which is significantly lower in patients than that of controls 66.09 ± 26.50 ng/ml at $p = 0.001$.

Table 4 shows the comparison between levels of total serum calcium of patients and controls in relation to gender and demonstrates non-significant differences in both males and females.

Table 5 shows a comparison between patients and controls in relation to the levels of vitamin D3 and portrays that the mean level below 20 ng/ml among patients was 13.44 ± 0.9 which is lower than that of controls 15.25 ± 3.9 in a statistically significant way. Moreover, the mean level of 20–30 ng/ml of vitamin D3 among patients was 24.45 ± 3.08 which is lower than the level among the controls 26.97 ± 0.83 in a statistically significant way. Furthermore, above the level of 30 ng/ml, the difference was statistically non-significant.

Discussion

Benign paroxysmal positional vertigo was first described by Adler in 1897 [13], since that time, many risk factors and mechanisms have been described, and recently, during the last two decades, vitamin D3 has been described as a risk factor for BPPV.

Table 1 Comparison between patients and controls in relation to age, vitamin D level, and total serum calcium

Variables	Patients (Mean ± SD)	Controls (Mean ± SD)	*p*-value*	95% CI	
Age/years	45.80 ± 14.45	39.16 ± 13.19	0.063	− 0.379	13.666
Vit. D3 ng/ml	18.57 ± 9.88	64.12 ± 24.64	> 0.0001	− 55.209	− 35.896
Serum calcium mg/dl	8.57 ± 0.68	8.93 ± 0.92	0.084	− 0.053	0.773

**t*-test for independent two means

Table 2 Comparison between patients and controls in relation to gender

Gender	Patients No. (%)	Controls No. (%)	*p*-value*
Males	12 (40.0%)	9 (28.1%)	0.324
Females	18 (60.0%)	23 (71.9%)	
Total	30 (100%)	32 (100%)	

*Chi-square test

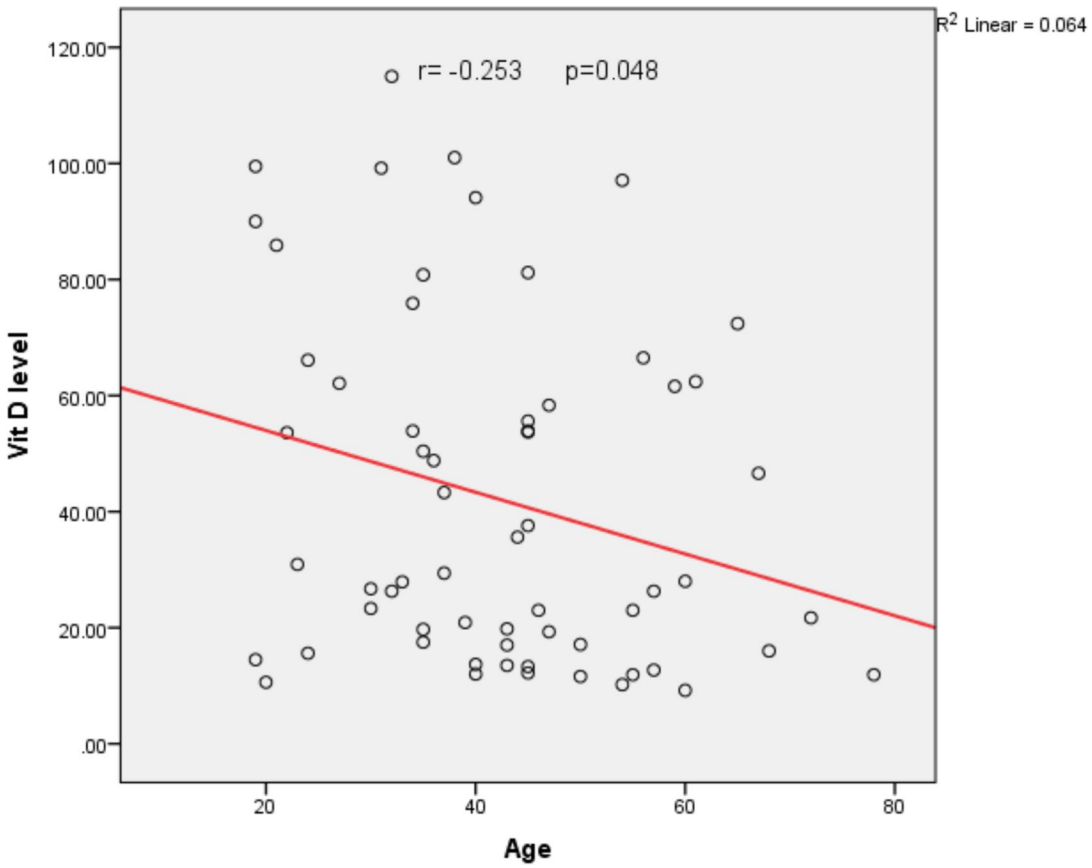

Fig. 1 Scattergram shows the relation between vitamin D3 level and age

Table 3 Comparison between levels of vitamin D3 of patients and controls in relation to gender

Vitamin D3 according to gender	Patients (Mean ± SD)	Controls (Mean ± SD)	*p*-value*	95% CI	
Males	20.33 ± 6.16	59.07 ± 19.51	0.001	31.286	46.194
Females	17.39 ± 11.77	66.09 ± 26.50	0.001	35.221	56.299

**t*-test for independent two means

Table 4 Comparison between levels of serum calcium mg/dl of patients and controls in relation to gender

Total serum calcium according to gender	Patients (Mean ± SD)	Controls (Mean ± SD)	*p*-value*	95% CI	
Males	8.76 ± 0.70	9.19 ± 0.63	0.014	0.092	0.768
Females	8.45 ± 0.66	8.82 ± 0.33	0.006	0.107	0.633

**t*-test for independent two means

Table 5 Comparison between patients and controls in relation to the levels of vitamin D3

Vit. D/ (ng/ml)	Patients (Mean ± SD)	Controls (Mean ± SD)	*p*-value*	95% CI	
Deficiency (> 20)	13.44 ± 0.9	15.25 ± 3.9	0.001	0.734	2.886
Insufficient (20–30)	24.45 ± 3.08	26.97 ± 0.83	0.001	1.39	3.65
Adequate (≥ 30)	62.10 ± 0.01	67.96 ± 22.56	0.16	− 2.383	14.103

Vitamin D3 is fundamental for the development of normal otoconia by maintaining normal calcium levels in the vestibular endolymph which is achieved by the calcium channel transport system in the inner ear and regulated by vitamin D3 receptors VDR [3].

In this study, the vitamin D3 level was evaluated in 62 participants, including 30 patients and 32 control participants.

The effect of age on BPPV can be explained by decreases in vitamin D3 levels with age. The scattergram shows vitamin D3 levels decreased by getting older, and this could be multifactorial which are poor solar exposure, obesity, and chronic disease [14].

In this study, the mean level of serum vitamin D3 in patients with BPPV was 18.57 ± 9.88 ng/ml, whereas in the control group, it was 64.12 ± 24.64 ng/dl $p = 0.000$. This statistically significant difference was in agreement with other studies, namely, Elmoursy and Abdelmaksoud et al. of Egypt [15, 16], Dhameliya et al. of India [17], Sarsitthithum et al. of Thailand [18], Yang et al. and GU et al. of China [19, 20], Carneiro de Sousa et al. of Portugal [21], and Çelik et al. of Turkey [22].

In 2019, Ding J. et al. aimed in their study to evaluate serum vitamin D3 levels in 174 patients with BPPV and 348 healthy participants. They found a relationship between the occurrence and recurrence of BPPV and low serum vitamin D3 and concluded that low serum vitamin D3 level is associated with the occurrence and recurrence of BPPV [23].

In 2020, Chen J. et al. in their meta-analysis evaluated the risk factors for BPPV recurrence, and vitamin D3 was one of these risk factors [24]. Moreover, in 2020, Yang B. et al. in reviewing their meta-analysis of 18 studies up to 2019, the risk factors of vitamin D3 deficiency on BPPV also concluded that vitamin D3 is a risk factor for BPPV [19].

In 2017, Talaat et al. in their study aimed to detect the effect of treatment of vitamin D3 deficiency on the recurrence rate of BPPV and found that the improvement of vitamin D3 level may reduce recurrence [7].

In 2017, Maslovara et al. aimed in their study on 40 patients with BPPV to measure serum vitamin D3 and determine whether there is a difference in the serum levels of vitamin D3 between patients with and without recurrence and found no significant differences in recurrence but most of them had vitamin D3 deficiency and need correction [25].

On the contrary, studies from Karataş et al. of Turkey [26] and Goldschagg et al. of Germany [27] found no statistically significant difference between low serum vitamin D3 level and the occurrence of BPPV attributing such an elusive finding to the common vitamin D3 deficiency in general population i.e. the relation is just coincidental. Moreover, Işık et al. of Turkey [28] in his study showed no significant difference in vitamin D3 and total serum calcium levels between the BPPV group and the control group. He explained the reason as vitamin D3 inadequacy was very common even in healthy populations and the study had been conducted in low solar exposure periods, i.e., from October to December. Büki et al. [2] from Austria found that the serum vitamin D3 level in BPPV is low similar to the general Austrian population.

Regarding total serum calcium level, this study shows no statistically significant difference in the total serum calcium between patients and the control group, the mean of both groups was 8.57 ± 0.68 mg/dl and 8.93 ± 0.46 mg/dl, respectively, $p = 0.084$. This result is in agreement with Elmoursy of Egypt [15] who found no statistically significant difference in either total or ionized serum calcium. Kahraman et al. of Turkey concluded that there is a possible correlation between both Vitamin D deficiency and decreased ionized serum calcium not only in patients with osteoporosis [29].

Unfortunately, we have some limitations in this study, namely, the small number of patients and the short follow-up period so we did not study the recurrence rate for patients with vitamin D3 deficiency.

Conclusions and recommendations

We believe that there is a possible association between vitamin D3 deficiency and BPPV. Moreover, there was no significant difference concerning total serum calcium between patients and the control group. We recommend further studies with a larger sample of patients with longer follow-up periods for the patients to study the relation between vitamin D3 deficiency and recurrence rate.

Acknowledgements

Not applicable.

Research involving human participants and/or animals/informed consent

An informed consent of the patient for the usage of clinical information and images was explained and duly taken from the patient. The authors have not disclosed any personal information regarding the patient or his identity and have used graphical images.

Authors' contributions

OA analyzed and interpreted the patient data regarding the evaluation of serum vitamin D3 and drafted the manuscript. HA performed the clinical trial and helped in writing the manuscript. AM supervised the work and finalized the manuscript writing. All authors read and approved the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Research Ethics Committee (MREC) in Iraq. Written informed consent before enrollment was obtained from all

participants. Additional verbal informed consent was obtained from all individual patients for whom identifying information is included in the article.

Consent for publication
A written informed consent for publication was obtained from all participants using the institutional consent form for publication.

Competing interests
The authors declare that they have no competing interests. Each of the authors has contributed to, read, and approved this manuscript. None of the authors has any conflict of interest, financial or otherwise.

Received: 1 June 2024 Accepted: 30 August 2024
Published online: 17 September 2024

References

1. Von Brevern M, Radtke A, Lezius F, Feldmann M, Ziese T, Lempert T et al (2007) Epidemiology of benign paroxysmal positional vertigo: a population based study. J Neurol Neurosurg Psychiatry 78(7):710–715
2. Büki B, Ecker M, Jünger H, Lundberg YW (2013) Vitamin D deficiency and benign paroxysmal positioning vertigo. Med Hypotheses 80(2):201–204
3. Jeong SH, Kim JS, Shin JW, Kim S, Lee H, Lee AY et al (2013) Decreased serum vitamin D in idiopathic benign paroxysmal positional vertigo. J Neurol 260(3):832–838
4. Jeong SH, Kim JS, Kim HJ, Choi JY, Koo JW, Choi KD et al (2020) Prevention of benign paroxysmal positional vertigo with vitamin D supplementation: A randomized trial. Neurology 95(9):e1117–e1125
5. Johnsson LG, Rouse RC, Wright CG, Henry PJ, Hawkins JE (1982) Pathology of neuroepithelial suprastructures of the human inner ear. Am J Otolaryngol Neck Med Surg 3(2):77–90
6. Gizzi M, Ayyagari S, Khattar V (1998) The familial incidence of benign paroxysmal positional vertigo. Acta Otolaryngol 118(6):774–777
7. Talaat HS, Kabel AMH, Khaliel LH, Abuhadied G, El-Naga HAERA, Talaat AS (2016) Reduction of recurrence rate of benign paroxysmal positional vertigo by treatment of severe vitamin D deficiency. Auris Nasus Larynx 43(3):237–41
8. Parham K, Leonard G, Feinn RS, Lafreniere D, Kenny AM (2013) Prospective clinical investigation of the relationship between idiopathic benign paroxysmal positional vertigo and bone turnover: A pilot study. Laryngoscope 123(11):2834–2839
9. Holick MF (2003) Vitamin D: A millenium perspective. J Cell Biochem 88(2):296–307
10. Di Rosa M, Malaguarnera M, Nicoletti F, Malaguarnera L (2011) Vitamin D3: a helpful immuno-modulator. Immunology 134(2):123–139
11. Alnori H, Alassaf FA, Alfahad M, Qazzaz ME, Jasim M, Abed MN (2020) Vitamin D and Immunoglobulin E Status in Allergic Rhinitis Patients Compared to Healthy People. J Med Life 13(4):463–468
12. Melis A, Rizzo D, Gallus R, Leo ME, Turra N, Masnaghetti D et al (2020) Relationship between calcium metabolism and benign paroxysmal positional vertigo in north Sardinia population. J Vestib Res Equilib Orientat 30(6):375–382
13. Semont A, Freyss G, Vitte E (1988) Curing the BPPV with a liberatory maneuver. In: Advances in oto-rhino-laryngology. pp 290–3
14. Fujita N, Wada Y, Matsunaga T (1990) Benign Paroxysmal Positional Vertigo. In: Practica Otologica, Supplement. Springer London, Munich, Germany, pp 66–70
15. Elmoursy M (2021) Vitamin D assessment in patients with benign paroxysmal positional vertigo. Al-Azhar Assiut Med J 19:111–8
16. Abdelmaksoud AA, Fahim DFM, Bazeed SES, Alemam MF, Aref ZF (2021) Relation between vitamin D deficiency and benign paroxysmal positional vertigo. Sci Rep 11(1):16855
17. Dhameliya JD, Chandra UK, Vishwakarma SK, Ganganpalli D, Verma A (2020) Investigating the Association Between Serum Vitamin D Deficiency and Idiopathic Benign Paroxysmal Positional Vertigo. Int Clin Neurosci J 7(3):122–126
18. Sarsitthithum K, Wisupagan T, Kiatthanabumrung S, Jariengprasert C (2023) The Association Between Serum Vitamin D Levels and Benign Paroxysmal Positional Vertigo. Ear Nose Throat J 102(7):473–477. https://doi.org/10.1177/01455613211008561
19. Yang B, Lu Y, Xing D, Zhong W, Tang Q, Liu J et al (2020) Association between serum vitamin D levels and benign paroxysmal positional vertigo: a systematic review and meta-analysis of observational studies. Eur Arch Oto-Rhino-Laryngology 277(1):169–177
20. Gu X, Dong F, Gu J (2018) Analysis of effect of 1α-hydroxyvitamin D3 on benign paroxysmal positional vertigo and risk factors. Exp Ther Med 15(3):2321–2326
21. Sousa P, Pereira D, Magalhaes P, Duarte DC (2019) Vitamin D deficiency and benign paroxysmal positioning vertigo. Hear Balanc Commun 17(2):179–81
22. Çelik H, Yardım A, Ertaş A, Varışlı B, Ocak Ö (2021) Evaluation of Serum 25-Hydroxyvitamin Vitamin D, Vitamin B12, and Folate Levels in Patients with Benign Paroxysmal Positional Vertigo. Eurasian J Emerg Med 20(1):19–24
23. Ding J, Liu L, Kong WK, Chen XB, Liu X (2019) Serum levels of 25-hydroxy vitamin D correlate with idiopathic benign paroxysmal positional vertigo. Biosci Rep 39(4):20190142
24. Chen J, Zhang S, Cui K, Liu C (2021) Risk factors for benign paroxysmal positional vertigo recurrence: a systematic review and meta-analysis. J Neurol 268(11):4117–4127
25. Maslovara S, Butkovic Soldo S, Sestak A, Milinkovic K, Rogic-Namacinski J, Soldo A (2018) 25 (OH) D3 levels, incidence and recurrence of different clinical forms of benig paroxysmal positional vertigo. Braz J Otorhinolaryngol 84(4):453–459
26. Karataş A, Acar Yüceant G, Yüce T, Hacı C, Taylan Cebi I, Salviz M (2017) Association of benign paroxysmal positional vertigo with osteoporosis and vitamin D deficiency: A case controlled study. J Int Adv Otol 13(2):259–265
27. Goldschagg N, Teupser D, Feil K, Strupp M (2021) No evidence for a specific vitamin D deficit in benign paroxysmal positional vertigo. Eur J Neurol 28(9):3182–3186
28. Cikrikci Isik G, Cevik Y, Emektar E, Corbacioglu SK (2017) Analysis of Vitamin D and Calcium Levels in Benign Paroxysmal Positional Vertigo. Eurasian J Emerg Med 16(3):128–132
29. Kahraman SS, Ozcan O, Arli C, Ustun I, Erduran R, Akoglu E et al (2016) Calcium homeostasis during attack and remission in patients with idiopathic benign paroxysmal positional vertigo. Otol Neurotol 37(9):1388–1392

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