

Betahistine for Residual Dizziness after the Epley Maneuver in Posterior Canal Benign Paroxysmal Positional Vertigo: A Randomized Double-Blind Placebo-Controlled Trial

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Abstract

Introduction:

Residual dizziness may occur after canalith repositioning procedures for posterior canal benign paroxysmal positional vertigo (BPPV) and can impair quality of life (QoL). This study assessed whether short-term betahistine improves QoL and promotes the resolution of residual dizziness after the Epley maneuver in patients with posterior canal BPPV.

Materials and Methods:

This randomized, double-blind, placebo-controlled trial screened 46 patients with posterior canal BPPV, all of whom underwent an Epley maneuver. Ten patients with persistent positional nystagmus at the 1-week reassessment were excluded before randomization, and the remaining 36 patients were randomized to receive betahistine 48 mg/day for 7 days or placebo after a successful Epley maneuver. Outcomes were assessed using the Visual Vertigo Analogue Scale (VVAS) and the Dizziness Handicap Inventory (DHI). The primary outcome was QoL improvement, while the secondary outcome was resolution of residual dizziness, defined as non-vertiginous dizziness in the absence of positional vertigo and positional nystagmus, assessed over 4 weeks.

Results:

All 36 randomized patients (18 per group) received the allocated intervention, completed follow-up, and were included in the analysis. VVAS and DHI scores improved significantly in both groups ($p < 0.001$), with no significant between-group differences. At 4 weeks, residual dizziness resolved in 77.8% of patients receiving betahistine and 66.7% of those receiving placebo, although the between-group difference was not statistically significant ($p = 0.693$).

Conclusions:

Short-term betahistine after a successful Epley maneuver did not significantly improve QoL compared with placebo, although the residual dizziness resolution rate was numerically higher in the betahistine group.

Keywords: Benign paroxysmal positional vertigo; Residual dizziness; Betahistine; Epley maneuver; Quality of life

Received date: 15 Jul 2026

Accepted date: 17 Aug 2026

**Please cite this article;* Patanasukit K, Supakmontri T, Tananuchittikul P. Betahistine for Residual Dizziness after the Epley Maneuver in Posterior Canal Benign Paroxysmal Positional Vertigo: A Randomized Double-Blind Placebo-Controlled Trial *Iran J Otorhinolaryngol.* 2026;38(5):393-400. Doi: 10.22038/ijorl.2026.97375.4208

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Introduction

Benign paroxysmal positional vertigo (BPPV) is a peripheral vestibular disorder characterized by brief episodes of positional vertigo. Posterior semicircular canal involvement accounts for approximately 90% of BPPV cases and is diagnosed by characteristic nystagmus elicited during the Dix–Hallpike maneuver (1). Canalith repositioning procedures are recommended as the first-line treatment for BPPV, with the Epley maneuver being the most widely used (2). Although these maneuvers are effective, approximately two-thirds of patients continue to experience persistent non-spinning dizziness, imbalance, or lightheadedness, collectively termed residual dizziness, after an otherwise successful treatment (3).

Residual dizziness has been reported in 29.6–76.9% of patients and may persist for weeks to months. However, its pathophysiology remains unclear, and the proposed mechanisms include residual otolith debris, otolith dysfunction, delayed central vestibular compensation, autonomic dysfunction, anxiety, and vestibular decline with age (4).

Among these mechanisms, concomitant otolith dysfunction has attracted particular attention. Persistent utricular and saccular dysfunction, demonstrated by abnormal oVEMP and cVEMP responses after successful repositioning, may contribute to residual dizziness (5). Hoseinabadi et al. reported a higher BPPV recurrence rate in patients with abnormal otolith function than in those with normal function (40% vs. 6.7%) (6).

These findings suggest that persistent otolith dysfunction may contribute to incomplete recovery after successful repositioning. Betahistine, a histamine analogue that acts predominantly as an H₃ receptor antagonist, promotes inner ear microcirculation and may facilitate otolith debris clearance and vestibular compensation (7). Despite its widespread use, evidence for this indication remains limited and inconsistent. This study evaluated short-term betahistine therapy for improving the quality of life and promoting the resolution of residual dizziness over 4 weeks after a successful Epley maneuver in patients with posterior canal BPPV.

Materials and Methods

Study Design

This prospective, randomized, double-blind, placebo-controlled trial was conducted at

Thammasat University Hospital from 1 June 2023 to 31 December 2024.

This study was approved by the Institutional Review Board and Ethics Committee for Human Research of the study center (MTU-EC-OL-0-270/65). Written informed consent was obtained from all participants before enrolment. All procedures involving human participants were conducted in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The trial followed the Consolidated Standards of Reporting Trials (CONSORT) guidelines and was retrospectively registered with the Thai Clinical Trials Registry (TCTR20260304003) on 4 March 2026, after completion of data collection. Prospective registration was not undertaken because this requirement was not recognized at the time of study initiation. The trial was subsequently registered when this requirement was identified during manuscript preparation.

Patient Selection

Forty-six patients aged 18–80 years with posterior canal BPPV confirmed by a positive Dix–Hallpike maneuver were screened. All patients underwent canalith repositioning and were reassessed at the 1-week follow-up before randomization. Patients were excluded for lateral, anterior, or multicanal BPPV; vestibular suppressant use within 1 month before enrolment, including dimenhydrinate, betahistine, hyoscine, scopolamine, diazepam, or gabapentin; persistent positional nystagmus consistent with posterior canal BPPV at follow-up; or refusal to participate. Successful repositioning was confirmed by the absence of positional nystagmus on repeat Dix–Hallpike testing, after which eligible patients were randomized to betahistine or placebo. The 10 patients with persistent positional nystagmus were excluded before randomization; no participant was excluded after randomization.

Sample Size

The sample size was calculated from Guneri and Kustutan (1), who evaluated betahistine after the Epley maneuver in patients with posterior canal BPPV. Based on mean Dizziness Handicap Inventory (DHI) scores of 38.39 and 50.33, standard deviations of 11.55 and 14.47, a two-sided α of 0.05, and 80% power ($\beta = 0.20$), the minimum sample size was 38 participants. Allowing for an anticipated

attrition rate of 20%, 46 participants were targeted. Ten of the 46 screened patients were excluded before randomization because of persistent positional nystagmus at the 1-week reassessment, leaving 36 participants for randomization and analysis. Therefore, the final sample consisted of two participants fewer than the calculated minimum of 38.

Randomization and Blinding

Participants were assigned 1:1 to receive betahistine or placebo using computer-generated block randomization. Randomization

was performed after the 1-week reassessment, following all eligibility exclusions. The 36 eligible participants were allocated equally (18 per group), and all randomized participants received the allocated intervention and were included in the analysis. Study medications were prepared, labelled, and coded by an independent pharmacist. Allocation was concealed using sequentially numbered, sealed opaque envelopes. Participants, treating physicians, and outcome assessors remained blinded throughout the study (Figure 1).

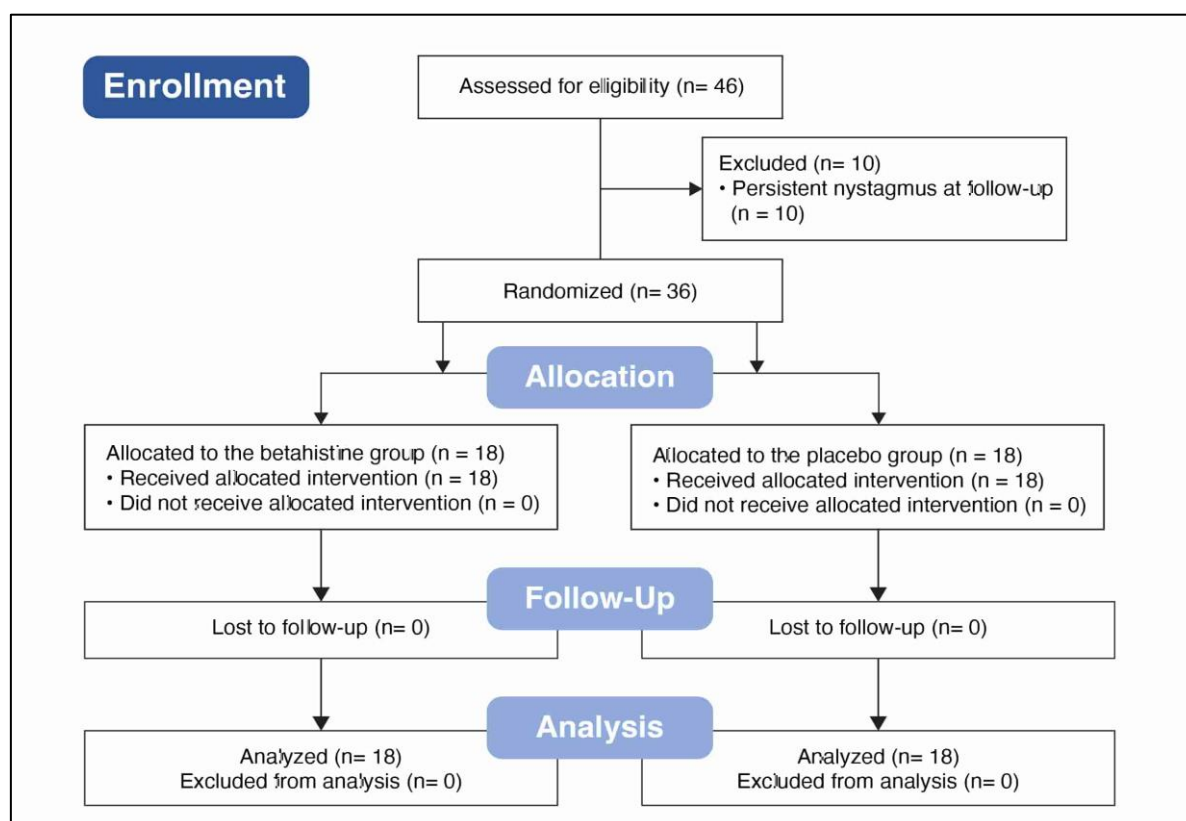


Fig 1. CONSORT flow diagram of participant enrollment, randomization, follow-up, and analysis.

Intervention

Following a successful Epley maneuver, participants received betahistine 48 mg/day or a matching placebo for 7 days. No postural restrictions were imposed.

All participants received a single Epley maneuver performed by the same otolaryngologist. Treatment success was confirmed at the 1-week reassessment; participants with persistent positional nystagmus were excluded before randomization and offered further repositioning outside the trial. No repeat Epley maneuver was performed during the trial period.

Definition and Assessment of Residual Dizziness

Residual dizziness was defined as non-vertiginous dizziness, such as lightheadedness, floating, swaying, or unsteadiness, in the absence of positional vertigo and nystagmus on repeat Dix–Hallpike testing after a successful Epley maneuver (5,8). Positional rotatory vertigo was considered unresolved or recurrent BPPV, and symptoms attributable to other identifiable causes were excluded. Residual dizziness was assessed weekly for 4 weeks as a dichotomous patient-reported outcome (present or absent) by an investigator blinded to

treatment allocation. Resolution was defined as the first assessment with complete absence of symptoms and no subsequent recurrence. The VVAS and DHI assessed symptom severity and impact but were not used to define residual dizziness or its resolution.

Outcome Measures

Baseline demographic and clinical data were also collected. Quality of life, the primary outcome, was assessed using the Visual Vertigo Analogue Scale (VVAS) (9) and DHI (10) at baseline, 1 week, and 1 month.

Residual dizziness resolution, the secondary outcome, was assessed weekly for 4 weeks after treatment. The Thai version of the DHI (DHI-TH) has been formally translated and validated in Thai patients with vestibular disorders, demonstrating good internal consistency (Cronbach's $\alpha = 0.87$) and excellent test-retest reliability (intraclass correlation coefficients = 0.91–0.97).

Construct validity was supported by moderate correlations with the Thai SF-36 ($r = -0.40$ to -0.63) (10).

Statistical Analysis

Analyses were performed using Stata version 14 (StataCorp, College Station, TX, USA). Continuous variables are reported as mean $\pm$ SD or median (IQR), and categorical variables as frequencies and percentages. Paired t-tests assessed within-group differences, while independent t-tests, chi-square tests, and

Fisher's exact tests assessed between-group differences. Significance was set at $p < 0.05$.

Results

Forty-six patients were assessed for eligibility and underwent the Epley maneuver. At the 1-week reassessment, 10 patients (21.7%) had persistent positional nystagmus and were excluded before randomization.

The remaining 36 patients were randomized to receive betahistine or placebo (18 per group). All randomized participants received their allocated intervention, completed the 4-week follow-up, and were included in the analysis, with no loss to follow-up or post-randomization exclusion (Figure 1). Baseline demographic and clinical characteristics, including age, sex, laterality, body mass index, comorbidities, and symptom duration, did not differ significantly between the groups (all $p > 0.05$) (Table 1).

Both groups showed significant improvements in the VVAS and DHI scores from baseline at 1 week and 1 month after treatment (all $p < 0.001$), with no significant between-group differences at any follow-up assessment (all $p > 0.05$) (Tables 2 and 3). Residual dizziness resolution over the 4-week follow-up did not differ significantly between the groups. By week 4, dizziness had resolved in 14/18 patients (77.8%) receiving betahistine and 12/18 (66.7%) receiving placebo ($p = 0.693$) (Figure 2).

Table 1. Baseline demographic and characteristics of study participants

	Betahistine (n=18)	Placebo (n=18)	p-value
Age, years	60.28 $\pm$ 18.64	54.5 $\pm$ 11.58	0.273
Sex			
Male	3 (16.67)	5 (27.78)	0.691
Female	15 (83.33)	13 (72.22)	
Affected side			
Right	13 (72.22)	11 (61.11)	0.480
Left	5 (27.78)	7 (38.89)	
BMI, kg/m ²	24.75 $\pm$ 5.4	24.39 $\pm$ 2.71	0.805
Comorbidity			
Diabetes mellitus	2 (11.11)	2 (11.11)	1.000
Dyslipidemia	4 (22.22)	4 (22.22)	1.000
Symptom onset, days	4.5 [1–14]	7 [3–14]	0.654

Data are presented as frequency (%), mean ($\pm$ standard deviation), or median [interquartile range].

Table 2. Changes in Visual Vertigo Analogue Scale (VVAS) Scores Over Time

Time point	Betahistine (n=18)	Placebo (n=18)	p-value
Baseline	53.83 ± 27.23	64.50 ± 19.70	0.187
1 week	13.83 ± 16.56	13.17 ± 20.66	0.916
p-value	<0.001*	<0.001*	
Change from Baseline (95% CI)	-40.00 (-51.00 to -29.00)	-51.33 (-63.83 to -38.84)	0.160
1 month	1.06 ± 4.48	1.67 ± 3.56	0.653
p-value	<0.001*	<0.001*	
Change from Baseline (95% CI)	-52.78 (-66.39 to -39.16)	-62.83 (-72.29 to -53.38)	0.209

Data are presented as the mean ± standard deviation (SD). Changes from baseline are presented with 95% confidence intervals (CI).

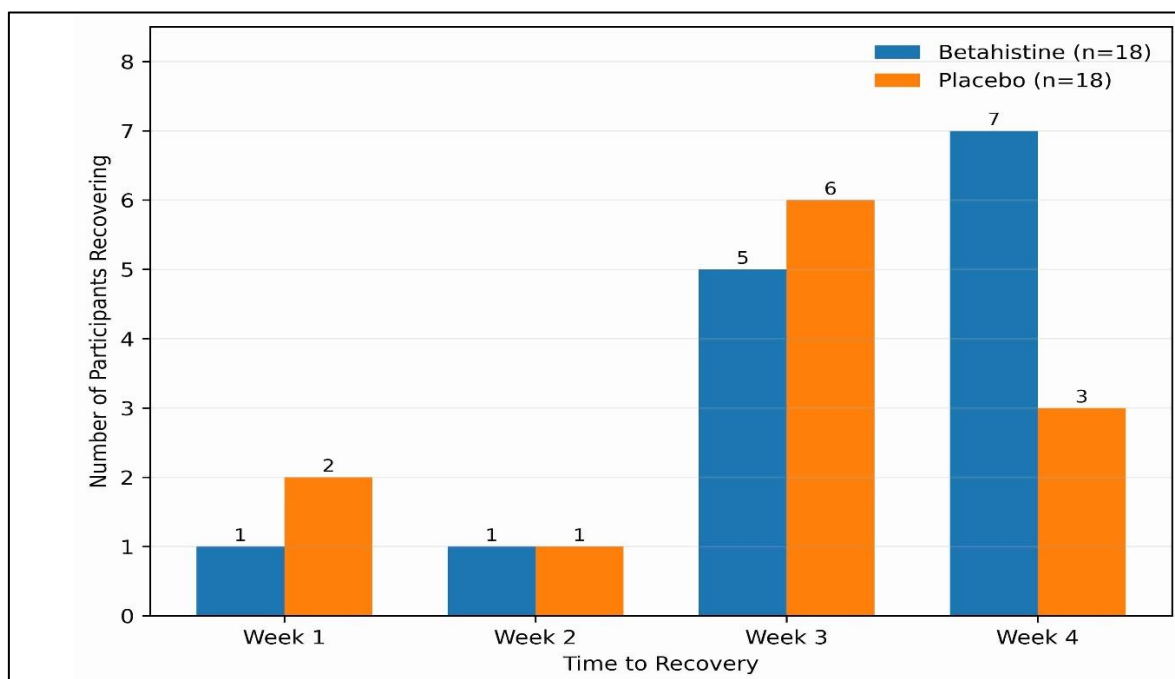
*Within-group comparisons versus baseline were performed using the paired t-test. Between-group comparisons were performed using the independent t-test. * p-value < 0.05 indicates statistical significance.

Table 3. Changes in Dizziness Handicap Inventory (DHI) Scores over Time

Time point	Betahistine (n=18)	Placebo (n=18)	p-value
Baseline	74.67 ± 20.93	74.44 ± 17.82	0.973
1 week	27.22 ± 21.88	21.00 ± 16.67	0.344
p-value	<0.001*	<0.001*	
Change from Baseline (95% CI)	-47.44 (-60.10 to -34.79)	-53.44 (-66.30 to -40.59)	0.488
1 month	1.89 ± 3.91	2.56 ± 5.61	0.682
p-value	<0.001*	<0.001*	
Change from Baseline (95% CI)	-72.78 (-82.79 to -62.76)	-71.89 (-80.59 to -63.19)	0.888

Data are presented as the mean ± standard deviation (SD). Changes from baseline are presented with 95% confidence intervals (CI).

*Within-group comparisons versus baseline were performed using the paired t-test. * p-value < 0.05 indicates statistical significance.

**Fig 2.** Time to recovery from residual dizziness in the betahistine and placebo groups during the 4-week follow-up period.

Discussion

The present study showed that betahistine did not significantly improve the quality of life or accelerate residual dizziness resolution after successful canalith repositioning. Residual dizziness is likely multifactorial, involving otolith organ dysfunction, incomplete otolith clearance, pre-existing vestibular deficits, impaired central vestibular compensation, autonomic dysfunction, and metabolic factors such as vitamin D deficiency (11). Several mechanisms extend beyond peripheral vestibular pathology and may not respond directly to betahistine.

Betahistine is thought to act mainly as a histamine H₃ receptor antagonist, increasing histamine turnover, improving inner ear microcirculation, and facilitating vestibular compensation (8,12). However, these pharmacological effects may not translate into meaningful clinical benefits when central and non-vestibular mechanisms are predominant. This may explain the lack of a significant benefit observed in this study.

In this randomized placebo-controlled study, both groups showed significant VVAS and DHI improvements over time, but no significant between-group differences occurred at any follow-up. These findings align with reports of limited short-term betahistine benefits. Acar et al. (13) found no significant DHI difference after 1 week, and Alsolamy et al. (14) reported no short-term improvement in a recent systematic review. However, longer treatment may enhance efficacy, with greater VVAS reduction after 4 weeks (14). In contrast, Guneri and Kustutan (1) reported better symptom control when betahistine was combined with canalith repositioning procedures. Differences in study design, outcome measures, treatment duration, and patient populations limit direct comparisons. Overall, the evidence for betahistine in residual dizziness remains inconclusive.

Evidence of the limited benefits of betahistine has also been reported in other vestibular disorders. In patients with vertigo and unsteadiness after acute and subacute head trauma, Jafarzadeh et al. found a greater improvement in DHI scores with betahistine combined with early vestibular rehabilitation than with betahistine alone, suggesting an additional benefit of vestibular rehabilitation (15). Similarly, vestibular rehabilitation has been

associated with reduced BPPV recurrence in patients with otolith dysfunction (6). A recent systematic review of four randomized controlled trials of betahistine after canalith repositioning found inconsistent results, with two trials reporting symptomatic benefits and two showing no significant advantage over control, concluding that the available evidence remains limited and heterogeneous (16). Consistent with these findings, our placebo-controlled trial found no significant benefit of betahistine, further suggesting that the current evidence does not support its routine use for residual dizziness after a successful Epley maneuver.

Both groups showed significant improvements, suggesting contributions from spontaneous recovery and placebo effects. Residual dizziness may improve over time (8) and has been linked to delayed central vestibular compensation (4), anxiety (8), and vitamin D deficiency (11). As betahistine primarily affects the peripheral vestibular system (5), its efficacy may be limited when central or non-vestibular mechanisms are predominant.

Although complete residual dizziness resolution was more frequent with betahistine than with placebo at 1 month (77.8% vs. 66.7%), the difference was not significant and should be interpreted cautiously, as it may reflect random variation rather than a true treatment effect.

This study had several limitations. First, although 46 patients were screened to allow for an anticipated 20% attrition, 10 (21.7%) were excluded before randomization because of persistent positional nystagmus, leaving 36 participants for randomization and analysis, two fewer than the calculated minimum of 38. The resulting sample size may have limited the statistical power to detect between-group differences. Second, the trial was retrospectively registered, which may raise concerns regarding selective outcome reporting, although the study protocol and prespecified outcomes were approved by the Institutional Review Board before participant enrolment. Third, residual dizziness was ascertained as a dichotomous patient-reported outcome, and no objective measure of otolith function, such as cVEMP, oVEMP, or subjective visual vertical, was obtained; therefore, participants with concomitant otolith dysfunction, who may be least likely to respond to pharmacotherapy, could not be identified. Fourth, the single-center

design may have limited the generalizability of the results. Fifth, the 4-week follow-up period may not capture long-term recovery trajectories. In addition, the optimal betahistine dose and duration remain uncertain, and a longer treatment may yield different outcomes.

Future studies should use larger multicenter cohorts and longer follow-up periods to determine the optimal dose, duration, and long-term effectiveness of betahistine after successful canalith repositioning.

Conclusion

In this randomized placebo-controlled study, short-term betahistine did not significantly improve dizziness-related quality of life or residual dizziness resolution after successful canalith repositioning compared with placebo. Although symptom resolution was more frequent with betahistine treatment, the difference was not statistically significant. These findings suggest that short-term benefits may be limited and should be interpreted in the context of natural recovery.

Acknowledgements

The authors would like to thank Ms. Worarachanee Imjaijitt, who served as the biostatistician for this study; Thammasat University Hospital for providing access to the data used in this study; and Editage (www.editage.com) for English-language editing.

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