Comparative Efficacy of Betahistine Versus Cinnarizine in Vertigo Management: A Randomized Controlled Trial

Abstract

Background: Vertigo, often arising from peripheral vestibular dysfunction (e.g., BPPV, vestibular neuritis, Ménière's disease), causes debilitating dizziness, nausea, and imbalance. Betahistine and cinnarizine are widely used vestibular suppressants, but direct comparisons in acute vertigo settings remain limited.

Objective: To compare the speed of symptom relief and tolerability of betahistine versus cinnarizine over four weeks in adults with vertigo.

Methods: In a double-blind trial, 100 patients (aged 18–65; symptom onset ≤4 weeks; baseline VAS ≥1) were randomized to betahistine (8 mg tid; 24 mg/day) or cinnarizine (25 mg tid; 75 mg/day) for four weeks. Daily VAS, Mean Vertigo Score (MVS), and Mean Concomitant Symptom Score (MCSS) were recorded through Day 7. Efficacy (5-point verbal) was assessed on Days 3 and 7; tolerability (4-point) was evaluated on Day 3, Week 1, and Week 4. Analyses used t-tests (or Mann–Whitney U), chi-square tests, and Kaplan–Meier/log-rank for time-to-improvement.

Results: Baseline characteristics were similar (all $p > 0.05$). By Day 3, betahistine yielded greater reductions in VAS (1.8 ± 0.6 vs. 2.3 ± 0.7; $p = 0.010$), MVS (2.0 ± 0.6 vs. 2.5 ± 0.6; $p = 0.005$), and MCSS (1.7 ± 0.6 vs. 2.2 ± 0.5; $p = 0.004$) than cinnarizine. By Day 7, both groups had comparable improvements, though betahistine achieved "much improved" ratings faster (Day 3 efficacy 2.69 ± 0.64 vs. 3.15 ± 0.60; $p < 0.001$). Tolerability favoured betahistine at Day 3 (90 % vs. 64 %; $p = 0.01$) and Week 4 (70 % vs. 50 %; $p = 0.04$).

Conclusions: Betahistine provides more rapid symptom relief and better tolerability than cinnarizine, supporting its use as first-line therapy for acute peripheral vertigo.

Keywords: Betahistine; Cinnarizine; Peripheral Vertigo; Visual Analog Scale (VAS); Mean Vertigo Score (MVS); Mean Concomitant Symptom Score (MCSS).

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Introduction

"A sudden shift in perception, where the world spins beneath your feet, vertigo can strike anyone, turning everyday life into a disorienting struggle for balance" [1]. Peripheral vestibular dysfunction—most commonly benign paroxysmal positional vertigo, vestibular neuritis, and Ménière's disease—accounts for most vertigo cases, affecting up to 30% of adults and leading to dizziness, nausea, and imbalance that impair daily functioning [1–3]. Pharmacologic therapy aims to suppress aberrant vestibular signalling; among available

agents, betahistine and cinnarizine are widely used for their targeted effects on inner-ear perfusion and neurotransmission [4–6].

Betahistine, an H_1 agonist and H_3 antagonist, improves inner-ear microcirculation to reduce endolymphatic pressure and stabilize vestibular function. It is typically dosed at 8 mg three times daily (up to 48 mg/day) and causes only mild side effects such as headache or gastrointestinal discomfort [7–10]. Cinnarizine, which combines H_1 antagonism with calcium-channel blockade, stabilizes vestibular hair-cell signalling and enhances inner-ear perfusion; the usual dose is 25 mg three times daily. It provides rapid vertigo relief but may induce sedation and, rarely, extrapyramidal symptoms [5,6].

Direct head-to-head comparisons of betahistine and cinnarizine in pure vertigo populations remain scarce. Small trials of combination regimens (e.g., betahistine plus dimenhydrinate) suggest additive benefits over monotherapy [6,7], but the individual efficacy and tolerability of each agent are not clearly defined [8]. Pharmacokinetic differences—such as betahistine's rapid hepatic metabolism versus cinnarizine's greater blood–brain-barrier penetration—underscore the need to clarify onset of action and duration of symptom control [7,9]. This randomized controlled trial compares betahistine and cinnarizine in adult patients with vertigo over four weeks, assessing symptom reduction (using the Vertigo Symptom Scale and patient diaries), time to meaningful improvement, and adverse-event profiles to guide optimal antihistamine selection.

Material and Methods

Study Design and Participants

This single-center, randomized, double-blind, parallel-group trial was conducted at the Park Hospital, from February 2024 to April 2025. Institutional ethics approval was obtained, and all participants gave written informed consent. Adults aged 18–65 years with acute or subacute vertigo of presumed peripheral vestibular origin (BPPV, vestibular neuritis, or Ménière's disease) were screened. Eligible subjects had symptom onset within four weeks and a baseline VAS score ≥1. Exclusions included central-origin vertigo, chronic vestibular disorders (>3 months), vestibular suppressant use within seven days, hypersensitivity to study drugs, significant hepatic/renal impairment, pregnancy/lactation, and major comorbidities.

Randomization and Interventions

After screening, 100 participants were randomized 1:1 to receive either betahistine or cinnarizine. A computer-generated block randomization (block size = 4) ensured balanced allocation; assignments were concealed in sealed, opaque envelopes. Both drugs were over-encapsulated to appear identical.

- **Betahistine Group:** Betahistine 8 mg orally three times daily (24 mg/day) for four weeks.
- **Cinnarizine Group:** Cinnarizine 25 mg orally three times daily (75 mg/day) for four weeks.

Doses were taken at approximately 8 am, 2 pm, and 8 pm. Adherence was monitored by pill counts at each visit.

Outcome Measures

Participants recorded daily scores in evening diaries. Outcome score definitions are provided in Table 1.

Variable	Scoring items
VAS (0–4)	0 = No symptom; 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Very severe
MVS (0–4)	Mean of 5 vertigo-related items, each 0 = No symptom to 4 = Very severe
MCSS (0–4)	Mean of 4 concomitant symptoms, each 0 = No symptom to 4 = Very severe
Efficacy (1–5)	1 = Very much improved; 2 = Much improved; 3 = Slightly improved; 4 = Not improved; 5 = Deteriorated
Tolerability (1–4)	1 = Very good; 2 = Good; 3 = Moderate; 4 = Poor

Assessments occurred at baseline (Day 0), daily through Day 7 (VAS, MVS, MCSS), Day 3 and Day 7 interviews (efficacy), and Week 4 (tolerability).

Statistical Analysis

Analyses were by intention-to-treat. Continuous scores used t-tests (or nonparametric tests), categorical outcomes used chi-square, and time-to-event used Kaplan–Meier with log-rank. A $p < 0.05$ was considered significant (SPSS v26.0).

Results

Table 2. Baseline Demographics and Clinical Characteristics

Variable	Betahistine (n = 50)	Cinnarizine (n = 50)	p value
Age (years)	45.0 ± 12.0	38.0 ± 15.0	0.09
Sex, n (%)			0.72
• Male	28 (56 %)	30 (60 %)	
• Female	22 (44 %)	20 (40 %)	
Symptom duration (days)	5.5 ± 2.0	5.6 ± 2.3	0.84

(Values are n (%) or mean ± SD; all p value > 0.05)

Table 3: Comparison of VAS, MVS, and MCSS Scores Between Betahistine and Cinnarizine Groups at Baseline, Day 3, and Day 7.

Outcome (0–4)	Time Point	Betahistine (n = 50)	Cinnarizine (n = 50)	p value
VAS	Baseline	3.0 ± 0.5	3.1 ± 0.6	0.45
	Day 3	1.8 ± 0.6	2.3 ± 0.7	0.010
	Day 7	0.8 ± 0.4	1.2 ± 0.5	0.002
MVS	Baseline	3.2 ± 0.6	3.1 ± 0.7	0.52

	Day 3	2.0 ± 0.6	2.5 ± 0.6	0.005
	Day 7	1.0 ± 0.5	1.5 ± 0.6	0.001
MCSS	Baseline	2.8 ± 0.7	2.9 ± 0.6	0.65
	Day 3	1.7 ± 0.6	2.2 ± 0.5	0.004
	Day 7	0.9 ± 0.4	1.3 ± 0.5	0.003

Table 4: Comparison of Efficacy Scores for Betahistine Versus Cinnarizine at Day 3 and Day 7

Time Point	Cinnarizine (n = 50)	Betahistine (n = 50)	p value
Day 3	3.15 ± 0.60	2.69 ± 0.64	< 0.001
Day 7	2.39 ± 0.56	2.43 ± 0.90	0.79

(Mean ± SD; p < 0.05 Indicates Significant Difference)

Table 5: Tolerability Ratings for Betahistine versus Cinnarizine at Day 3, Week 1, and Week 4.

Time Point	Tolerability Rating	Betahistine (n = 50)	Cinnarizine (n = 50)	p value
Day 3	Very good (1)	40 (80 %)	30 (60 %)	
	Good (2)	8 (16 %)	12 (24 %)	
	Moderate (3)	2 (4 %)	6 (12 %)	
	Poor (4)	0 (0 %)	2 (4 %)	0.02*
Week 1	Very good (1)	45 (90 %)	32 (64 %)	
	Good (2)	4 (8 %)	10 (20 %)	
	Moderate (3)	1 (2 %)	6 (12 %)	
	Poor (4)	0 (0 %)	2 (4 %)	0.01*
Week 4	Very good (1)	35 (70 %)	25 (50 %)	
	Good (2)	10 (20 %)	15 (30 %)	
	Moderate (3)	5 (10 %)	8 (16 %)	
	Poor (4)	0 (0 %)	2 (4 %)	0.04*

(n = 50 per group at each time point; values are n [%]

***p < 0.05 indicates significant difference favoring betahistine)**

Results:

A total of 100 participants were enrolled and randomized equally to the betahistine (n = 50) and cinnarizine (n = 50) groups. All participants completed the study, and no major protocol deviations occurred. Baseline demographics and clinical characteristics are summarized in Table 2. Mean age was 45.0 ± 12.0 years in the betahistine group and 38.0 ± 15.0 years in the cinnarizine group (p = 0.09). Sex distribution was comparable (56 % male vs. 60 % male; p = 0.72), as was mean symptom duration (5.5 ± 2.0 days vs. 5.6 ± 2.3 days; p = 0.84).

Changes in symptom scores (VAS, MVS, MCSS) from baseline through Day 7 are shown in Table 3. At baseline, mean VAS, MVS, and MCSS scores did not differ significantly between groups (VAS: 3.0 ± 0.5 vs. 3.1 ± 0.6, p = 0.45; MVS: 3.2 ± 0.6 vs. 3.1 ± 0.7, p = 0.52; MCSS: 2.8 ± 0.7 vs. 2.9 ± 0.6, p = 0.65). By Day 3, both groups showed symptom improvement, but betahistine recipients had significantly lower mean scores: VAS decreased to 1.8 ± 0.6 versus 2.3 ± 0.7 with cinnarizine (p = 0.010); MVS decreased to 2.0 ± 0.6 versus 2.5 ± 0.6 (p =

0.005); and MCSS decreased to 1.7 ± 0.6 versus 2.2 ± 0.5 ($p = 0.004$). By Day 7, improvements persisted and remained superior in the betahistine group: VAS was 0.8 ± 0.4 versus 1.2 ± 0.5 ($p = 0.002$); MVS was 1.0 ± 0.5 versus 1.5 ± 0.6 ($p = 0.001$); and MCSS was 0.9 ± 0.4 versus 1.3 ± 0.5 ($p = 0.003$).

Efficacy ratings (0–4 scale) at Day 3 and Day 7 are reported in Table 4. On Day 3, mean efficacy score was significantly lower (better) with betahistine (2.69 ± 0.64) compared to cinnarizine (3.15 ± 0.60; $p < 0.001$). By Day 7, mean scores converged (betahistine 2.43 ± 0.90 vs. cinnarizine 2.39 ± 0.56; $p = 0.79$), indicating no significant difference at that time point.

Tolerability ratings at Day 3, Week 1, and Week 4 are detailed in Table 5. On Day 3, 80 % of betahistine patients rated tolerability as "very good" versus 60 % of cinnarizine patients ($p = 0.02$). At Week 1, "very good" ratings increased to 90 % in the betahistine group compared to 64 % in the cinnarizine group ($p = 0.01$). By Week 4, 70 % of betahistine patients still reported "very good" tolerability versus 50 % of cinnarizine patients ($p = 0.04$). Across all three time points, betahistine demonstrated significantly better tolerability.

Discussion

Vertigo represents a substantial burden on patients, manifesting as a false sensation of movement along with accompanying symptoms such as nausea, vomiting, tinnitus, and gait instability [10] Effective management often relies on pharmacotherapy to suppress aberrant vestibular signaling, with betahistine and cinnarizine among the most prescribed agents [10]. Betahistine enhances cochlear and vestibular microcirculation—likely reducing endolymphatic pressure—whereas cinnarizine blocks calcium channels in vestibular hair cells and improves inner-ear perfusion [9,12].

Rapid symptom relief is particularly important in acute vertigo, and in our study, betahistine provided faster improvement than cinnarizine. By Day 3, participants receiving betahistine reported significantly greater reductions in VAS, MVS, and MCSS scores compared to those on cinnarizine ($p < 0.01$ for all), indicating expedited vestibular stabilization [13]. Pianese et al. similarly noted that betahistine's vasodilatory action produces significant symptom relief within five days, whereas cinnarizine and other calcium antagonists often require up to two weeks for maximal effect [14]. By Day 7, efficacy scores converged ($p = 0.79$), mirroring Djelilović-Vranic et al.'s findings in Ménière's disease patients where no difference was observed between betahistine and cinnarizine at one-week [15]. Together, these data suggest that betahistine's H_1-agonist/H_3-antagonist mechanism accelerates vestibular compensation, while cinnarizine's calcium-channel blockade catches up by the end of the first week.

The tolerability difference was also notable. On Day 3, 90 % of betahistine-treated patients rated tolerability as "very good" versus 60 % of those on cinnarizine ($p = 0.01$), and by Week 4 this gap persisted (70 % vs. 50 %, $p = 0.04$). Morozova et al. reported that cinnarizine recipients experienced more sedation and fatigue than those on betahistine in a crossover trial of recurrent vertigo ($p < 0.05$) [16], while Yetiser et al. found higher rates of drowsiness and extrapyramidal symptoms with cinnarizine compared to betahistine ($p < 0.01$) [17]. Mira et

al. also noted that, in patients with peripheral vestibular vertigo, betahistine was associated with minimal gastrointestinal discomfort and virtually no central nervous system effects, resulting in superior adherence compared to other vestibular suppressants [18]. Because excessive sedation can hinder vestibular rehabilitation and increase fall risk, betahistine's superior safety profile supports its role as the preferred first-line agent in acute peripheral vertigo.

Conclusion

Betahistine and cinnarizine both effectively alleviate peripheral vertigo within one week; however, betahistine provides significantly faster symptom relief by Day 3 and maintains a better tolerability profile throughout treatment. This suggests that betahistine's – mechanism enhancing inner-ear microcirculation—offers more prompt vestibular stabilization without the sedation commonly seen with cinnarizine. Consequently, betahistine should be considered the preferred first-line agent for acute or subacute peripheral vertigo.

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