Article published online: 2022-04-13

Therapeutic Effect of the Correction of Vitamin D Deficiency in Patients with Benign Paroxysmal Positional Vertigo – A Randomized Clinical Trial

Jimena Mancera Sánchez[1] Juan Carlos Hernaiz Leonardo[1] Julia Kioko Ishiwara Niembro[2] Juan Carlos Lesser[1]

[1] Ear Nose and Throat Department, Instituto Nacional de Rehabilitación, Mexico City, Mexico
[2] Department of Otoneurology, Instituto Nacional de Rehabilitacion Luis Guillermo Ibarra Ibarra, Mexico City, Mexico

Address for correspondence Jimena Mancera Sánchez, MD, Instituto Nacional de Rehabilitacion, Mexico 14389, Mexico (e-mail: dramancera.orl@gmail.com).

Int Arch Otorhinolaryngol 2022;26(4):e666–e670.

Abstract

Introduction Benign paroxysmal positional vertigo (BPPV) appears during the same age group in which vitamin D and calcium deficiencies are evident. Vitamin D deficiency could predispose to BPPV, since these two entities share a demineralization process.

Objective To establish the otological impact of vitamin D supplementation in patients with its deficiency who suffer from BPPV.

Methods This was a randomized clinical trial. A total of 35 patients with vitamin D deficiency (< 30 ng/ml) and BPPV were divided into 2 groups: Group 1 (control group): treatment with repositioning maneuvers; and Group 2: treatment with repositioning maneuvers and vitamin D supplementation.

Results A follow-up of between 6 and 13 months and a log rank test revealed that the probability of recurrence between the experimental groups was significantly different, with group 2 having a decreased recurrence of vertigo ($p = 0.17$). Scores in the Dizziness Handicap inventory (DHI) in patients treated with vitamin D supplementation were smaller (10 ± 9) when compared with a score of 36 ± 9 in the control group.

Conclusion Plasmatic values of 25-hydroxyvitamin D have an impact in patients with BPPV, who present an improvement in their quality of life when their vitamin D levels are replaced with supplementation. Benign paroxysmal positional vertigo could stop being perceived as a purely otologic disease.

Keywords
- benign paroxysmal positional vertigo
- deficiency
- vitamin D

Introduction

Benign paroxysmal positional vertigo (BPPV) is the most common cause of peripheral vertigo, affecting 2.4% of the population worldwide.[1,2] Benign paroxysmal positional vertigo appears during the same age group as vitamin D and calcium deficiencies (between the 5th and the 7th decades of life). Vitamin D deficiency is quite common; it is present in up to 60% of the general population, and could predispose for BPPV, since these 2 entities share a demineralization process.[3]

The conventional treatment for BPPV is based in canalicular repositioning maneuvers, which have variable results and recurrence rates as high as 50% during the next 5 years

received
July 15, 2020
accepted after revision
February 14, 2021
published online
April 13, 2022

DOI https://doi.org/10.1055/s-0041-1730992.
ISSN 1809-9777.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

after the 1st episode.[4–6] The age at which this type of vertigo becomes more frequent is the same in which vitamin D and calcium (Ca^{2+}) deficiencies are more common and, more importantly, in which its consequences appear as well. Several studies have observed the relationship between the deficit of theses micronutrients and BPPV.[7–10]

The function of the semicircular canals and otoliths reduces with time.[11] With aging, there is a degeneration of the type I and II sensitivity ciliary cells. A degeneration of otoliths is also observed as part of a demineralization process related to age. These structures suffer from fractures of their bodies as part of a demineralization process, since they are structures with a high level of Ca^{2+} within their inorganic perimeter.[12] This natural process may be accelerated in patients with vitamin D deficiency, therefore making otoliths unstable.

The pathophysiology of BPPV is based on the migration of otoliths out of their conventional site in the utricular macula and into the semicircular canals.[13] Furthermore, we must observe this disease as part of a whole in the physiologic disequilibrium in a molecular level. Calcium and vitamin D participate in the homeostasis of the otoliths; therefore, it is expected that their deficiency will relate with the appearance of this type of peripherical vertigo.[14] Structural modifications such as decreased density and size were observed with electronic microscopy of otoliths extracted from adult female rats with induced osteopenia and osteoporosis due to ovary resection.[15] Moreover, Zuca et al. proved that an increase in Ca^{2+} resorption due to vitamin D deficiency may generate an increase in the concentration of Ca^{2+} in the endolymph and reduce the dissolution capability of the dislocated otoliths.[16]

Various studies have demonstrated the relationship between decreased bone density and BPPV: a systematic revision by Yu et al. containing 7 studies, the study by Vibert et al.,[15] in which 75% of women between 50 and 85 years old with diagnosis of BPPV had osteopenia or osteoporosis; a revision of 101 patients with BPPV who had a positive relation with postmenopausal women, and the study by Jang et al, who reported that patients with low column and hip bone density had a higher vertigo recurrence rate and required more repositioning maneuvers.[1,17,18]

In addition, a Study by Talaat et al. proved that, by increasing plasmatic levels of 25-hydroxyvitamin $D > 10$ ng/ml, 82% of the patients had a statistically significant decrease in the number of recurrent vertigo episodes compared with patients with levels < 10 ng/ml.[7] Talaat also concluded that levels of 25-hydroxyvitamin D were significantly lower in patients with recurrent BPPV compared with the group of nonrecurrent BPPV ($p < 0.05$).[3] Jeong et al. demonstrated that in patients with values between 10 and 20 ng/ml, the risk of having BPPV increased 3.8 times, while in patients with levels < 10 ng/ml, the risk was 23 times higher.[8]

Sheikhzadeh et al. did an experimental study that became a role model for ours, in which he divided patients into two groups; the first was composed of patients with BPPV treated with both vitamin D supplements and repositioning maneuvers and the second was a control group treated with the conventional maneuvers. The intensity of the disease was aggravated in the control group patients, compared with a state of stability without vertigo episodes during 6 months in the supplemented group ($p = 0.001$).[10]

The present study seeks to establish the impact of vitamin D replacement in patients with deficiency of this element in our center, the National Institute of Rehabilitation Luis Guilleremo Ibarra Ibarra, who, in addition, suffer from BPPV, as an extra to the conventional treatment with repositioning maneuvers. A better comprehension of the relationship between BPPV and other metabolic diseases will help to find innovative treatment strategies that decrease recurrences, generating a positive impact in the well-being of our patients by decreasing falls, fractures, hospitalizations, and expenses generated by work absenteeism.[19]

Patients and Methods

Thirty-four patients from both the otoneurology and otorhinolaringology departments the National Institute of Rehabilitation Luis Guillermo Ibarra Ibarra, in Mexico City with clinical diagnosis of BPPV using Dix-Hallpike or McClure maneuvers, were randomly chosen using Microsoft Excel (Microsoft Inc., Redmond, WA, USA) software. As inclusion criteria, patients had to have 25-hydroxyvitamin D deficiency (< 30 ng/ml) corroborated by laboratory blood tests. Sixty patients were recruited during 2 years, of which 2 had normal Vitamin D values, 9 were lost to follow-up, 5 were excluded for being diagnosed with osteoporosis and, therefore, were already under Ca^{2+} and vitamin D supplementation, 5 were excluded because of an abnormal videonistagmography (VNG), 2 with Meniere diagnosis and 1 with a cerebral vascular event diagnosis. Other exclusion criteria included paresis or preponderance of 25% in VNG, all diseases that cause vertigo other than BPPV, and patients with kidney diseases.

The patients were asked to fill in the Dizziness Handicap Inventory (DHI) during the time of diagnosis and again between 6 and 12 months after treatment. All patients signed the informed consent form and received the conventional repositioning maneuvers after diagnosis. After having their laboratory tests done for 25-hydroxyvitamin D and Ca^{2+} to identify any state of hypercalcemia which would exclude them, the patients were randomly separated into 2 groups: Group 1 was treated with a vitamin D supplement (Colecalciferol 1,600 U) with personalized dosage depending on their serum levels (►**Appendix A**), and group 2 was only treated with repositioning maneuvers.

All patients were informed of which foods are rich in vitamin D with a list recommended by a nutritionist, and received information on the importance of moderate sun exposure. Patients were asked to attend the emergency consultation if they presented a vertigo attack to have strict control of these episodes. In addition, all patients received monthly calls to track the number of episodes they had.

Table 1 Overall Comparisons

	Chi-squared	Standard deviation	Significance
Log Rank (Mantel-Cox)	5.697	1	.017

Equality test for distribution survival for the different levels of the protocol's status.

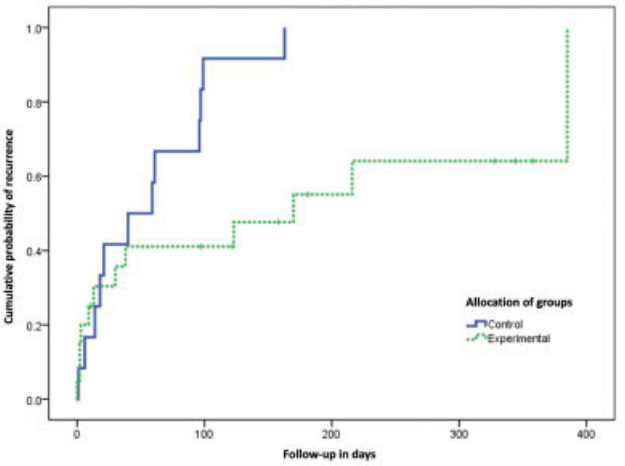

Fig. 1 Accumulated probability of recurrence per group.

Results

In the descriptive analysis of the independent variable (values of 25-hydroxyvitamin D), we observed a mean of 18.5 ng/ml with a standard deviation (SD) of 6.8 before treatment, which increased to a mean 26.2 ng/ml (SD 4.9) after repositioning. (►**Table 1**). The average age of our patients was 62 years old (SD 13 years old). Regarding gender, 88.3% of our patients were female. The mean number of vertigo episodes during the study (5 episodes), was the same in both the experimental and control groups, with a SD of 12, which was higher in the control group. The most affected canal was the posterior (98% of patients), while only 2 patients had canalolithiasis, and 1 had cupulolitiasis of the horizontal semicircular canal.

Only patients who perceived hearing loss, aural fullness or tinnitus were evaluated with audiometry; therefore, not all patients had this auxiliary test. The pure tone averages of both ears showed superficial to moderate hearing loss with a range from 27 to 36 dB. There were no notorious asymmetries (>10 dB) between both ears in the same patient.

A Kaplan-Meier graph was used to display the follow-up through time (in days) of both groups, with a minimum of 180 days (6 months) and a maximum of 400 days (13 months) as well as the probability of the patients of presenting a recurrence in the form of vertigo episodes. A log rank test was used in which the probability of recurrence between groups significantly differed ($p = 0.017$). (►**Fig. 1**)

From a total possible of 100 points, the mean score in the DHI before treatment was very similar in both groups, 55 ± 16 in the control group and 57 ± 18 in the experimental group. After the reposition of vitamin D, this index decreased to a mean of 10 ± 9 in the experimental group, while the mean of the control group changed to 36 ± 9.

Discussion

Similar to what is observed in the literature, our population with BPPV is composed mainly by senior women (88%) with a mean age of 61 years old, being the posterior semicircular canal the most affected (92% of cases).

With 25-hydroxyvitamin D repositioning, we were able to improve the levels of the patients to mild deficiency and, in most of them, to sufficiency, according to the post treatment mean levels of 26.2 ng/ml with a SD of 4.9. This confirmation of an adequate supplementation, without leading the patients to a toxic state, gives us a security range to establish this repositioning method as a safe and successful one, as established by Aguilar del Rey.[20]

There was a marked decrease in the DHI scores in the experimental group compared with the control group. This leads us to think that vitamin D plays a beneficial role in the perception of stability and physical, functional and emotional well-being of patients suffering from BPPV, independently of the number of episodes that they present. This may be attributed to the direct effect of this vitamin in the vestibule, by improving the mineralization of the otocinia, as was described by Jeong et al.[8] This theory is supported by the clinical stability demonstrated by the patients who had a vitamin D repositioning and absence of vertigo recurrences. The accumulated probability of presenting a recurrence was significantly lower ($p = 0.017$) in the treated group. This is similar to the results expressed by Sheikhzadeh et al. and Talaat et al., who observed absence of vertigo episodes during 6 months in the group treated with vitamin D plus reposition maneuvers ($p = 0.001$).[10]

A difference from the aforementioned studies was that most of our patients had a follow-up > 6 months, which could give more opportunity for recurrences to appear, due to the natural history of the disease, in which the possibility of new episodes duplicates each year.[9]

Additionally, patients perceived a sense of improvement demonstrated with the lower scores in the DHI, with a mean decrease of 47 points, which could be attributed to an indirect effect of vitamin D on muscular tone and balance derived from an improvement in the muscular skeletal system. Whichever is the targeted physiological and anatomical site of vitamin D (physiognomy of the otolith and\or muscular skeletal system), we observed the existence of a beneficial effect perceived by patients with BPPV after the elevation of this liposoluble vitamin. A weakness in our study was the difference in vestibular rehabilitation that was given by the different practitioners who saw our patients. All doctors work in the same hospital; however, each has different training and points of view in the rehabilitation treatment for BPPV.

It would be useful for future investigations to consider the different vestibular rehabilitation techniques and the number of repositioning maneuvers that the patients receive. In addition, it would be useful to continue with this protocol during a longer period to increase our sample size, allowing even more concise conclusions.

Conclusion

Plasmatic values of 25-hydroxyvitamin D have an impact in patients suffering from recurrent BPPV, who present an improved quality of life when their levels are improved with supplements of this vitamin. Benign paroxysmal positional vertigo is a disease that must not be considered as purely otologic. The reposition of vitamin D together with repositioning maneuvers should be given as a treatment in this type of vertigo. Moreover, more studies are needed to study this relationship in the long term ($>$ 2 years) to find a more proactive management for the prevention of recurrent episodes of vertigo, considering the equilibrium of disorders of bone replacement.

Conflict of Interests

The authors have no conflict of interests to declare.

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Appendix A Vitamin D Reposition

Patient serum 25/ hidroxyvitamin D levels	Dosage of vitamin D	Duration of treatment	Maintenance	Dosage per day Valmetrol pills 1600 UI
< **10 ng/ml**	180,000 UI	1 month	16,000 UI once a week	4 pills for 1 month 1.5 pills during 6 months
10-19 ng ml	16,000 UI	Once a week during 8-10 weeks	16,000 UI once a week	1.5 a day during 8-10 weeks 1.5 pill daily.
20-29 ng/ml	16,000 UI	Once a week during 5 weeks.	16,000 every 15 days during 5 weeks.	1.5 pills every day during 5 weeks. 1.5 pills every 15 days.

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