Vitamin D Supplementation for Benign Paroxysmal Positional Vertigo: A Systematic Review

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Objective: Benign paroxysmal positional vertigo (BPPV) is commonly attributed to displaced otoconia. These have been shown to have biomineralization close to that of bone, and vitamin D deficiency has been associated with BPPV. We aim to systematically review the available literature on vitamin D supplementation and BPPV intensity and recurrence in adults.
Databases Reviewed: PubMed, MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Current Controlled Trials, and ClinicalTrials.gov.
Methods: We systematically reviewed the available literature from 1947 to April 2020. The study protocol was registered in the PROSPERO database (trial registration: CRD42020183195).
Results: A total of 179 abstracts were identified and screened by two independent reviewers. Based on inclusion and exclusion criteria, six studies were selected and subjected to a quality assessment. In one randomized clinical trial (RCT), vitamin D supplementation was found to reduce annual recurrence rate of vertigo in patient with BPPV and subnormal serum vitamin D levels compared with placebo (odds ratio, 0.69; 95% confidence interval, 0.54–0.90). Non-RCTs demonstrated the possibility of a null effect in the random effects model (odds ratio, 0.08; 95% confidence interval, 0.00–1.56). The RCT considered as low risk of bias. All of the nonrandomized studies were assessed as serious risk of bias.
Conclusions: The intervention studies identified consistently demonstrated a decrease in BPPV recurrence with supplementation of vitamin D in patients with subnormal vitamin D levels. Although there is a paucity of high-quality studies, the present literature does highlight a role for optimization of vitamin D levels in patients with BPPV.
Key Words: Benign paroxysmal positional vertigo—Dizziness—Vertigo—Vitamin D deficiency—Vitamin D supplementation.

Otol Neurotol **43:**e704–e711, 2022.

INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is the most common neurootologic disorder, and accounts for nearly one-half of patients with peripheral vestibular dysfunction. BPPV has a lifetime prevalence of 2.4% (1). The prevalence of BPPV increases with age, and the elderly with BPPV are more likely to have reduced activities of daily living scores, to sustain falls, and to have depression (2).

BPPV is most commonly attributed to displaced otoconia from the utricular macula into the semicircular canals (3). Otoconia are made of a largely organic core of glycoproteins and a predominantly inorganic periphery of calcium carbonate (4). Otoconia forms within a low-calcium endolymph via an active, tightly controlled and ordered process (5). Recent studies have shown that biomineralization of otoconia has similarities to that of bone and teeth (6,7), and that bone metabolism has a connection to BPPV (8). Studies have shown an association between BPPV and osteoporosis (9), and animal studies have demonstrated dysfunctional otoconia formation in osteoporosis (10).

It has been shown that serum vitamin D levels are significantly lower in individuals with BPPV and that vitamin D deficiency is an independent risk factor for BPPV (11). As such, vitamin D supplementation may help prevent BPPV. Indeed, some studies have shown that vitamin D supplementation are associated with a reduction in the recurrence of BPPV (12,13). However, many studies have small sample sizes fail to achieve statistical significance to demonstrate causation. We aim to systematically review the available literature on vitamin D supplementation and BPPV intensity and recurrence. An understanding of the effects of vitamin D supplementation in BPPV will help inform treatment options and recommendations.

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L.C. and G.K. contributed equally to the article.
The authors disclose no conflicts of interest.
DOI: 10.1097/MAO.0000000000003586

METHODS

A systematic review of the literature was performed according to the recommendations of the Cochrane handbook (14). The review was reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (15). The study protocol was registered in the PROSPERO database (Trial Registration: CRD42020183195) in April 2020.

Study Selection

We engaged an experienced librarian to assist in developing the search strategy and conducting the literature search. A comprehensive search was conducted in electronic databases including MEDLINE (PubMed and OVID), EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Current Controlled Trials, ClinicalTrials.gov and relevant gray literature sources including abstracts and conference presentations. Results were limited to publications from inception to April 29, 2020.

Search Strategy and Eligibility Criteria

The search used a combination of controlled vocabulary and keywords to identify relevant studies, detailed in Appendix A of the electronic appendix. A search was conducted for ongoing and completed trials including the WHO trials registry platform. As well, we performed a review of bibliographies of included studies and relevant reviews. The MeSH terms/controlled vocabulary/keywords used included: "BPPV," "vitamin D," "cholecalciferol," and "vitamin D deficiency." Syntax was adjusted according to the needs of each database. Only papers in the English language were included. Studies were limited to investigations of human participants. Randomized, cohort studies, and case series of at least 10 participants were eligible for the study. Studies of adults (18 years of age and older) diagnosed with BPPV that evaluated the use of vitamin D supplementation as a treatment strategy were eligible for the review. The diagnostic criteria for BPPV were accepted as per the Barany society definition (1).

Two reviewers independently screened all retrieved records. Level 1 screening entailed a broad screen based on record titles and/or abstracts. A liberal accelerated process was adopted—one reviewer required to include a study, but two to exclude it. The full-text of all records passing Level 1 screening were retrieved for Level 2 screening. Level 2 screening confirmed final eligibility. Discrepancies were resolved by consensus or by involving a third team member. To be included, studies had to report quantitative data for at least one of the study's primary or secondary outcomes.

Data Extraction

Electronic data collection forms were implemented in Microsoft Excel using a standardized data extraction form. Two independent reviewers extracted trial details pertaining to the participants, vitamin D interventions, and results of BPPV outcomes. The primary outcome was the effect of vitamin D supplementation on BPPV recurrence. Other relevant outcomes were extracted, such as effect of vitamin D supplementation on BPPV intensity; effect of vitamin D supplementation on disease-specific quality of life measures among patients with BPPV; effect of vitamin D supplementation on general quality of life measures; adverse effects of vitamin D supplementation among patients with BPPV.

If studies reported results for an outcome at multiple time points during the intervention, the longest available data was extracted within the time points of interest for statistical analyses. For example, if a study reported data at 3, 4, and 6 months, we only extracted and analyzed the data for the 6-month follow-up. For an extension trial, if the initial treatment intervention was switched, we used the outcome data before that point. When a trial published multiple reports or follow-up points, we collected all reports into a single study and reported the data from the longest follow-up.

Risk of bias Assessment

Internal validity of study design and conduct was assessed by two reviewers independently. Discrepancies were resolved by consensus or by involving a third team member. Risk of bias was assessed using the Cochrane Collaboration's risk of bias tool for randomized clinical trials (RCTs) (RoB 2.0) and the Risk of Bias in Nonrandomized Studies-of Interventions (ROBINS-I) tool for non-RCTs. The Cochrane Collaboration's risk of bias tool for RCTs comprises five domains including random sequence generation, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of reported result. For each domain, an outcome of low, unclear, or high risk is recorded, then an overall risk of bias judgment is determined through the combination of all domains. The ROBINS-I tool assesses bias across six domains including confounding bias, participant selection, intervention classification, departure from intended interventions, missing data, measurement of outcomes, and selection of reported results. For each domain, an outcome of low, moderate, serious, critical, and no information for risk of bias is recorded. An overall risk of bias judgment is then determined through combination of all domains.

Data Synthesis

Study characteristics were summarized narratively. Study results were presented separately for each outcome. Study results extracted from the original publication were reported as mean outcomes, the numbers of participants experiencing an event or odds ratio. Trials were combined in a random-effects meta-analysis using R Studio Version 1.2.5019. A p value less than 0.05 was considered significant. The I^2 statistic was computed to assess statistical heterogeneity, with I^2 greater than 50% indicating significant heterogeneity. The Peto odds ratio methods was performed for zero cell counts, which can lead to bias in results (16). A subgroup analysis was performed to account for heterogeneity in study design.

RESULTS

Search Results and Study Characteristics

A flowchart of study retrieval and selection is provided in Fig. 1. One hundred seventy-eight (n = 178) records were identified through database searching and one (n = 1) through review of references, of which 51 records were duplicates. Title and abstract screening by two review authors led to the exclusion of noneligible articles (e.g., letters, conference abstracts where articles of completed studies were not available, studies where vitamin D supplementation and BPPV were not discussed, and non-English articles). The final results from a preliminary study were made available in the course of this systematic review (17). Only the final publication was included in the study analysis (18). Fifty-two studies of the 179 titles and abstracts were selected for full-text analysis. After reviewing articles in full-text, a total of six studies met our eligibility criteria and were included in the qualitative assessment, consisting of five non-RCTs (12,13,19–21) and one RCT (17).

The pertinent characteristics of the studies included in the review are illustrated in Table 1. The studies were published between 2013 and 2019. Among the five included

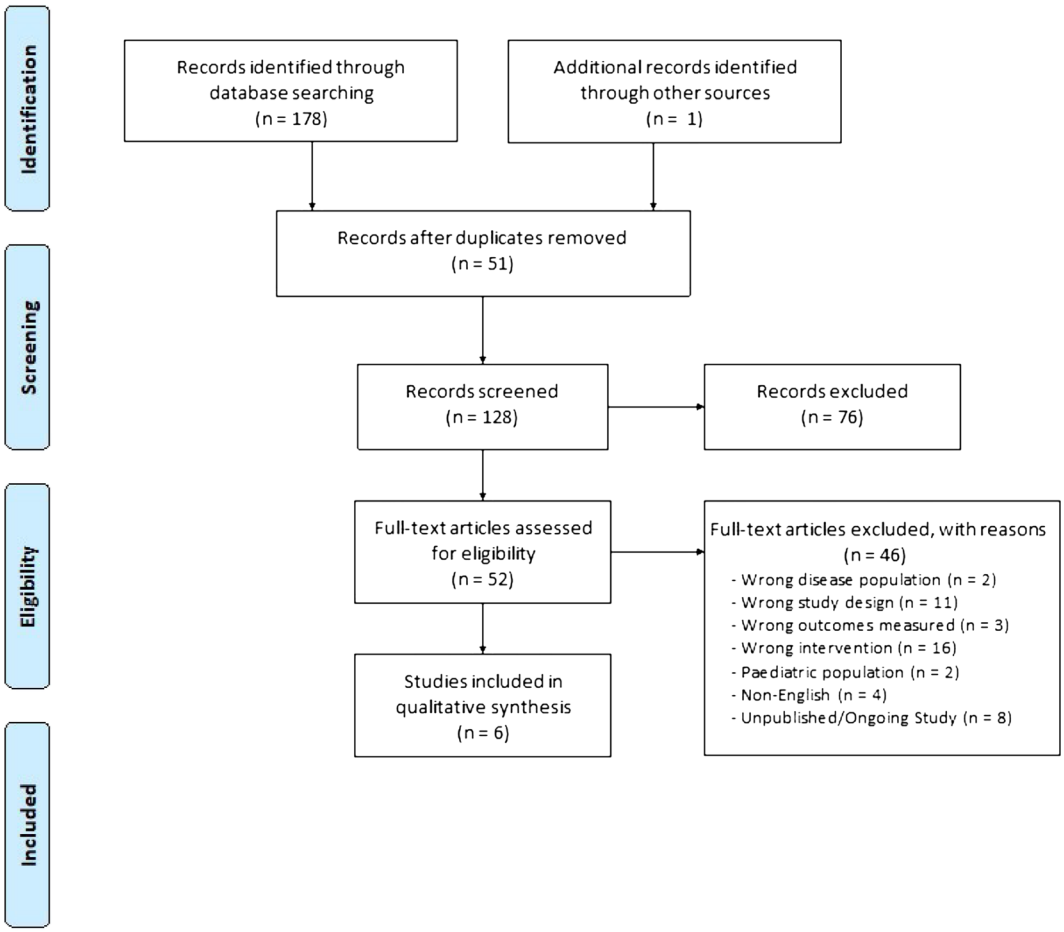

FIG. 1. PRISMA flow diagram. Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, the PRISMA group (2009). Preferred reporting items for systematic reviews and Meta-analyses: The PRISMA statement. BMJ [Internet] (15).

studies, a total of 1,320 participants were analyzed. Study sizes ranged from 10 to 1,050 participants; mean ages ranged from 50.4 to 67; and there was a female predominance in the participants. The details of the inclusion and exclusion criteria of participants in the included studies are summarized in eTable 1 under Appendix B of the electronic appendix. Study follow-up duration ranged from 6 to 18 months. Only three studies (12,18,19) specified the diagnostic criteria for BPPV used in the study inclusion criteria. Four of six studies reported outcomes for patients with recurrent BPPV, whereas two of six studies did not describe the historical details (first attack vs recurrent) of the participants

TABLE 1. *Baseline characteristics of included studies*

Author (Year)	Type of Study	Country	No. Participants	Mean Age	No. Females (%)	Follow-Up (mo)
Buki (2013)	Nonrandomized preintervention and postintervention trial	Austria	18 (10 of which with 25(OH) D < 20 ng/ml were treated)	67	11 (0.61)	8
Carneiro De Sousa (2019)	Nonrandomized controlled trial	Portugal	10	64	10 (1.0)	12
Jeong (2020)	Randomized controlled trial	South Korea	1,050	62.2 in TG; 61.6 in CG	283 (63.6) in TG; 333 (65.0) in CG	5.5 on average
Sheikhzadeh (2016)	Nonrandomized controlled trial	Iran	81 (assigned to three groups[a])	NR	45 (0.556)	6
Talaat (2016)	Nonrandomized controlled trial[b]	Saudi Arabia	93	50.4	51 (0.548)	18
Califano (2019)	Nonrandomized preintervention and postintervention trial	Italy	68	60.2	40 (0.588)	12

[a]Participants were assigned to three groups, each n = 27: 1) Treated group: vitamin D deficient, treated with vitamin D + rehabilitation; 2) Nontreated group: vitamin D deficient, treated only with rehabilitation 3) Control group: Normal vitamin D, treated only with rehabilitation.

[b]Groups were not assigned by investigators; all were supplemented with vitamin D. 28 participants who had elevation in serum Vit D3 level were allocated to subgroup 1, 65 with elevation <10 ng/ml were assigned to subgroup 2. In other words, allocation was based on whether or not participants were presumably compliant with vitamin D supplementation.

BPPV indicates benign paroxysmal positional vertigo; CG, control group; NR,ot reported; TG, treatment group.

TABLE 2. *Effect of vitamin D supplementation observed in included studies*

Author (Year)	Population	Intervention	Comparator	Mean 25(OH)D Level (ng/ml)	Mean 25(OH)D Level at Last Follow-up	Outcomes Reported
Buki (2013)	Adults with BPPV	Cholecalciferol (8,000 IU daily × 2 wk, 4,000 IU daily × next 2 wk, then 8,000 IU weekly) for patients with 25(OH)D levels under 20 ng/ml	Same group, pretreatment	23 (13.75 in with recurrent BPPV)	NR	No recurrence of BPPV
Carneiro De Sousa (2019)	Adults with at least two episodes of BPPV in the previous 2 yr requiring emergency care	Cholecalciferol (5,000 IU daily if deficiency; 800 IU daily if insufficiency)	No supplementation	13.6 (TG: 14; CG: 13.2)	35.2 for TG; no data on CG	No recurrence of BPPV in TG compared with persistent episodes in CG needing emergency care and chronic dizziness complaints
Jeong (2020)	BPPV with subnormal serum vitamin D levels	Oral administration of vitamin D 400 IU and 500 mg of calcium carbonate twice a day	No supplementation	13.3 in TG; no data on CG	24.2 in TG; no data on CG	Reduced annual recurrence rate in TG compared with CG (0.83 vs 1.10 recurrences per 1 person-year; incident rate ratio 0.76; absolute rate ratio −0.27, NNT 3.70)Proportion with BPPV recurrence was lower in TG compared with CG (37.8% vs 46.7%, $p = 0.005$)
Sheikhzadeh (2016)	BPPV with at least 2 attacks over 6 mo, and with vitamin D deficiency	Cholecalciferol (50,000 IU weekly × 2 mo, then 50,000 IU monthly × 6 mo) + Epley maneuver	Epley maneuver	11.4 in TG, 10.7 in non-TG, 33.8 in CG	35.5 for TG; 11.1 in non-TG, 36.2 in CG	VAS scores (where 0 indicated no vertigo and 10 indicated severe attacks of vertigo) significantly improved from baseline in TG (7±1.3 vs 0.22± 0.42) and CG (6.8 ± 1.01 vs 0.3 ± 0.82) compared with non-TG (7.22 ± 1.01 vs 6.9 ± 0.94)
Talaat (2016)	Unilateral, idiopathic, posterior canal BPPV with 25-OH D3 level ≤10 ng/ml	"Subgroup (SG) I": cholecalciferol (50,000 IU three times a week × 1 mo, then 50,000 IU once every 2 wk) + Calcium citrate 600 mg twice daily	"Subgroup II": Same treatment as Subgroup I, but participants were found to have vitamin D3 increase <10, and assumed noncompliant	6.8 (6.7 in SG I, 68 in SG II)	28.3 in SG I; 8.7 in SG II	SG I with fewer subjects with recurrence (4 vs 28), less attacks of recurrence (5 vs. 43) and less attack/subject ratio (0.18 in text/0.28 in table vs 0.66). OR for development of recurrence in subjects with severe Vit D deficiency—4.54
Califano (2019)	Adults with BPPV	10,000 to 50,000 IU weekly, in relation to the laboratory data, with the overall limit of 600,000 IU in a year	Same group, pretreatment	18.2	NR	Reduced annual recurrence (14 vs. 74) rate compared with pretreatment of hypovitaminosis D

BPPV indicates benign paroxysmal positional vertigo; CG, control group; IU, International Units; non-TG = nontreated group; NR, not reported; NNT, number needed to treat; OR, odds ratio; TG, treated group; VAS, visual analog score.

with BPPV. All studies included participants with BPPV and vitamin D insufficiency or deficiency. Only one study specified outcomes for patients with posterior canal BPPV (20). Vitamin D supplementation varied from 800 international units (IU) daily to 50,000 IU weekly. The characteristics of the study population, interventions and outcomes were summarized in Table 2.

Three studies (18–20) reviewed the effects of vitamin D supplementation on BPPV episode recurrence rates in 1,060 patients with BPPV. The studies were heterogenous in their study design and duration of treatment (12–18 mo). Vitamin D supplementation was associated with a significant decrease in odds of BPPV recurrence in the single RCT (odds ratio [OR], 0.69; 95% confidence interval [CI], 0.54–0.90; Fig. 2A). (18) The meta-analysis of non-RCTs demonstrated the possibility of a null effect in the random effects model (OR, 0.08; 95% CI, 0.00–1.56; Fig. 2B). Talaat et al. (20) investigated the effects of vitamin D supplementation in 93 men and women with BPPV and reported a subgroup analysis according to degree of improvement in serum vitamin D3 levels. Treatment for all patients consisted of three times a week 50,000 IU for 1 month, then once every 2 weeks 50,000 IU, as well as Calcium citrate 600 mg twice daily. Participants were stratified according to improvement in serum vitamin D3 level by greater than 10 ng/ml and participants that were observed to have an improvement in vitamin D3 levels less than 10 ng/ml, which were implied to have had poor compliance with vitamin D supplementation. The authors reported that the group compliant with vitamin D supplementation, that is, the subgroup that demonstrated an elevation in serum vitamin D3 level greater than 10 ng/ml, had fewer subjects with recurrence, less attacks of recurrence, and less attack/subject ratio. By contrast, the participants in the study from de Sousa et al. (16) were limited to 10 female patients with vitamin D deficiency. The treatment group received 5,000 IU of vitamin D per day for vitamin D deficiency and 800 IU of vitamin D per month for vitamin D insufficiency.

Two uncontrolled preintervention and postintervention trials (Fig. 2C) (12,21) demonstrated a reduction of BPPV episodes in 144 patients treated for vitamin D deficiency in a random effects model (OR, 0.14; 95% CI, 0.01–1.46).

Only one non-RCT (13) reported on clinical symptom scores associated with BPPV intensity in participants that received treatment for vitamin D deficiency. Participants with recurrent BPPV were assigned to three groups according to their vitamin D levels: 1) patients with subnormal vitamin D levels that received vitamin D supplementation, as well as the Epley maneuver; 2) patients with subnormal vitamin D levels treated with only Epley maneuver; and 3) patients with normal vitamin D levels treated with only Epley maneuver. The authors found that the deficient BPPV participants treated with vitamin D supplementation and Epley maneuvers had a significant improvement in visual analog scores from baseline (7 versus 0.2) as compared with deficient BPPV participants that received Epley alone (7 versus 6.9), and BPPV patients without vitamin D deficiency that received Epley alone (7 vs. 0.3).

No studies reported outcomes from effect of vitamin D supplementation on general quality of life, nor did any studies report outcomes according to disease-specific or generic quality of life measures. No studies reported on adverse effects of vitamin D supplementation among patients with BPPV.

Risk of Bias

The results of the risk of bias assessment can be found in Table 3. The study presented by Jeong et al. in 2020 (18) was the only RCT to be assessed by RoB 2.0 tool. It was

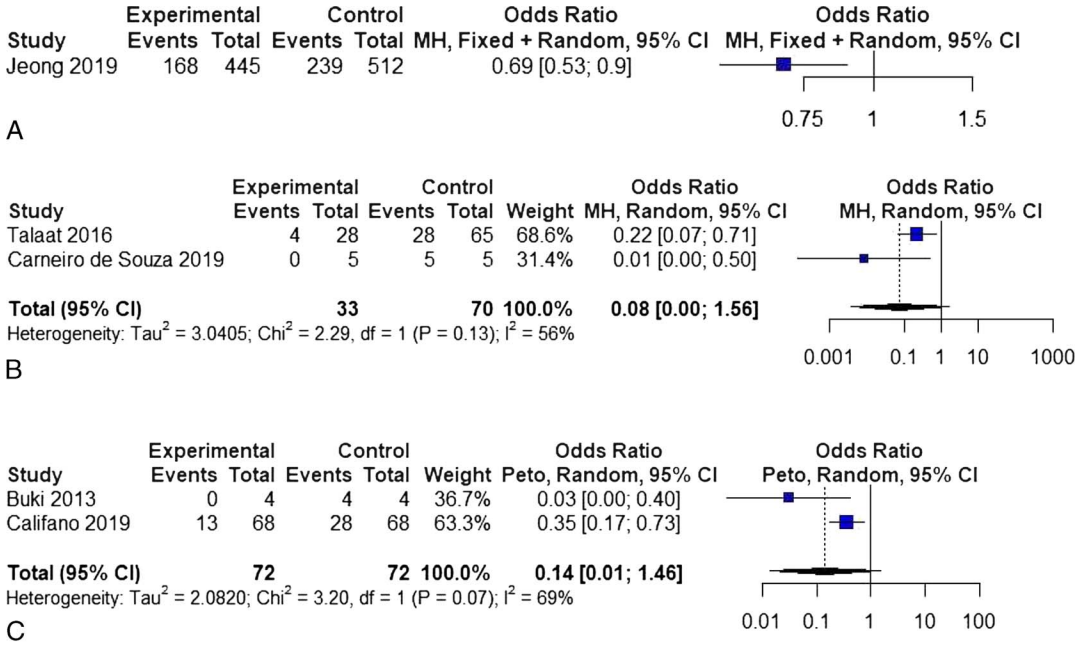

FIG. 2. Forest plot comparison of vitamin D supplementation in preventing recurrences of BPPV by study design *A*, RCT *B*, nonrandomized intervention trials *C*, preintervention and postintervention studies. RCT indicates randomized clinical trial.

the only study to be considered as low risk of bias in the overall evaluation. The study was classified as low risk of bias in all five domains evaluated. The remaining controlled trials were nonrandomized, and were assessed by ROBINS-I tool. All nonrandomized studies were classified as moderate risk for bias because of confounding, two studies were classified as low risk for bias in participant selection, whereas the other three were classified as moderate risk. Considering bias in classification of interventions all but one study was classified as serious risk of bias. Two of the nonrandomized studies had no information regarding missing data. None of the nonrandomized studies reported an intention-to-treat analysis. None of the nonrandomized studies provided information regarding a prespecified analysis plan. Overall, the reporting of all nonrandomized studies was very poor. All of the nonrandomized studies presented at least one domain judged as moderate risk, and at least three domains judged as not interpretable. All of the nonrandomized studies were considered as serious risk of bias.

DISCUSSION

This study provides an overview of the current body of literature investigating the supplementation of vitamin D in BPPV patients with and without vitamin D deficiency. The clinical trials identified in this systematic review consistently demonstrated a decrease in BPPV recurrence and improvement in clinical symptom scores with supplementation of vitamin D in patients with subnormal vitamin D levels. Of note, significant improvement in outcomes for patients with BPPV was observed irrespective of dosing regimens for vitamin D therapy. The results from Talaat et al. (20) would suggest that clinicians should target an improvement in vitamin D3 of >10 ng/ml for greater benefit in BPPV outcomes. When used in conjunction with rehabilitation, vitamin D supplementation demonstrated a notable long-term beneficial effect in vitamin D-deficient patients with BPPV as compared with using rehabilitation alone (13). We recommend testing patients with BPPV for serum vitamin D levels, and treating patients with vitamin D insufficiency or deficiency, with follow-up in measurements of serum vitamin D to ensure return to normalcy.

The studies included in this systematic review were limited by study design. The majority of the identified interventional studies demonstrated high risk of bias, predominantly because of nonrandomized study design. Diagnostic criteria for BPPV was not specified in any of the intervention studies identified. Of note, three studies were published after publication of the consensus statement on the diagnostic criteria for BPPV from the Barany Society (1), that is, Carneiro de Sousa et al. (19), Califano et al. (21), and Jeong et al. (18), failed to reference the statement in the selection of the study population of the trial. As the details of the diagnostic criteria for the study population were unclear in the majority of the identified studies, it is possible that the study population may not wholly represent the target population. Although half of the studies (19–21) reported outcomes at 12 months or longer, the other half included reported out-

TABLE 3. *Risk of bias assessment of randomized and non-RCTs*

RCTs	Random Sequence Generation	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall		
Jeong (2020)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk		
Nonrandomized Clinical Trials	Bias because of confounding	Bias in participant selection	Bias in classification of interventions	Bias because of departures from intended interventions	Bias because of missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
Carneiro de Souza (2019)	Moderate risk	Low risk	Serious risk	Not interpretable	Low risk	Not interpretable	Not interpretable	Serious risk
Sheikhzadeh (2016)	Moderate risk	Moderate risk	Moderate risk	Not interpretable	Low risk	Not interpretable	Not interpretable	Serious risk
Talaat (2016)	Moderate risk	Moderate risk	Serious risk	Not interpretable	Low risk	Not interpretable	Not interpretable	Serious risk
Buki (2013)	Moderate risk	Moderate risk	Serious risk	Not interpretable	Not interpretable	Not interpretable	Not interpretable	Serious risk
Califano (2019)	Moderate risk	Low risk	Serious risk	Not interpretable	Not interpretable	Not interpretable	Not interpretable	Serious risk

Risk of bias assessment was performed using the Cochrane Collaboration's risk of bias tool for RCTs. Each domain was classified as either unclear, low or high risk. The ROBINS-I tool was used for nonrandomized clinical trials. Each domain was classified as low risk, moderate risk, serious risk, and critical risk or not interpretable. An overall bias assessment was then made using the same scale.

RCT indicates randomized clinical trial; ROBINS-I, Risk of Bias in nonrandomized studies-of interventions

comes at less than 12 months or did not report duration of follow-up. As a chronic disease, adequate follow-up of BPPV is necessary to adequately evaluate response to therapy. Of note, the authors included BPPV episode recurrence rates from one study (13) that were not included in the published article. We attempted to contact the authors of the original study but did not receive a response.

At the time that this study was initiated, no other systematic reviews on this topic were registered or published. However, during the course of this study, a systematic review from Jeong et al. (22) was published that suggested that vitamin D supplementation could provide a benefit in risk reduction against recurrences of BPPV. The study had a clear objective and was reported according to the PRISMA guidelines, and provided an insightful discussion with a focus on the biochemistry of otoconia and endolymph and vestibular organ physiology in relation to calcium and vitamin D. The Jeong et al. review drew similar conclusions to our study recommending vitamin D supplementation in patients with BPPV. This study does however demonstrate important limitations. First, the study failed to include the study from Büki et al. (12) in the meta-analysis. Second, the study conclusions were drawn from a meta-analysis of a randomized controlled trial, nonrandomized controlled trials, and preintervention and postintervention studies. The authors did not account for differences in study design integrating the study results or the risk of correlated outcomes in preintervention and postintervention studies. As a result, the overall risk ratios by either the fixed or random-effects models as determined by this study may be misleading and likely skewed by combining the analysis of studies of very different designs, in particular, the randomized controlled trial. This is evident in sensitivity analysis performed by the authors that demonstrate significant heterogeneity in the study (88%) and found that this heterogeneity was decreased after exclusion of the RCT. In contrast, our review compared included studies according to their study designs (Fig. 2).

In implementing our search strategy and study design, as per the Cochrane handbook and reporting the results according to the PRISMA guidelines, we were able to effectively appraise the individual studies. As we used a strict methodologic strategy in our review design, our systematic review was limited to six studies. We excluded four studies that were not published in the English literature, which has the potential to exclude relevant data. Despite these limitations, we are able to conclude that this study provided a substantial overview of the current literature related to vitamin D supplementation in BPPV.

It would be prudent for future studies to use standardized diagnostic criteria for BPPV as outlined by the Barany Society (1). Of note, the study presented by Sheikhzadeh et al., Talaat et al., and Califano et al. did not seem to use a confirmatory nystagmus test as an inclusion criterion for participants to their studies (eTable 1). There is also a need for more robust and higher quality studies to make strong recommendations regarding vitamin D supplementation in BPPV, including standardized dosing and appropriate treatment regimens for patients with BPPV. Reporting the effect of vitamin D supplementation on disease-specific or generic quality of life measures, as well as long-term studies on adverse effects of vitamin D supplementation, would further direct guidelines on vitamin D supplementation in BPPV. Cost-effectiveness analyses would provide additional insight into socioeconomic benefits of vitamin D supplementation before becoming standard of care for BPPV patients.

Finally, it would be of interest for future studies to control for the potentially confounding variables and investigate the extent to which optimization of vitamin D has a role in reducing the frequency of BPPV in certain sub-populations of BPPV. First, it would be of interest to study the extent to which vitamin D optimization is effective for BPPV successfully treated with repositioning maneuvers at time of initiation of vitamin D therapy, versus BPPV not yet resolved at time of initiation of vitamin D therapy. Of note, Büki et al., Carneiro et al. and Jeong et al. had specified successful repositioning as an inclusion criterion to their study, but not for Sheikhzadeh et al., Talaat et al., or Califano et al. (eTable 1). Second, seasonal variations would be important to control for, and consideration should be made for BPPV occurrences during different seasons with different sun exposures, particularly in cases of short follow-up studies. No studies included in this review had studied seasonal variations. Third, the distinction between BPPV secondary to head-trauma versus nonhead trauma and the extent to which vitamin D optimization is effective for both groups would be interesting to study. In this review, we note that Sheikhazadeh et al., Talaat et al. and Califano et al. had excluded head-trauma–related BPPV, but Büki et al., Carneiro de Sousa et al. and Jeong et al. did not specify this (eTable 1).

CONCLUSION

This study provides a review of the current literature regarding the role of vitamin D supplementation in patients diagnosed with BPPV. This review identified a significant paucity of high-quality RCTs and highlighted the low quality of the current evidence. Nevertheless, the present literature does highlight a role for optimization of vitamin D levels in patients with BPPV. Given the evidence demonstrating significant effect of vitamin D therapy to reduce frequency of BPPV episodes and improve quality of life, it would beneficial for clinicians to consider investigating for and treating vitamin D deficiency in patients with BPPV.

Acknowledgments: The authors would like to thank Risa Shorr of The Ottawa Hospital Library Services for assistance in the preparation and execution of the search algorithm for this systematic review.

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