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Original Article

Effect of calcium and vitamin D supplementation on recurrence of benign paroxysmal positional vertigo in osteoporotic patients

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Abstract: Objective: To investigate whether calcium and vitamin D supplementation can reduce the recurrence of benign paroxysmal positional vertigo (BPPV) and improve quality of life in patients with osteoporosis. Methods: In this retrospective study, 334 patients with primary osteoporosis and posterior semicircular canal BPPV were included and divided into three groups based on treatment: Group A (n = 103; intravenous calcium gluconate infusion [20 mL diluted in 250 mL 5% glucose per day for 15 days per course, four courses total]), Group B (n = 112; intramuscular injection of vitamin D_2, 150,000 IU every 15 days for two doses, then monthly for two additional doses over 3 months), and Group C (n = 119; supplementation with both calcium and vitamin D_2 using the protocols of Group A and B). Dizziness Handicap Inventory (DHI) scores, BPPV recurrence, serum calcium and vitamin D levels, bone turnover markers, adverse effects, and Short Form Health Survey (SF-36) quality-of-life scores were compared among the groups. Results: At 6 months post-treatment, DHI scores were 40.57 ± 3.67 in Group A, 41.25 ± 4.11 in Group B, and 32.63 ± 2.11 in Group C. The score in Group C was significantly lower than those in Groups A and B ($P < 0.001$), while Groups A and B showed comparable scores ($P = 0.2991$). Additionally, Group C exhibited a significantly lower BPPV recurrence rate at 12 months post-treatment ($P = 0.030$ vs. Group A; $P = 0.021$ vs. Group B) and 24 months post-treatment ($P = 0.016$ vs. Group A; $P = 0.017$ vs. Group B). Serum calcium ($P < 0.001$ vs. both Groups A and B) and vitamin D levels ($P = 0.0191$ vs. Group A; $P = 0.0423$ vs. Group B) were significantly higher in Group C compared with the other two groups. Moreover, Group C showed improved bone metabolism, as indicated by higher procollagen type I N-terminal propeptide (P1NP) levels ($P < 0.05$) and lower beta-crosslaps (β-CTX) levels ($P < 0.05$) than the other two groups. Quality-of-life scores were significantly improved in Group C across several domains, including physical functioning, role-physical, role-emotional, mental health, and social functioning (all $P < 0.001$). Notably, adverse effects were comparable among the groups (all $P > 0.05$, Fisher's exact test). Conclusion: Combined calcium and vitamin D supplementation may reduce BPPV recurrence and improve quality of life in patients with osteoporosis.

Keywords: Calcium, vitamin D, recurrence rate, benign paroxysmal positional vertigo, primary osteoporosis

Introduction

Benign paroxysmal positional vertigo (BPPV) is one of the most common peripheral vestibular disorders a with high prevalence among patients with vertigo. Patients may experience sudden and intense dizziness during head movements, such as rolling over, tilting the head backward, or bending forward [1]. The pathogenesis is primarily associated with calcium carbonate particles originating from the utricle, which enter the semicircular canals and stimulate hair cells within the canals, leading to vertigo, dizziness, or nystagmus [2]. The overall incidence of BPPV is approximately 2.4%, with a preference in the elderly population; For

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people aged ≥ 70 years, the incidence can be as high as 10% [3, 4]. BPPV is clinically significant not only because it is common, but also because it substantially impacts patients' quality of life, activities of daily living, and mental health [5]. Furthermore, BPPV exhibits a high recurrence rate, particularly among patients with osteoporosis. Consequently, further investigation into the pathogenesis of BPPV and the exploration of effective prevention strategies are warranted [6].

Osteoporosis is a systemic skeletal disorder characterized by reduced bone mass and impaired bone microarchitecture, leading to increased bone fragility and an elevated fracture risk. The disease reflects an imbalance between bone resorption and formation, manifested by increased osteoclast activity and decreased osteoblast activity [7, 8]. Osteoporosis most commonly affects postmenopausal women, primarily due to estrogen deficiency, though it can also occur in elderly men. Some patients develop the condition due to secondary factors such as long-term glucocorticoid therapy or endocrine disorders [9, 10]. Both osteoporosis and BPPV are age-related conditions that frequently coexist in the same patient. Primary osteoporosis has been recognized as an independent risk factor for BPPV, suggesting a potential link between systemic calcium metabolism abnormalities and vestibular dysfunction [11, 12].

Otoconia are composed of calcium carbonate crystals embedded in a protein matrix, and tis structural stability relies on optimal calcium homeostasis within the inner ear. Experimental and clinical evidence indicates that vitamin D deficiency and calcium metabolism disorders can compromise otolith integrity and promote detachment, thereby increasing the risk of recurrent BPPV episodes [13]. Osteoporosis represents a state of systemic calcium loss, which may further compromise otolith stability, leading to more frequent vertigo episodes. A clinical study by Miśkiewicz-Orczyk et al. reported significantly higher BPPV recurrence rates in osteoporotic patients compared with healthy controls, further supporting the association between bone health and inner ear function [14]. Recent evidence indicates that correcting vitamin D deficiency can effectively reduce BPPV recurrence. For example, Jeong et al. reported that vitamin D supplementation markedly reduced the BPPV recurrence rate [15]. Similar conclusions were drawn by Chua et al. and Lin et al., with both studies reporting improved vestibular function after vitamin D supplementation [16, 17]. However, most of these studies did not specifically focus on patients with osteoporosis, and there is a lack of systematic comparisons among calcium supplementation alone, vitamin D supplementation alone, and combined therapy.

Calcium and vitamin D play crucial roles in bone health and are commonly used as foundational treatments for osteoporosis in clinical practice. Calcium helps maintain bone density and participates in various important physiological functions, while vitamin D enhances intestinal calcium absorption and maintains stable serum calcium and phosphorus levels, which are essential for normal bone formation [18]. Clinical guidelines recommend calcium and vitamin D supplementation to slow the progression of osteoporosis. Although canalith repositioning remains the primary treatment for acute BPPV, effective management of risk factors such as osteoporosis is equally important for preventing recurrence. As fundamental components of osteoporosis treatment, the efficacy of different calcium and vitamin D supplementation regimens in reducing BPPV recurrence among patients with osteoporosis remains unclear. Therefore, this study compared the effects of calcium supplementation alone, vitamin D supplementation alone, and combined supplementation on recurrence rates and quality of life in patients with primary osteoporosis complicated by BPPV, aiming to provide evidence for clinical prevention and treatment strategies.

Materials and methods

Patient selection criteria

Inclusion Criteria: (1) Age ≥ 50 years; (2) A confirmed diagnosis of primary osteoporosis, based on a bone mineral density (BMD) T-score ≤ -2.5 or a documented clinical diagnosis; (3) Posterior semicircular canal BPPV (PSC-BPPV) diagnosed by an otolaryngologist/or neurologist based on typical symptoms and a positive Dix-Hallpike test [19]; (4) Voluntary agreement to undergo one of the predefined supplementation protocols; (5) Ability to complete at least 24 months of follow-up, including scheduled

assessments such as the Dizziness Handicap Inventory (DHI), Short Form Health Survey (SF-36), and routine laboratory tests.

Exclusion Criteria: (1) Secondary osteoporosis or secondary BPPV (e.g., hyperparathyroidism, chronic kidney disease, thyroid dysfunction, vestibular neuritis, head trauma, uncontrolled hypertension); (2) Intolerance of, or contraindication to, calcium or vitamin D supplements; (3) Current use of other anti-osteoporosis agents (e.g., bisphosphonates, calcitonin, denosumab).

Study design and patient grouping

This retrospective study analyzed clinical data from 334 patients diagnosed with primary osteoporosis and posterior semicircular canal BPPV who were treated at The Third Affiliated Hospital of Southern Medical University between January 2021 and December 2023. All patients received cabaseline standard treatment and were additionally assigned to one of three supplementation strategies in routine care. Patients were not prospectively randomized; treatment selection was determined by clinicians during routine care based on factors such as serum vitamin D levels, calcium levels, medication tolerance, or clinical judgment. Patients were retrospectively divided into three groups according to the regimen they received. Group A (Calcium Supplementation Group, n = 103): Intravenous calcium gluconate infusion (20 mL diluted in 250 mL 5% glucose per day for 15 days per course, four courses total); Group B (Vitamin D Supplementation Group, n = 112): Intramuscular vitamin D_2 injection at 150,000 IU every 15 days for two doses, then monthly × 2 for three months. Group C (Calcium + Vitamin D Group, n = 119): A combination of both treatment regimens. Although treatment types differed, all regimens adhered to the hospital's standardized protocols regarding dosage and frequency, which ensured clinical consistency. As this retrospective analysis did not involve sample size calculation, the sample size was determined by the total number of patients who met the inclusion and exclusion criteria and received one of the three standardized supplementation regimens during the study period (n = 334). This study was approved by Ethics Committee of the Third Affiliated Hospital of Southern Medical University, and informed consent was waived due to the retrospective nature of data collection. All patient data were fully anonymized prior to analysis.

Treatment protocols

All enrolled patients received the following standard treatment. The three study groups (A, B, C) differed in the additional supplementation provided on top of this standard regimen.

Standard treatment: Oral calcium vitamin D3 tablets (Pfizer Pharmaceuticals Co., Ltd., National Drug Approval No. H10950029) were administered at 600 mg per day for a duration of 30 days per cycle. The treatment was extended to three consecutive courses if no hypercalcemia or hepatic/renal impairment occurred during treatment.

Epley Maneuver for Canalith Repositioning was applied exclusively to patients diagnosed with PSC-BPPV. The patient was placed on the treatment bed with their head rotated 45° toward the affected side. The healthcare provider then swiftly assisted the patient into a supine position, with the head hanging over the edge of the bed. The head was then rotated 90° towards the healthy side, followed by a continuation of the head's movement with the body to further rotate 90° towards the healthy side, allowing the patient lying on their side on the treatment bed with the head rotated 135° from the supine position. Finally, the patient was assisted to return to a sitting position, completing one treatment cycle. Each position was maintained for at least 30-60 seconds or until nystagmus subsided. The entire treatment process was repeated until the absence of dizziness or nystagmus in any position, followed by additional 2-3 cycles performed thereafter. The same repositioning procedure was repeated in patients who experienced recurrence during follow-up.

Calcium supplementation group: In addition to standard treatment, patients received intravenous infusion therapy with calcium gluconate injection (Shandong Xinhua Pharmaceuticals Co., Ltd., National Drug Approval No. H37020733; 20 mL diluted in 250 mL of 5% glucose solution). Each treatment course consisted of a 15-day continuous infusion, followed by a 15-day drug-free interval. Four such courses were administered, resulting in a total treatment period of 120 days (approximately 4

months). This regimen was consistent across all patients in this group as per hospital protocol.

Vitamin D supplementation group: In addition to standard management, patients in this group received intramuscular injections of vitamin D_2 (Jiangxi Gannan Hexin Pharmaceuticals Co., Ltd., National Drug Approval No. H20054433). 150,000 IU was administered intramuscularly every 15 days for the first two doses, followed by monthly injections for the subsequent two doses. A total of four doses were given over approximately 90 days (about 3 months). This schedule aligns with routine clinical practice at the Third Affiliated Hospital of Southern Medical University. Since the standard formulation of vitamin D_2 is 300,000 IU per vial, half a vial was used per injection.

Combined calcium and vitamin D supplementation group: Patients in this group received both intravenous calcium supplementation and intramuscular vitamin D_2 injections, in addition to the routine treatment described earlier. Specifically, calcium gluconate (20 mL diluted in 250 mL of 5% glucose): a 15-day continuous infusion per course, with a 15-day interval between courses, for a total of four courses. Vitamin D_2 was administered at the same dosage as described for the vitamin D group: 150,000 IU every 15 days for the first two injections, then monthly for another two doses. All patients in this group followed the same protocol, in line with the hospital's treatment standards.

Dizziness handicap inventory (DHI)

The Dizziness handicap inventory (DHI) was used to evaluate the impact of dizziness on patients' daily lives [20]. This 25-item scale covers three dimensions, including physical, emotional, and functional aspects. Each item is rated on a three-point scale, with higher scores indicating more severe functional impairment. The DHI ranges from 0 to 100 points, where higher scores reflect more severe negative impacts of dizziness on patients' lives. In this study, DHI was measured at baseline and at 6 months post-treatment initiation.

Assessment of bone metabolism markers

Bone metabolism markers are routinely used in clinical practice to assess bone metabolic status in osteoporotic patients. Fasting venous blood samples were collected at baseline and at the 24-month follow-up to assess bone metabolism. Bone formation was evaluated by measuring serum Procollagen Type I N-Terminal Propeptide (P1NP), and bone resorption was evaluated by measuring serum Beta-CrossLaps (β-CTX). Analyses were performed using electrochemiluminescence immunoassays on a Cobas e801 analyzer (Roche Diagnostics), in accordance with the manufacturer's instructions.

Quality of life assessment

Health-related quality of life was assessed using the Short Form-36 (SF-36) survey. This well-validated instrument encompasses several dimensions of physical and mental health [21]. The domains analyzed in this study included physical functioning, role limitations due to physical health, emotional well-being, cognitive function, and social participation. A higher score indicates better quality of life. In this study, the SF-36 questionnaire demonstrated good internal consistency with a Cronbach's alpha value of 0.814. Patients completed the SF-36 questionnaire at the conclusion of the 24-month follow-up period.

Statistical methods

Statistical analyses were performed using SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) and compared among groups using one-way ANOVA or Welch's ANOVA (when variances were unequal, as determined by Levene's test) followed with post-hoc Tukey's test. Categorical variables were presented as frequencies and percentages and compared using chi-square tests or Fisher's exact tests, as appropriate. In addition, multivariate linear regression for continuous outcomes (e.g., DHI score changes and SF-36 scores) and logistic regression for binary outcomes (e.g., BPPV recurrence at each time point) were conducted to account for potential confounding factors-such as age, gender, baseline serum calcium and vitamin D levels. Due to lack of information on dietary calcium intake, sunlight exposure, and other anti-osteoporosis medications, these variables were not adjusted in the analysis. All statistical tests were two-sided with a significance threshold of $P < 0.05$.

Table 1. Comparison of baseline characteristics among the three groups

Parameter	Group A (n = 103)	Group B (n = 112)	Group C (n = 119)	F (Overall)	*P* (Overall)
Age (years)	67.23 ± 4.61	66.52 ± 5.24	67.12 ± 4.84	0.669	0.513
Sex (Male/Female)	32/71	35/77	38/81	0.022	0.989
BMI (kg/m^2)	25.12 ± 2.33	24.99 ± 1.91	25.13 ± 1.76	0.170	0.844
BMD (g/cm^2)	0.78 ± 0.12	0.79 ± 0.11	0.77 ± 0.13	1.007	0.366
Disease Duration (years)	4.12 ± 1.05	3.98 ± 1.23	4.07 ± 1.82	0.250	0.779
Serum Calcium (mg/dL)	7.11 ± 3.06	7.08 ± 3.07	7.09 ± 3.64	0.002	0.998
Vitamin D (ng/mL)	19.11 ± 3.25	19.26 ± 4.75	18.65 ± 3.88	0.707	0.494
PTH (pg/mL)	9.19 ± 4.22	8.89 ± 3.17	9.08 ± 3.61	0.180	0.835

Note: Vitamin D levels were measured as 25-hydroxyvitamin D (25(OH)D). Group A: calcium supplementation; Group B: vitamin D supplementation; Group C: calcium + vitamin D supplementation; BMI: body mass index; BMD: bone mineral density; PTH: parathyroid hormone.

Table 2. Comparison of DHI scores among groups before and 6 months after treatment

Timepoint	Group A (n = 103)	Group B (n = 112)	Group C (n = 119)	F (Overall)	P (Overall)	P (A vs B)	P (A vs C)	P (B vs C)
Before treatment	60.23 ± 5.48	59.78 ± 6.12	61.11 ± 6.37	1.459	0.2341	0.8482	0.5242	0.2160
After treatment	40.57 ± 3.67	41.25 ± 4.11	32.63 ± 2.11	316.1	< 0.001	0.2991	< 0.001	< 0.001
Δ Value (Post-Pre)	-19.66 ± 4.90	-18.53 ± 6.48	-28.48 ± 6.10	68.86	< 0.001	0.4665	< 0.001	< 0.001

Note: Group A: calcium supplementation; Group B: vitamin D supplementation; Group C: calcium + vitamin D supplementation; DHI: Dizziness Handicap Inventory.

Results

Comparison of baseline characteristics among groups

Analysis of baseline characteristics showed no significant differences among groups in terms of age, gender distribution, body mass index (BMI), bone mineral density (BMD), disease duration, serum calcium level, vitamin D levels, or PTH levels (all P > 0.05), indicating comparability among groups for evaluating treatment outcomes in BPPV patients with primary osteoporosis (**Table 1**).

Comparison of DHI scores among groups before and 6 months after treatment

Before treatment, the mean DHI scores in the A, B, and C groups were 60.23 ± 5.48, 59.78 ± 6.12, and 61.11 ± 6.37, respectively, with no significant difference among groups (P = 0.2341).

After 6 months of treatment, DHI scores decreased in all three groups, with Group C demonstrating the lowest DHI score (32.63 ± 2.11), followed by Group A (40.57 ± 3.67) and B (41.25 ± 4.11) (both P < 0.001, vs. Group A/B); However, no significant difference was found between groups A and B (P = 0.2991).

Similarly, the most pronounced change in DHI score (Δ value) was observed in group C (-28.48 ± 6.10), as compared to the change in Group A (-19.66 ± 4.90, P < 0.001) and group B (-18.53 ± 6.48, P < 0.001); However, no significant difference was found between groups A and B (P = 0.4665) (**Table 2**).

Incidence of BPPV recurrence

Recurrence was defined as the reappearance of vertigo symptoms and positional nystagmus after successful repositioning therapy and at least two consecutive weeks of symptom-free status. To evaluate the impact of the three treatment strategies on BPPV recurrence, recurrence rates were analyzed at 6, 12, and 24 months after treatment.

At post-treatment 6 months, the recurrence rates were 13.59% in Group A, 16.07% in Group B, and 6.72% in Group C. Although Group C exhibited the lowest recurrence rate, the overall differences among the three groups was not statistically significant (χ^2 = 5.152, P = 0.076. At post-treatment 12 months, recurrence rates

Table 3. Comparison of Incidence of BPPV recurrence among groups

Time Period	Group A (n = 103)	Group B (n = 112)	Group C (n = 119)	χ^2	P (Overall)	P (A vs B)	P (A vs C)	P (B vs C)
Post-treatment 6 months	14 (13.59%)	18 (16.07%)	8 (6.72%)	5.152	0.0761	-	-	-
Post-treatment 12 months	19 (18.45%)	22 (19.64%)	10 (8.40%)	6.795	0.0334	0.8235	0.0268	0.0135
Post-treatment 24 months	27 (26.21%)	29 (25.89%)	16 (13.45%)	7.196	0.0274	0.9573	0.0164	0.0170

Note: Group A: calcium supplementation; Group B: vitamin D supplementation; Group C: calcium + vitamin D supplementation; BPPV: Benign paroxysmal positional vertigo.

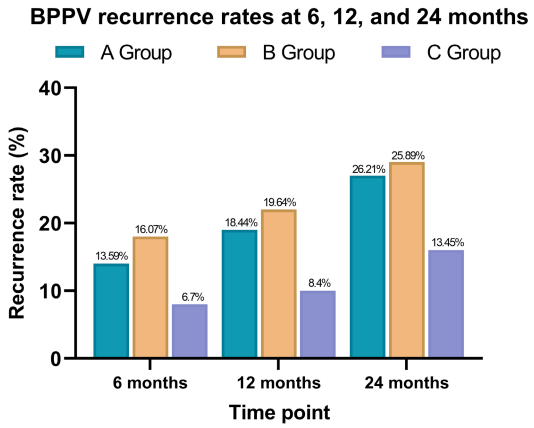

Figure 1. Comparison of Benign Paroxysmal Positional Vertigo (BPPV) recurrence rates among three treatment groups at 6, 12, and 24 months. Group C (combined calcium and vitamin D supplementation) consistently demonstrated the lowest recurrence rates across all time points, with statistically significant differences observed at 12 and 24 months compared to Groups A (calcium alone) and B (vitamin D alone). These findings highlight the potential long-term benefit of combined supplementation in reducing recurrence risk of BPPV in patients with primary osteoporosis. BPPV: Benign paroxysmal positional vertigo.

were 18.45% (A), 19.64% (B), and 8.40% (C), with a significant overall difference (χ^2 = 6.795, P = 0.033). Pairwise comparisons showed that the recurrence rate was significantly lower in Group C than that in both Group A (P = 0.0268) and Group B (P = 0.0135), while the difference between Groups A and B was not significant (P = 0.8235). At post-treatment 24 months, recurrence rates were 26.21% (A), 25.89% (B), and 13.45% (C), with a significant overall difference (χ^2 = 7.196, P = 0.027). Further comparisons revealed that Group C had significantly lower recurrence rates than Group A (P = 0.016) and Group B (P = 0.017), whereas Groups A and B did not differ significantly (P = 0.957). These findings suggest that combined calcium and vitamin D supplementation may reduce long-term BPPV recurrence risk, particularly evident at 12 and 24 months (**Table 3**; **Figure 1**).

Serum calcium and vitamin D levels at the end of study

At the end of the study, serum calcium and vitamin D levels were assessed in all participants. The mean serum calcium levels were 9.12 ± 0.47 mg/dL in Group A, 9.23 ± 0.58 mg/dL in Group B, and 9.72 ± 0.64 mg/dL in Group C, with a significant overall difference among the groups (P < 0.001). Further pair-wise comparisons showed that Group C had significantly higher serum calcium levels than both Group A (P < 0.001) and Group B (P < 0.001), while the difference between groups A and B was not significant (P = 0.3437). The mean vitamin D levels were 25.45 ± 6.35 ng/mL in Group A, 25.76 ± 6.81 ng/mL in Group B, and 27.81 ± 6.22 ng/mL in Group C, with a significant overall difference among groups (P = 0.0116). Further pairwise comparisons showed that Group C had significantly higher vitamin D levels than Group A (P = 0.0191) and Group B (P = 0.0423), while the difference between Groups A and B was not statistically significant (P = 0.9377) (**Table 4**; **Figure 2**).

Changes in bone metabolism markers before and after treatment

Before treatment, the mean P1NP (μg/L) levels in Groups A, B, and C were 35.12 ± 8.45, 34.89 ± 7.92, and 35.45 ± 8.61, respectively, with no significant difference among the groups (P (Overall) = 0.876). After 24 months of treatment, P1NP levels increased to 38.45 ± 9.28 in Group A, 39.11 ± 8.94 in Group B, and 42.32 ± 9.15 in Group C, with a significant difference among groups (F = 5.79; P (Overall) = 0.003); Group C demonstrated significantly higher P1NP levels compared to Groups A (P = 0.002) and B (P = 0.008).

Table 4. Comparison of serum calcium and vitamin D levels among groups after treatment

Parameter	Group A (n = 103)	Group B (n = 112)	Group C (n = 119)	F (Overall)	P (Overall)
Serum calcium (mg/dL)	9.12 ± 0.47	9.23 ± 0.58	9.72 ± 0.64	36.42	< 0.001
Vitamin D (ng/mL)	25.45 ± 6.35	25.76 ± 6.81	27.81 ± 6.22	4.513	0.0116

Note: Group A: calcium supplementation; Group B: vitamin D supplementation; Group C: calcium + vitamin D supplementation.

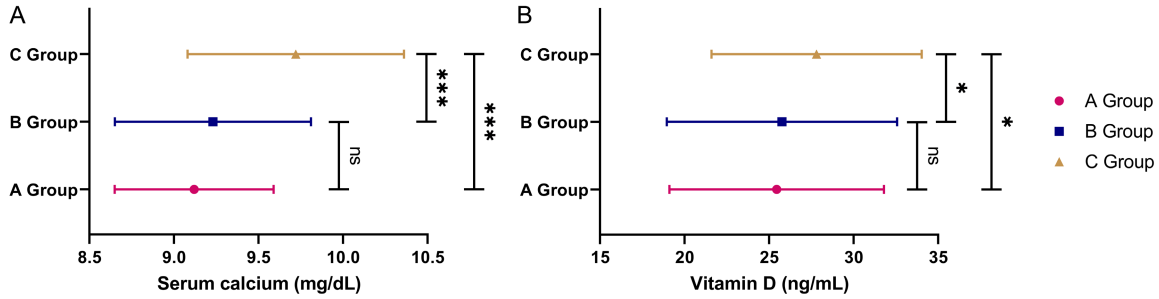

Figure 2. Comparison of serum calcium and vitamin D levels after treatment. A: Serum calcium (mg/dL); B: Vitamin D (ng/mL); Group A: calcium supplementation; Group B: vitamin D supplementation; Group C: calcium + vitamin D supplementation. ns: no significant difference; *: P < 0.05; ***: P < 0.001.

Table 5. Comparison of bone metabolism markers P1NP and β-CTX among groups before and 24 months after treatment

Timepoint	Group A (n = 103)	Group B (n = 112)	Group C (n = 119)	F (Overall)	P (Overall)	P (A vs B)	P (A vs C)	P (B vs C)
P1NP (μg/L)								
Before treatment	35.12 ± 8.45	34.89 ± 7.92	35.45 ± 8.61	0.13	0.876	0.838	0.776	0.609
After treatment	38.45 ± 9.28	39.11 ± 8.94	42.32 ± 9.15	5.79	0.003	0.594	0.002	0.008
β-CTX (ng/mL)								
Before treatment	0.49 ± 0.10	0.48 ± 0.11	0.50 ± 0.12	0.94	0.392	0.694	0.430	0.223
After treatment	0.35 ± 0.07	0.36 ± 0.09	0.32 ± 0.08	7.39	< 0.001	0.199	0.005	< 0.001

Note: Group A: calcium supplementation; Group B: vitamin D supplementation; Group C: calcium + vitamin D supplementation; P1NP: Procollagen Type I N-Terminal Propeptide; β-CTX: Beta-CrossLaps.

For β-CTX (ng/mL), the mean values were 0.49 ± 0.10, 0.48 ± 0.11, and 0.50 ± 0.12 in Groups A, B, and C, respectively, with no significant pre-treatment differences among groups (P(Overall) = 0.392). Post-treatment, β-CTX levels decreased to 0.35 ± 0.07 in Group A, 0.36 ± 0.09 in Group B, and 0.32 ± 0.08 in Group C, showing a significant overall difference among groups (F = 7.39; P (Overall) < 0.001). Specifically, Group C demonstrated significantly lower β-CTX levels compared to Groups A (P = 0.005) and B (P < 0.001), while no significant differences were found between groups A and B (**Table 5**).

Adverse events

Adverse events were monitored throughout the study, including hypercalcemia, nausea/vomiting, constipation, renal stones, and hypercalciuria. The incidence of hypercalcemia was 1.9% in Group A, 0.9% in Group B, and 2.5% in Group C; nausea/vomiting was reported in 3.9%, 2.7%, and 4.2% of participants; constipation occurred in 5.8%, 6.2%, and 4.2%; kidney stones occurred in 1.9%, 0.9%, and 1.7%; and hypercalciuria occurred in 4.9%, 3.6%, and 5.0% of participants in Groups A, B, and C, respectively. No significant differences were found in the incidence of any adverse events among the three groups (all P > 0.05). These results indicate that combined calcium and vitamin D supplementation was well tolerated and did not increase the risk of adverse effects (**Table 6**).

Quality of life assessment

At the end of the study, health-related quality of life was assessed using the SF-36 question-

Table 6. Comparison of the incidence of adverse events among groups [n (%)]

Adverse events	Group A (n = 103)	Group B (n = 112)	Group C (n = 119)	Statistical Test	*P* Value
Hypercalcemia	2 (1.9%)	1 (0.9%)	3 (2.5%)	Fisher's exact test (pairwise)	A vs B: 0.608 A vs C: > 0.999 B vs C: 0.622
Nausea/vomiting	4 (3.9%)	3 (2.7%)	5 (4.2%)	Fisher's exact test (pairwise)	A vs B: 0.712 A vs C: > 0.999 B vs C: 0.723
Constipation	6 (5.8%)	7 (6.2%)	5 (4.2%)	Chi-square test (overall)	0.767
Renal stones	2 (1.9%)	1 (0.9%)	2 (1.7%)	Fisher's exact test (pairwise)	A vs B: 0.608 A vs C: > 0.999 B vs C: > 0.999
Hypercalciuria	5 (4.9%)	4 (3.6%)	6 (5.0%)	Fisher's exact test (pairwise)	A vs B: 0.740 A vs C: > 0.999 B vs C: 0.750

Note: Group A: calcium supplementation; Group B: vitamin D supplementation; Group C: calcium + vitamin D supplementation.

Table 7. Comparison of quality of life scores (SF-36 Score) among groups

Domain	Group A (n = 103)	Group B (n = 112)	Group C (n = 119)	F (Overall)	P (Overall)	P (A vs B)	P (A vs C)	P (B vs C)
Physical functioning	75.27 ± 6.53	76.57 ± 7.28	82.84 ± 7.61	36.19	< 0.001	0.3799	< 0.001	< 0.001
Role-limitations	68.93 ± 8.35	71.45 ± 7.91	82.74 ± 8.57	89.72	< 0.001	0.0669	< 0.001	< 0.001
Emotion well-being	69.18 ± 8.62	71.94 ± 9.22	83.44 ± 9.87	75.45	< 0.001	0.0765	< 0.001	< 0.001
Cognitive function	71.23 ± 5.78	73.26 ± 5.11	82.10 ± 5.26	131.4	< 0.001	0.0169	< 0.001	< 0.001
Social function	72.10 ± 4.78	72.20 ± 6.23	81.78 ± 5.02	122.2	< 0.001	0.9888	< 0.001	< 0.001

Note: Group A: calcium supplementation; Group B: vitamin D supplementation; Group C: calcium + vitamin D supplementation; SF-36: Short Form Health Survey.

naire. As shown in **Table 7**, patients in Groups demonstrated significantly higher quality of life scores across all assessed domains, including physical functioning ($F = 36.19$, $P < 0.001$), role limitations ($F = 89.72$, $P < 0.001$), emotional well-being ($F = 75.45$, $P < 0.001$), cognitive function ($F = 131.4$, $P < 0.001$), and social participation ($F = 122.2$, $P < 0.001$). However, there were no significant differences between the Group A and B across the various domains except for cognitive function ($P = 0.0169$).

Discussion

This study evaluated the effects of calcium supplementation, vitamin D supplementation, and their combination on preventing BPPV recurrence and improving quality of life in patients with primary osteoporosis. The results indicate that combined supplementation offered broader benefits compared with either agent used alone, including a greater reduction in vertigo-related functional impairment, lower long-term recurrence rates, improved biochemical profiles, and enhanced quality of life across multiple domains, without increasing the incidence of adverse events.

Patients receiving the combined intervention exhibited the most notable improvement in dizziness-related symptoms, as reflected by the reduction in DHI scores. BPPV imposes a substantial burden on daily functioning and psychological well-being, making symptom relief a core therapeutic goal [22]. The superior outcome in the combination group may be attributed to the synergistic roles of calcium and vitamin D in maintaining inner ear homeostasis [23]. Otoconia are primarily composed of calcium carbonate, and their stability depends on tightly regulated calcium metabolism [24]. Vitamin D enhances intestinal calcium absorption and helps regulate calcium-phosphate balance, which may contribute to preserving otoconia integrity and reducing abnormal detachment. Previous studies have demonstrated

that vitamin D supplementation can reduce the risk of BPPV recurrence in vitamin D-deficient individuals [25]. Our results extend this notion by suggesting that concomitant calcium supplementation may provide additional benefit, particularly in osteoporotic patients who often exhibit systemic calcium dysregulation [26, 27].

With regard to long-term recurrence, the combination group experienced fewer episodes of BPPV at 12- and 24-months post-treatment compared with the single-agent groups, suggesting that the combined regimen may offer sustained stabilization of vestibular function. Osteoporosis is characterized by increased bone resorption and calcium loss, which may synergistically cause disturbance in the vestibular calcium environment, predisposing to otoconia detachment and subsequent BPPV recurrence [28]. Chua et al. and Lin et al. reported that vitamin D supplementation alone effectively reduced recurrence risk in older adults and patients with idiopathic BPPV; however, our study highlights the potential advantage of combined calcium and vitamin D supplementation in a specific population with underlying osteoporosis [16, 17]. The mechanism may involve improved systemic calcium availability and enhanced local ion equilibrium within the endolymph, thereby reducing the likelihood of otoconia detachment [29, 30].

Consistent with these clinical outcomes, biochemical assessments revealed higher serum calcium and vitamin D levels in the combination group after treatment, indicating more effective nutrient repletion with dual supplementation, likely owing to the interdependent relationship between vitamin D and calcium absorption [23, 31]. Vitamin D status is a key determinant of calcium bioavailability, while adequate calcium intake is required for vitamin D to exert its physiological effects. Our findings align with those reported by Talebi et al., supporting the notion that combined therapy produces a more favorable metabolic profile than monotherapy [32].

The assessment of bone turnover markers provided further mechanistic insight into the superior efficacy of the combined regimen. We found that combined supplementation not only corrected serum nutrient levels but also induced a more favorable bone metabolic state, characterized by a significant increase in the bone formation marker P1NP and a decrease in the bone resorption marker β-CTX, compared with either supplement alone. This synergistic effect on bone remodeling underscores a fundamental advantage of the combined approach in osteoporotic patients [33]. Since otoconia stability is intimately linked to systemic calcium metabolism, this enhanced stabilization of the skeletal system likely contributes to a more stable vestibular environment. Reduced bone resorption may decrease the flux of calcium ions into the bloodstream, potentially minimizing aberrant crystallization or dissolution of otoconia in the inner ear [34]. Thus, the significant reduction in BPPV recurrence observed in the combination group may be partly attributable to this systemic improvement in bone turnover, which goes beyond the effects of merely supplementing either nutrient alone.

In addition to clinical and biochemical improvements, patients in the combination group reported better outcomes in multiple quality-of-life domains assessed by the SF-36, including physical functioning, role limitations due to physical health, emotional well-being, cognitive function, and social participation. BPPV recurrence not only causes physical discomfort but also contributes to anxiety, functional restriction, and reduced social engagement [35, 36]. The comprehensive improvement observed with combined supplementation implies that effective management of BPPV recurrence may help restore overall well-being and functional autonomy. This observation resonates with the systematic review by Madrigal et al., which emphasized the multifaceted impact of BPPV on quality of life, and further suggests that addressing nutrient deficiencies in high-risk populations may produce broader health benefits [5].

Furthermore, the combination regimen did not increase the occurrence of adverse effects relative to either supplementation alone. The incidence of hypercalcemia, gastrointestinal symptoms, constipation, renal stones, and hypercalciuria was comparable across groups, indicating that the combined approach was well tolerated in this patient population [37].

It is noteworthy that the mean BMI of participants in all groups was in the overweight range (approximately 25 kg/m^2), which may reflect the specific demographic characteristics of the

study population or age-related changes in body composition. While a higher BMI is often associated with higher bone mineral density, its complex relationship with osteoporosis risk and BPPV recurrence warrants further investigation. Baseline levels of PTH, P1NP, and β-CTX-commonly assessed bone metabolism indices in osteoporotic patients-were comparable across all three groups, reinforcing the initial homogeneity in bone turnover status and supporting the validity of subsequent intergroup outcome comparisons.

Despite these encouraging findings, several limitations should be acknowledged. First, the retrospective design and non-randomized treatment allocation meant that the choice of supplementation regimen was based on clinical judgment rather than a strict protocol, potentially introducing selection bias. Second, important confounding variables such as dietary calcium intake, sun exposure, and concomitant use of other anti-osteoporosis medications were not accounted for in the analysis due to data availability constraints. Third, the single-center nature of the study and the moderate sample size may affect the generalizability of the results. Additionally, although vitamin D is essential for calcium absorption, the choice of monotherapy with either calcium or vitamin D in some patients was based on individualized clinical judgment, potentially reflecting factors such as pre-existing nutrient levels, patient-specific tolerability, or physician preference in routine practice, rather than a standardized protocol. Future prospective, multicenter studies with larger sample sizes and longer follow-up periods are warranted to confirm these observations. Further investigation into the molecular mechanisms by which calcium and vitamin D influence otoconia stability may provide deeper insights into recurrence prevention.

Future research should also evaluate potential effect modifiers, such as the severity of osteoporosis or baseline vitamin D status, to identify patient subgroups most likely to benefit from combined supplementation. Moreover, exploring the roles of other nutrients implicated in bone and vestibular health, such as vitamin K_2 and magnesium, could provide a more comprehensive nutritional strategy. Ultimately, the goal is to develop evidence-based, personalized management protocols that effectively reduce the burden of recurrent BPPV in vulnerable populations, such as those with osteoporosis.

Conclusions

Concurrent calcium and vitamin D supplementation in patients with primary osteoporosis is associated with a lower BPPV recurrence rate and improved quality of life compared with either treatment alone. These findings highlight the potential benefit of concurrently addressing skeletal and vestibular health. However, given the retrospective design and limited scope of the study, the results should be interpreted with caution. Larger prospective trials are required to confirm these associations and to clarify whether the relationship is causal. Nevertheless, the present findings may provide a useful reference for clinicians and inform future research on integrated management strategies for osteoporosis complicated by BPPV.

Disclosure of conflict of interest

None.

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