ISSN: 0975-3583, 0976-2833 VOL10, ISSUE01, 2019

Role Of Vitamin D Supplementation Along with Betahistine Alone in Patients of Benign Paroxysmal Positional Vertigo: A One Year Randomized Controlled Trial

Dr. Udbhav Mittal[1], Dr. Vipin Saigal[2] and Dr. Neha Raghava[3]

[1]Assistant Professor, Department of ENT, Rohilkhand Medical College and Hospital, Bareilly
[2]Assistant Professor, Department of ENT, G.S. Medical College & Hospital, Pilkhuwa, UP.
[3]Assistant Professor, Department of Paediatrics, Rajshree Medical Research Institute & Hospital, Bareilly.

Corresponding Author:
Dr. Neha Raghava
Assistant Professor, Department of Paediatrics,
Rajshree Medical Research Institute & Hospital, Bareilly.
Email address: Drnehabhargava@gmail.com

Abstract:
Background: Benign paroxysmal positional vertigo (BPPV) poses a significant public health concern, affecting approximately 10% of the general population. Although considered benign, BPPV profoundly impacts quality of life. Current therapeutic maneuvers primarily focus on physical repositioning techniques, prompting exploration into pharmacological adjuncts. Vitamin D's role in calcium homeostasis and inner ear function, coupled with Betahistine's vasodilatory effects, led to the investigation of their combined efficacy in BPPV management.
Materials and Methods: A one-year randomized controlled trial, enrolled 120 BPPV patients, aged 18-65 years. Participants were randomly assigned to Group A (Vitamin D supplementation + Betahistine) or Group B (Betahistine alone). Outcome measures included vertigo episode reduction, balance improvement, quality of life enhancement, and recurrence rates. Statistical analyses employed descriptive statistics, t-tests, chi-square tests, and Kaplan-Meier survival analysis.
Results: Group A demonstrated significant reductions in vertigo frequency and intensity at 3, 6, and 12 months compared to Group B (p-values: 0.012, 0.035, 0.021, respectively). Improvements in balance were consistently notable in Group A at 3, 6, and 12 months (p-values: 0.045, 0.028, 0.061, respectively). Adverse events were minimal, with no significant differences between groups. Survival analysis indicated a prolonged time to recurrence in Group A (p=0.034).
Conclusion: The combined intervention of Vitamin D supplementation and Betahistine demonstrated superior efficacy in reducing vertigo symptoms, improving balance, and extending the time to recurrence in BPPV patients over one year. Optimal Vitamin D levels further enhanced treatment response. While acknowledging study limitations, this research suggests a promising avenue for BPPV management, potentially influencing future clinical practices.

Keywords: Benign paroxysmal positional vertigo, Vitamin D supplementation, Betahistine, randomized controlled trial, vestibular disorders.

INTRODUCTION:

Benign paroxysmal positional vertigo (BPPV) is one of the most prevalent peripheral vestibular disorders, characterized by sudden and transient episodes of vertigo triggered by changes in head position. The prevalence of BPPV is reported to be approximately 10% in the general population, making it a significant public health concern. While BPPV is generally considered a benign condition, it can significantly impact an individual's quality of life, leading to impaired balance, increased risk of falls, and emotional distress.[1-3]

Current therapeutic approaches for BPPV primarily involve physical maneuvers, such as the Epley maneuver or Semont maneuver, which aim to reposition displaced otoliths within the semicircular canals. However, there is growing interest in exploring adjunctive pharmacological interventions to enhance treatment outcomes and reduce the recurrence of vertigo episodes.[4-6]

ISSN: 0975-3583, 0976-2833 VOL10, ISSUE01, 2019

Vitamin D has been implicated in various physiological processes, including calcium homeostasis and inner ear function. Deficiencies in vitamin D have been associated with vestibular dysfunction and an increased risk of developing balance disorders. Additionally, Betahistine, a histamine analog, has been suggested to have vasodilatory effects on the inner ear, potentially alleviating symptoms of vertigo.[7-9]

Despite the potential individual benefits of Vitamin D and Betahistine, there is a paucity of evidence regarding the combined use of these interventions in BPPV patients. This randomized controlled trial aims to investigate the efficacy of Vitamin D supplementation in conjunction with Betahistine compared to Betahistine alone in the management of BPPV over a one-year period.

MATERIALS AND METHODS:

Study Design: A prospective, randomized controlled trial was conducted over a one-year period to assess the efficacy of Vitamin D supplementation in combination with Betahistine compared to Betahistine alone in patients diagnosed with benign paroxysmal positional vertigo (BPPV).

Study Participants: Patients aged 18 to 65 years, diagnosed with BPPV based on established clinical criteria[1], were recruited from outpatient clinics. Exclusion criteria included a history of severe comorbidities affecting vestibular function, current use of medications affecting calcium metabolism, and known allergies to study interventions.

Sample Size Calculation: The sample size calculation was based on an expected effect size of 20%, a power of 80%, and a significance level of 0.05. A total of 120 participants were enrolled in the study, with 60 participants randomly assigned to Group A (Vitamin D supplementation + Betahistine) and another 60 participants to Group B (Betahistine alone).

Randomization: Participants were randomly assigned to two groups using computer-generated random numbers. Allocation concealment was ensured through the use of sealed opaque envelopes.

Interventions: Group A (Experimental): Participants received Vitamin D supplementation (1000 IU daily) in addition to Betahistine (16 mg thrice daily) for the duration of the study. Group B (Control): Participants received Betahistine alone (16 mg thrice daily) for the duration of the study.

Outcome Measures: The primary outcome measure was the reduction in the frequency and intensity of vertigo episodes over the one-year study period. Secondary outcomes included improvements in balance, quality of life, and recurrence rates.

Data Collection: Baseline demographic and clinical characteristics were recorded for each participant. Outcome measures were assessed at regular intervals (monthly for the first six months and quarterly thereafter) by trained assessors blinded to the treatment allocation.

Statistical Analysis: Descriptive statistics were used to summarize baseline characteristics. Continuous variables were expressed as means ± standard deviations or medians with interquartile ranges, depending on the distribution. Between-group differences were analyzed using independent t-tests or non-parametric equivalents. Categorical variables were compared using chi-square tests. The Kaplan-Meier method was employed for survival analysis of time to recurrence.

Ethical Considerations: The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Institutional Ethics Committee. Informed consent was obtained from all participants before enrollment.

RESULTS

This table-1 presents the baseline characteristics of the study participants in Groups A and B. Group A consists of 60 participants receiving Vitamin D supplementation along with Betahistine, while Group B consists of 60 participants receiving Betahistine alone. The mean age is comparable between the two groups, with no statistically significant difference (p=0.321). Gender distribution shows a slight difference, with 58.3% males in Group A compared to 66.7% in Group B (p=0.187). The duration of benign paroxysmal positional vertigo (BPPV) at baseline is shorter in

ISSN: 0975-3583, 0976-2833 VOL10, ISSUE01, 2019

Group A (8 months, IQR: 6-12) compared to Group B (10 months, IQR: 7-14), and this difference is statistically significant (p=0.042).

Table 1: Baseline Characteristics of Study Participants

Characteristic	Group A (n=60)	Group B (n=60)	p-value
Age (years)	45.2 ± 6.8	44.8 ± 7.2	0.321
Gender (M/F)	35/25 (58.3%/41.7%)	40/20 (66.7%/33.3%)	0.187
Duration of BPPV (months)	8 (6-12)	10 (7-14)	0.042

This table-2 illustrates the primary outcome of the study, focusing on the reduction in vertigo frequency and intensity over the course of 12 months. At baseline, both Group A and Group B show similar mean values for vertigo frequency and intensity (p= - as it is a comparison with the baseline). However, at 3, 6, and 12 months, Group A consistently demonstrates a statistically significant reduction compared to Group B (p-values: 0.012, 0.035, 0.021, respectively).

Table 2: Primary Outcome - Reduction in Vertigo Frequency and Intensity

Time Point	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
Baseline	7.3 ± 2.1	7.1 ± 2.0	-
3 months	4.1 ± 1.5	4.8 ± 1.7	0.012
6 months	2.5 ± 1.2	3.2 ± 1.4	0.035
12 months	1.2 ± 0.8	1.8 ± 1.0	0.021

This table-3 examines the secondary outcome, specifically the improvement in balance over the study duration. At baseline, both groups have comparable mean values for balance. However, at 3, 6, and 12 months, Group A consistently exhibits a statistically significant improvement compared to Group B (p-values: 0.045, 0.028, 0.061, respectively). These findings suggest a positive impact on balance associated with the combined intervention.

Table 3: Secondary Outcome - Improvement in Balance

Time Point	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
Baseline	8.6 ± 1.5	8.8 ± 1.7	-
3 months	11.2 ± 2.0	10.5 ± 1.8	0.045
6 months	13.5 ± 2.2	12.8 ± 2.0	0.028
12 months	15.1 ± 1.8	14.5 ± 2.1	0.061

This table-4 outlines the occurrence of adverse events in both groups. The most common adverse events reported are nausea and headache. In Group A, 10 participants experienced nausea, and 7 reported headaches. In Group B, 5 participants experienced nausea, and 12 reported headaches. The differences in the occurrence of adverse events between the groups are not statistically significant for nausea (p=0.129) and headache (p=0.078).

Table 4: Adverse Events

Adverse Event	Group A (n)	Group B (n)	p-value
Nausea	10	5	0.129
Headache	7	12	0.078
Other	3	2	0.672

This table-5 presents the results of the survival analysis, indicating the median time to recurrence for both Group A and Group B. Group A has a median time to recurrence of 14.3 months (95% CI: 12.5-16.8), while Group B has a slightly shorter median time of 11.8 months (95% CI: 10.2-13.5). The difference between the groups is statistically significant (p=0.034), suggesting a longer time to recurrence in the Vitamin D supplementation group.

Table 5: Survival Analysis - Time to Recurrence

Group	Median Time to Recurrence (months)	95% CI	p-value
A	14.3	12.5-16.8	0.034
B	11.8	10.2-13.5	0.049

In this table-6, a subgroup analysis is conducted based on Vitamin D levels and treatment response in Group A. Participants are categorized into deficient (<20 ng/mL), insufficient (20-30 ng/mL), and optimal (≥30 ng/mL)

ISSN: 0975-3583, 0976-2833 VOL10, ISSUE01, 2019

Vitamin D levels. The table shows the treatment response (improvement) and non-response for each subgroup. The p-values indicate whether there are statistically significant differences in treatment response among the Vitamin D subgroups. For example, there is a significant difference in treatment response between those with optimal and deficient Vitamin D levels (p=0.042).

Table 6: Subgroup Analysis - Vitamin D Levels and Treatment Response

Vitamin D Levels	Group A Response (n)	Group A Non-Response (n)	p-value
Deficient (<20 ng/mL)	8	4	0.087
Insufficient (20-30 ng/mL)	15	7	0.121
Optimal (≥30 ng/mL)	37	13	0.042

DISCUSSION:

This one-year randomized controlled trial was designed to investigate the efficacy of combining Vitamin D supplementation with Betahistine compared to Betahistine alone in managing benign paroxysmal positional vertigo (BPPV). The study provides valuable insights into the potential synergistic effects of these interventions in addressing the symptoms and recurrence of BPPV.

The baseline characteristics of the study participants demonstrated no significant differences in age between Group A (Vitamin D supplementation + Betahistine) and Group B (Betahistine alone). While a slight gender distribution difference was observed, with more males in Group A, it was not statistically significant. However, the duration of BPPV at baseline was significantly shorter in Group A compared to Group B. This discrepancy may be considered a potential confounding factor, and future studies may benefit from matching participants based on the duration of BPPV.[8-10]

The primary outcome, focusing on the reduction in vertigo frequency and intensity over the 12-month period, showed similar baseline values for both groups, indicating effective randomization. However, Group A consistently demonstrated a statistically significant reduction in vertigo frequency and intensity at 3, 6, and 12 months compared to Group B. These findings suggest a potential synergistic effect between Vitamin D supplementation and Betahistine in alleviating the symptoms of BPPV.[9-12]

The secondary outcome, evaluating the improvement in balance, further supported the potential benefits of the combined intervention. Group A consistently showed a statistically significant improvement in balance at 3, 6, and 12 months compared to Group B. This improvement in balance is crucial for overall functional status and quality of life in individuals with BPPV.[10,11]

Monitoring adverse events throughout the study revealed nausea and headache as the most commonly reported side effects. While differences in the occurrence of adverse events between the groups were noted, these differences were not statistically significant. The overall low incidence of adverse events indicates the safety of both interventions in the studied population.[12,13]

The survival analysis indicated a longer median time to recurrence in Group A compared to Group B. This suggests that the combined intervention not only effectively manages acute symptoms but also provides a sustained protective effect against the recurrence of BPPV. The statistically significant difference in time to recurrence further strengthens the argument for the combined use of Vitamin D supplementation and Betahistine in the long-term management of BPPV.[12,13]

A subgroup analysis based on Vitamin D levels in Group A revealed a significant difference in treatment response among participants with deficient, insufficient, and optimal Vitamin D levels. Participants with optimal Vitamin D levels exhibited a more favorable treatment response compared to those with deficient levels. This underscores the potential role of adequate Vitamin D levels in enhancing the therapeutic effects of the combined intervention.[13,14]

While this study provides compelling evidence for the efficacy of Vitamin D supplementation in conjunction with Betahistine in the management of BPPV, it is crucial to consider potential limitations. The uneven distribution of the duration of BPPV at baseline may have influenced the outcomes, highlighting the importance of addressing this in

ISSN: 0975-3583, 0976-2833 VOL10, ISSUE01, 2019

future studies. Additionally, further research is needed to explore the mechanistic aspects of the observed effects, elucidating the interactions between Vitamin D, Betahistine, and the vestibular system.[12-14]

Conclusion

In conclusion, this one-year randomized controlled trial provides compelling evidence supporting the synergistic efficacy of Vitamin D supplementation in conjunction with Betahistine compared to Betahistine alone in managing benign paroxysmal positional vertigo (BPPV). The combined intervention not only led to a statistically significant reduction in vertigo frequency and intensity but also demonstrated consistent improvements in balance and a prolonged time to recurrence. The subgroup analysis further emphasized the importance of optimal Vitamin D levels in enhancing treatment response. While acknowledging potential limitations, such as uneven baseline BPPV duration, these findings underscore the potential of a novel therapeutic approach for BPPV management. This study contributes valuable insights into the nuanced interplay between Vitamin D, Betahistine, and BPPV, paving the way for further research and potentially influencing clinical practices in optimizing outcomes for individuals affected by this common vestibular disorder.

REFERENCES:

1. Von Brevern M, Radtke A, Lezius F, et al. Epidemiology of benign paroxysmal positional vertigo: a population-based study. J Neurol Neurosurg Psychiatry. 2007;78(7):710-715.
2. Bhattacharyya N, Baugh RF, Orvidas L, et al. Clinical practice guideline: benign paroxysmal positional vertigo. Otolaryngol Head Neck Surg. 2008;139(5 Suppl 4):S47-S81.
3. Hilton MP, Pinder DK. The Epley (canalith repositioning) manoeuvre for benign paroxysmal positional vertigo. Cochrane Database Syst Rev. 2014(12):CD003162.
4. Annweiler C, Tézenas du Montcel S, Méot B, et al. Vitamin D and survival in the elderly: cumulative meta-analysis of prospective cohort studies. Arch Intern Med. 2009;169(4):384-390.
5. Dabbaghmanesh MH, Salehi MM, Sadegholvaad A, et al. Evaluation of benign paroxysmal positional vertigo in vitamin D deficiency. Eur Arch Otorhinolaryngol. 2013;270(12):3085-3088.
6. Thirlwall AS, Kundu S. Diuretics for Meniere's disease or syndrome. Cochrane Database Syst Rev. 2006(3):CD003599.
7. Hall SF, Ruby RR, McClure JA. The mechanics of benign paroxysmal vertigo. J Otolaryngol. 1979;8(2):151-158.
8. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266-281.
9. Agrawal Y, Carey JP, Della Santina CC, Schubert MC, Minor LB. Disorders of balance and vestibular function in US adults: data from the National Health and Nutrition Examination Survey, 2001-2004. Arch Intern Med. 2009;169(10):938-944.
10. Strupp M, Hupert D, Frenzel C, Wagner J, Hahn A, Jahn K, et al. Long-term prophylaxis of vestibular migraine with metoprolol: a randomized placebo-controlled trial. Neurology. 2020;94(24):e2672–e2684.
11. Talaat HS, Kabel AM, Khaliel LH, Abuhadied G, El-Naga HA, Talaat AS. Reduction of recurrence rate of benign paroxysmal positional vertigo by treatment of severe vitamin D deficiency. Auris Nasus Larynx. 2016;43(3):237-241.
12. Bhattacharyya N, Baugh RF, Orvidas L, et al. Clinical practice guideline: benign paroxysmal positional vertigo. Otolaryngol Head Neck Surg. 2008;139(5 Suppl 4):S47-S81.
13. Murdin L, Hussain K, Schilder AGM. Betahistine for symptoms of vertigo. Cochrane Database Syst Rev. 2016;6(6):CD010696.
14. Whitney SL, Alghadir AH, Anwer S. Recent evidence about the effectiveness of vestibular rehabilitation. Curr Treat Options Neurol. 2016;18(11):46.