Survey Report

Needs and Preferences for Combination of Cinnarizine + Dimenhydrinate in Vertigo.

Version No.: 1.1

The study was conducted according to the approved protocol and in compliance with the protocol, Good Clinical Practice (GCP), and other applicable local regulatory requirements.

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1 INTRODUCTION

Vertigo is a distressing symptom commonly associated with disorders of the vestibular system, affecting individuals' balance and quality of life. It typically caused by dysfunction in both peripheral (labyrinth and vestibular nerve) and central (vestibular nuclei, brainstem, cerebellum, cerebrum) components of the vestibular system, due to sensory mismatch in higher centers of equilibrium regulation [1,2]. Vertigo is a common and disabling symptom that impacts millions globally, with prevalence of 0.71% in rural Indian populations. It presents a substantial health challenge due to its potential to severely affect balance and quality of life [3]. Their lifetime prevalence is approximately 20 to 30% [2].

Effective management of vertigo is crucial due to its prevalence and association with various underlying disorders, presenting challenges in diagnosis and treatment [4,5]. Treatment for vertigo may involve medication, physical therapy, and psychotherapy, with surgery rarely needed. Moreover, in older patients typically involves vestibular rehabilitation exercises to improve balance and reduce symptoms. Medications like antihistamines (e.g., meclizine) or benzodiazepines (e.g., diazepam) may be used cautiously to alleviate acute episodes. Addressing underlying conditions contributing to vertigo, managing medications to avoid interactions, and promoting a safe environment to prevent falls are critical for management of vertigo [6].

Cinnarizine, a selective calcium channel antagonist with weak antihistamine properties, and dimenhydrinate, an antihistamine with anticholinergic effects targeting the central vestibular system, are established treatments for vertigo. Their combination in a fixed-dose form (20 mg cinnarizine + 40 mg dimenhydrinate) offers several advantages. It provides a dual mode of action that addresses both peripheral and central causes of vertigo, potentially enhancing symptomatic relief compared to monotherapy. Importantly, this combination allows for lower individual doses of each component, thereby reducing the risk of dose-related adverse effects while maintaining efficacy [5,7].

This questionnaire-based survey aimed to gather comprehensive insights from healthcare providers regarding their clinical practices and preferences related to the combination of cinnarizine and dimenhydrinate in treating vertigo. By

addressing the specific needs and preferences in vertigo management, this topic aims to optimize treatment strategies and improve outcomes for patients affected by this challenging condition.

2 RATIONALE OF THE STUDY

The rationale for this study was to evaluate the effectiveness and safety of combining cinnarizine and dimenhydrinate in treating vertigo, leveraging their dual action on both peripheral and central vestibular pathways to potentially enhance symptom relief while minimizing adverse effects associated with higher doses of individual medications. This research addressed the need for improved therapeutic options to manage the debilitating symptoms of vertigo more effectively, thereby enhancing patient outcomes and quality of life.

3 STUDY OBJECTIVE

The primary objective of this study was to evaluate the effectiveness, safety, patient adherence, and cost-effectiveness of the fixed-dose combination in treating vertigo.

4 METHODS

This study was designed as a prospective, randomized, double-blind, placebo-controlled trial assessing the combination therapy in vertigo patients. The survey included 15 questions related to prescribing practices, effectiveness and safety outcomes observed, management of adverse effects, monitoring protocols, factors influencing treatment decisions, and preferences in vertigo management. The study proceeded with participant recruitment based on predefined criteria related to vertigo symptoms. Following screening and confirmation of eligibility, participants were randomly assigned to either the treatment group receiving 20 mg cinnarizine plus 40 mg dimenhydrinate daily or the placebo group.

Baseline assessments established initial symptom severity and quality of life metrics. Treatment was administered according to a specified protocol, with regular follow-up visits to monitor symptom improvement, treatment adherence, and adverse effects. Data collected underwent rigorous statistical analysis to evaluate the efficacy, safety profile, patient adherence, and cost-effectiveness of the combination therapy. Ethical considerations included informed consent,

confidentiality measures, and adherence to regulatory guidelines throughout the study. The study aimed to provide valuable insights into optimizing vertigo management strategies through combined pharmacotherapy.

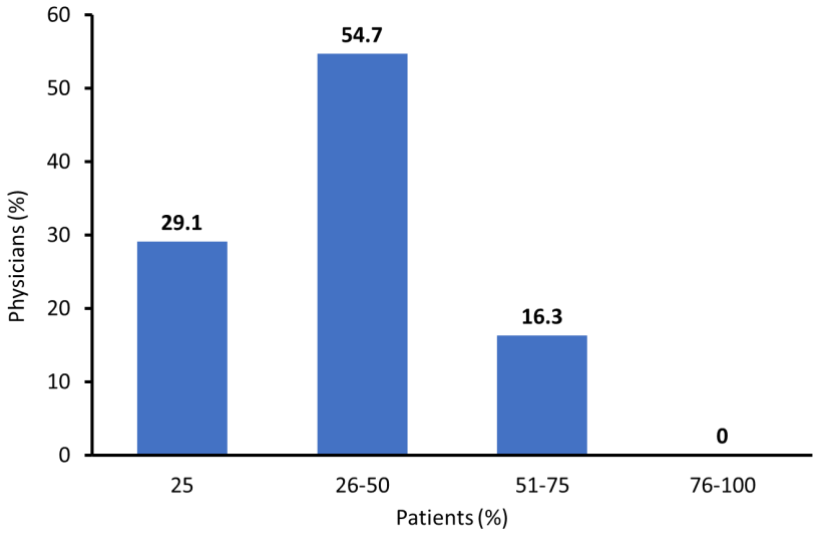
The target sample size for this study was 86 Indian physicians. This number was chosen to ensure a diverse and representative sample, allowing for meaningful statistical analysis of the survey data. This study encompassed obtaining informed consent from participants, ensuring the confidentiality of personal information, adhering to regulatory guidelines, and maintaining transparency in study procedures. Safety monitoring for adverse events and ethical review board approval were integral to maintaining ethical standards throughout the study.

5 RESULTS

A total of 86 HCPs participated in the survey. Below is the summary of the responses.

Question 1: In your clinical practice, of the total patient load what percentage of patients do you encounter patients with vertigo?

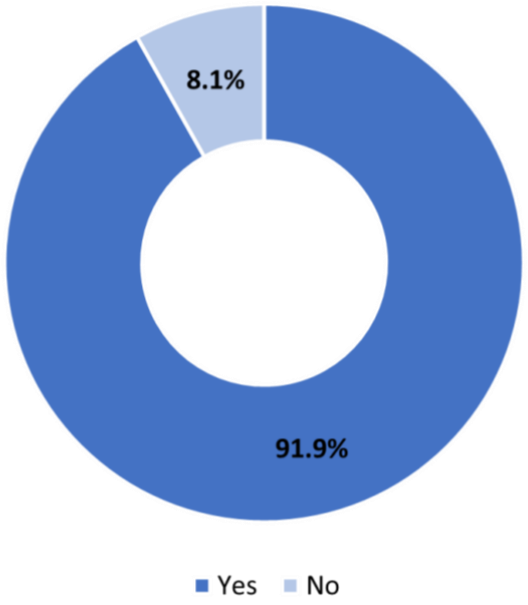
Options	Number of Physicians (N=86)
25%	25 (29.1)
26-50%	47 (54.7)
51-75%	14 (16.3)
76-100%	0
Data presented as n (%)	



- Majority of physicians (54.7%) encountered 26-50% of their total patients with vertigo during their clinical practice.
- Approximately, 29.1% of physicians encounter 25% of patients with vertigo during their daily clinical practice.
- A small group (16.3%) encountered 51-75% of patients with vertigo during their daily clinical practice.
- No physician reported about 76-100% of patients with vertigo during their daily clinical practice.

Question 2: In your clinical practice, do you consider the combination of cinnarizine and dimenhydrinate for the treatment of vertigo?

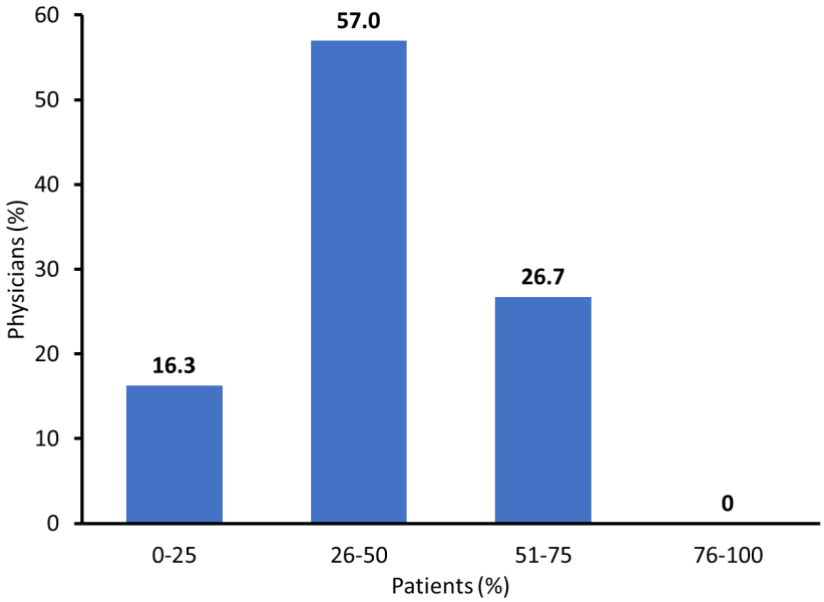
Options	Number of Physicians (N=86)
Yes	79 (91.9)
No	7 (8.1)
Data Presented as n (%).	



- Majority of physicians (91.9%) considered the combination of cinnarizine and dimenhydrinate for the treatment of vertigo in their clinical practices. In contrast, only 8.1% of physician did not considered the combination of cinnarizine and dimenhydrinate for the treatment of vertigo in their practice.

Question 3: In your clinical practice, if you consider the combination, what percentage of your vertigo patients receive this treatment?

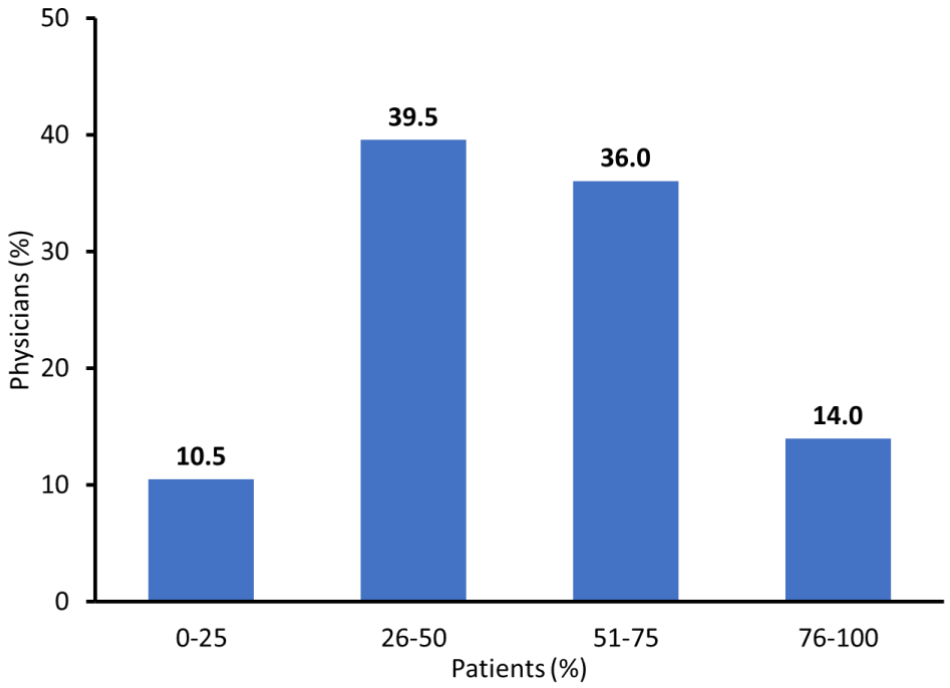
Options	Number of Physicians (N=86)
0-25%	14 (16.3)
26-50%	49 (57.0)
51-75%	23 (26.7)
76-100%	0
Data Presented as n (%).	



- The majority of physicians (57%) believed that after considering the combination, 26-50% of patients received the treatment for vertigo during their clinical practice.
- Approximately 26.7% of physicians believed that after considering the combination, 51-75% of patients received the treatment for vertigo.
- A smaller portion of physicians (16.3%) observed that after considering the combination, 0-25% of patients received the treatment for vertigo.
- In contrast, no physician provided their view on treating vertigo with the considered combination for 76-100% of patients.

Question 4: In your clinical practice, what percentage of your patients experienced a reduction in vertigo symptoms with the combination?

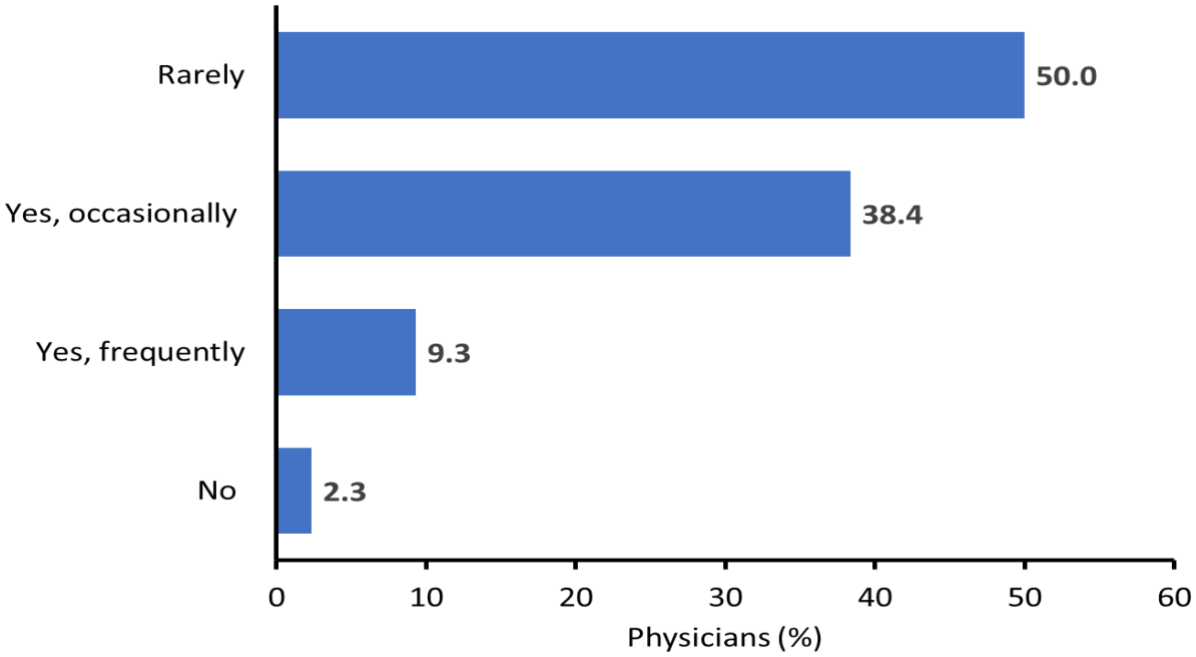
Options	Number of Physicians (N=86)
0-25%	9 (10.5)
26-50%	34 (39.5)
51-75%	31 (36.0)
76-100%	12 (14.0)
Data Presented as n (%).	



- In clinical practice, 39.5% of physicians observed that 26-50% of patients experienced a reduction in vertigo symptoms with the combination.
- Similarly, 36% of physicians observed that 51-75% of patients experienced a reduction in vertigo symptoms with the combination.
- Approximately 14% of physicians observed that 76-100% of patients experienced a reduction in vertigo symptoms with the combination.
- This was followed by 10.5% of physicians who observed 0-25% of patients experienced a reduction in vertigo symptoms.

Question 5: In your clinical practice, have you encountered any adverse effects with the combination?

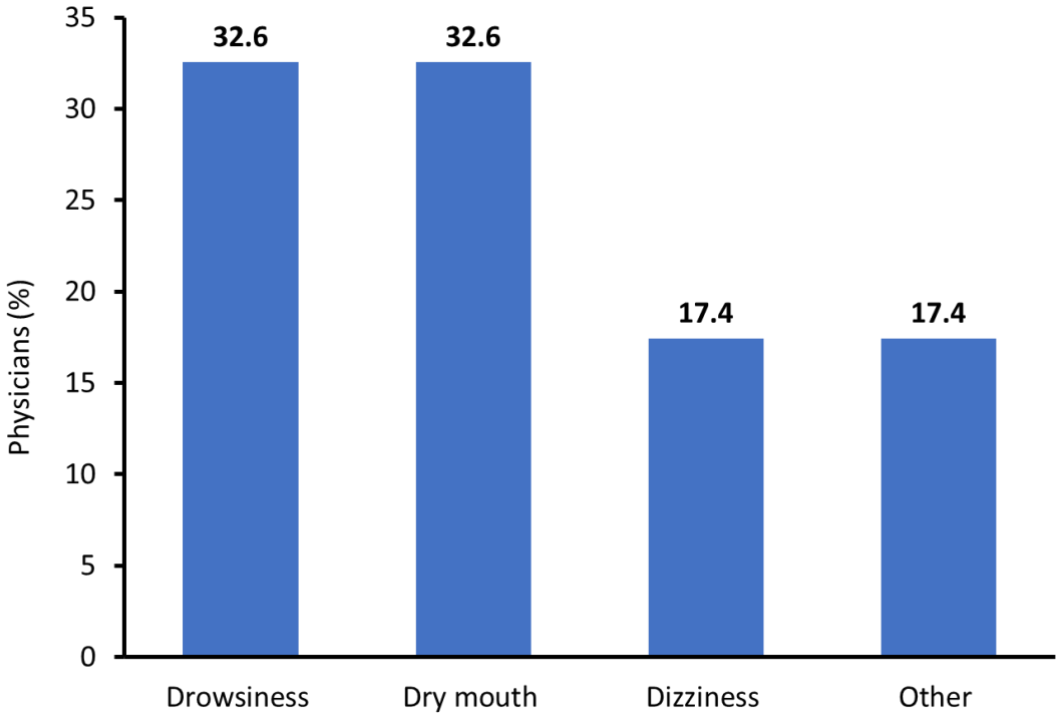
Options	Number of Physicians (N=86)
Rarely	43 (50.0)
Yes, occasionally	33 (38.4)
Yes, frequently	8(9.3)
No	2 (2.3)
Data Presented as n (%).	



- Approximately 50% of physicians had rarely encountered adverse effects with the combination in their clinical practice.
- Additionally, 38.4% of physicians had occasionally encountered adverse effects with the combination in their clinical practice.
- A small group of physicians (9.3%) had frequently encountered adverse effects with the combination, whereas only 2.3% of physicians had not encountered adverse effects with the combination.

Question 6: If yes, please specify the most common adverse effects you have observed. (Select all that apply)?

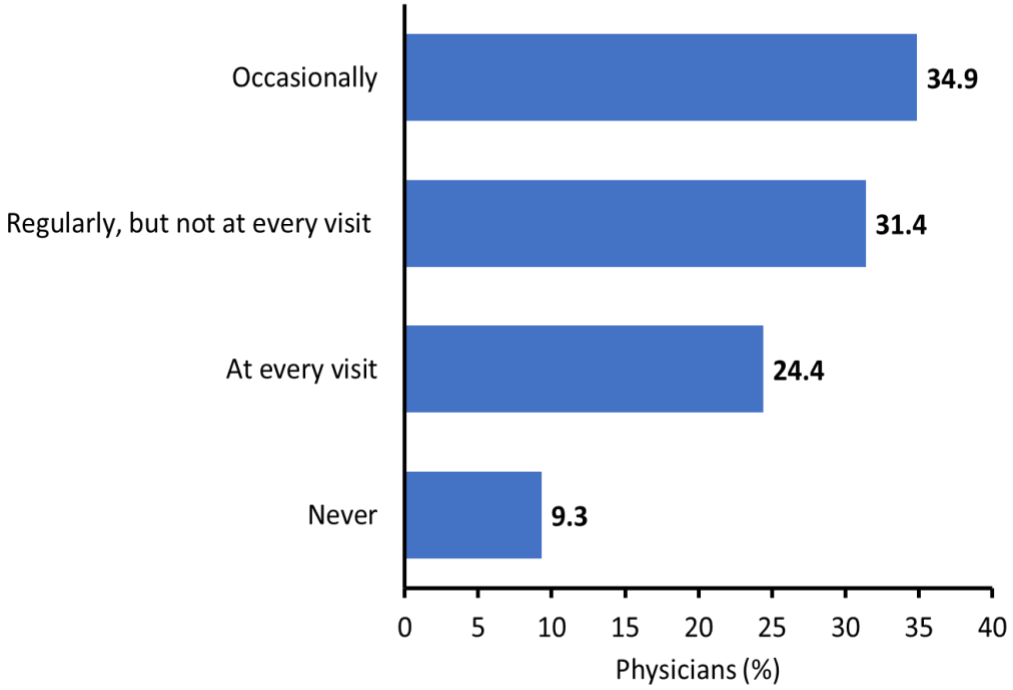
Options	Number of Physicians (N=86)
Drowsiness	28 (32.6)
Dry mouth	28 (32.6)
Dizziness	15 (17.4)
Other (please specify)	15 (17.4)
Data Presented as n (%).	



- About 32.6% of physicians observed drowsiness as the most common adverse effects.
- Similarly, 32.6% of physicians observed dry mouth as the most common adverse effects.
- This was followed by 17.4% observed the dizziness and again 17.4% observed other as common adverse effects.

Question 7: In your clinical practice, how often do you monitor patients receiving this combination for adverse effects?

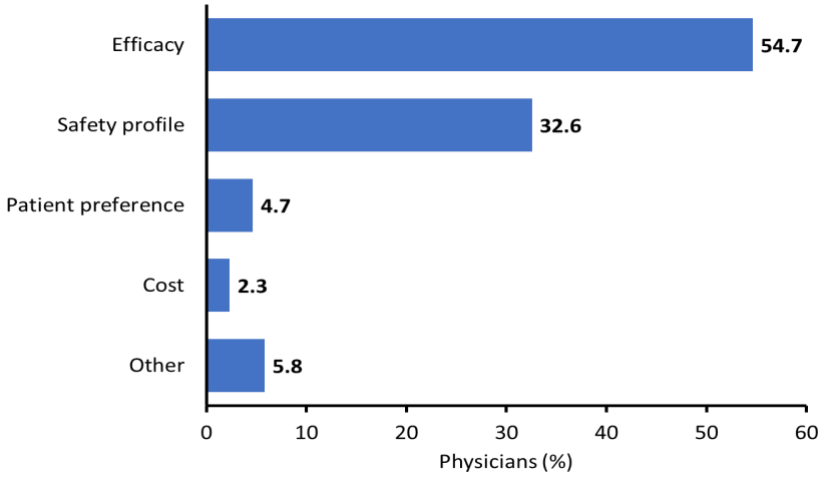
Options	Number of Physicians (N=86)
Occasionally	30 (34.9)
Regularly, but not at every visit	27 (31.4)
At every visit	21 (24.4)
Never	8 (9.3)
Data Presented as n (%).	



- In clinical practices, 34.9% of physician has monitored that occasionally patients receiving this combination for adverse effects.
- Similarly, 31.4% of physicians has monitored regularly, but not at every visit patients receiving this combination for adverse effects.
- Additionally, 24.4% of physicians has monitored it at every visit patients receiving this combination for adverse effects.
- A smaller group 9.3% of physicians has monitored no patients receiving this combination for adverse effects.

Question 8: What factors influence your decision to prescribe this combination for vertigo? (Select all that apply)

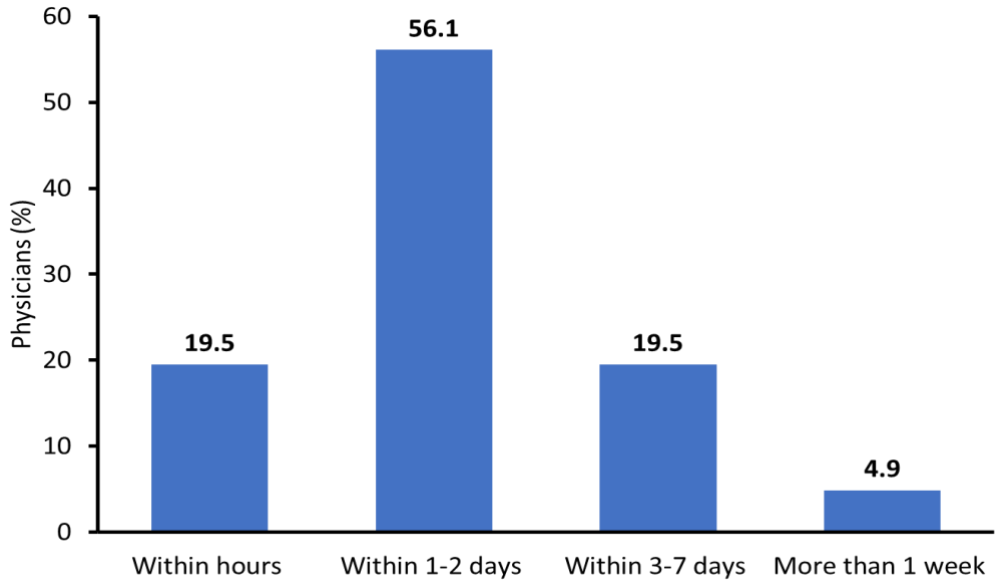
Options	Number of Physicians (N=86)
Efficacy	47 (54.7)
Safety profile	28 (32.6)
Patient preference	4 (4.7)
Cost	2 (2.3)
Other (please specify)	5 (5.8)
Data Presented as n (%).	



- A majority of physicians (54.7%) considered efficacy as the significant factor influencing their decision to prescribe this combination for vertigo during their practices.
- Approximately 32.6% of physicians considered the safety profile as a factor influencing their decision to prescribe this combination for vertigo during their practices.
- Additionally, 5.8% of physicians considered the other as a factor influencing their decision to prescribe this combination for vertigo during their practices.
- This was followed by 4.7% considered the patient preference and 2.3% % considered the cost as a significant factor influencing their decision to prescribe this combination for vertigo during their practices.

Question 9: In your experience, how quickly do patients typically experience relief from vertigo symptoms after starting this combination?

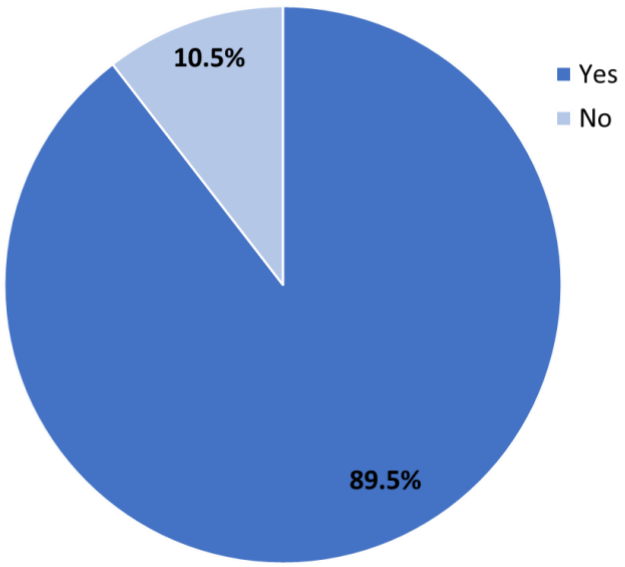
Options	Number of Physicians (N=86)
Within hours	16 (19.5)
Within 1-2 days	46 (56.1)
Within 3-7 days	16 (19.5)
More than 1 week	4 (4.9)
Data Presented as n (%).	



- Majority of physicians (56.1%) experienced patients typically get relief from vertigo symptoms within 1-2 days after starting this combination.
- This followed by 19.5% experienced it within hours and other 19.5% experienced it within 3-7 days.
- Only 4.9% of physicians experienced relief from vertigo symptoms more than 1 week after starting this combination.

Question 10: In your clinical practice. Do you consider the combination of cinnarizine and dimenhydrinate as a first-line treatment for vertigo?

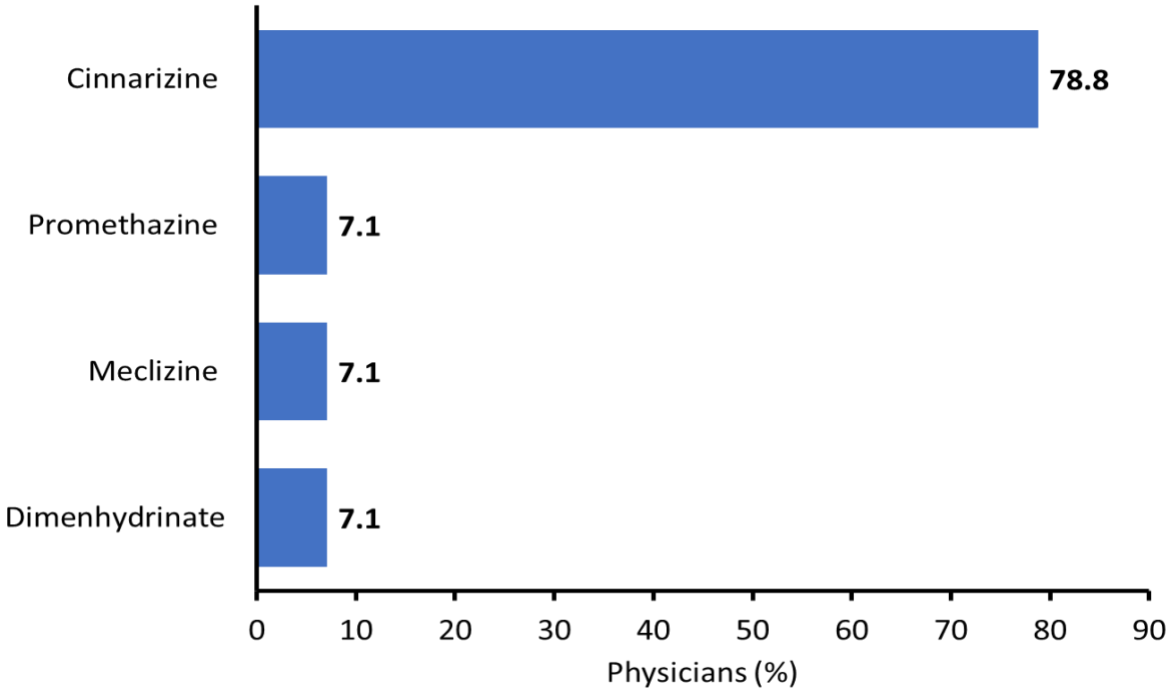
Options	Number of Physicians (N=85)
Yes	77 (89.5)
No	9 (10.5)
Data Presented as n (%).	



- In clinical practice majority of physicians (89%) considered combination of cinnarizine and dimenhydrinate as a first-line treatment for vertigo, whereas only 10.5% of physicians did not considered it as a first-line treatment for vertigo.

Question 11: In your clinical practice, what is your preferred treatment for vertigo patients?

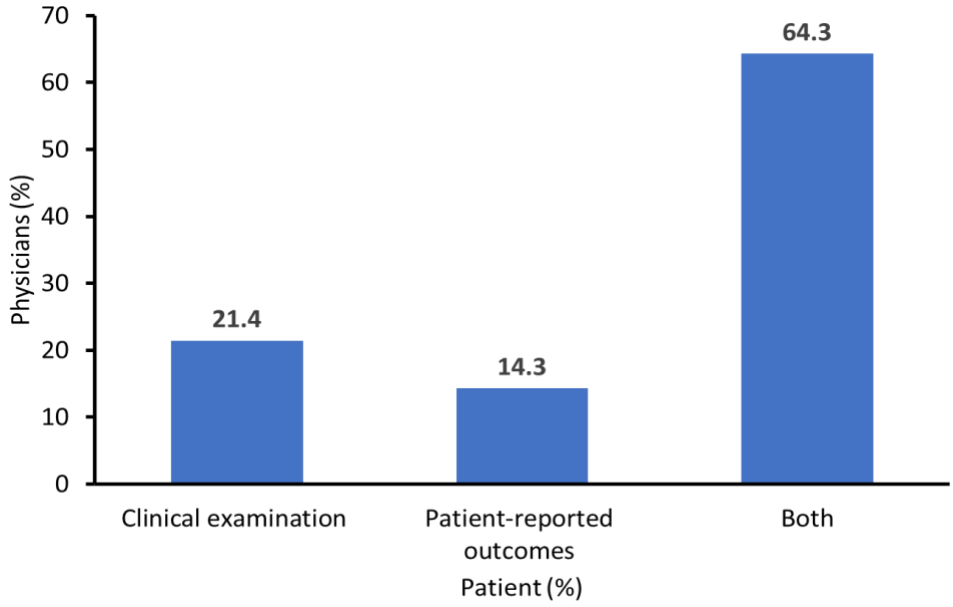
Options	Number of Physicians (N=85)
Cinnarizine	67 (78.8)
Promethazine	6 (7.1)
Meclizine	6 (7.1)
Dimenhydrinate	6 (7.1)
Data Presented as n (%).	



- Majority of physicians (78.8%) preferred Cinnarizine for the treatment of vertigo patients during their clinical practices.
- Additionally, 7.1% of physicians preferred promethazine, similarly 7.1% of physicians preferred meclizine and likewise other 7.1% preferred dimenhydrinate for the treatment of vertigo patients during their clinical practices.

Question 12: In your clinical practice, how do you assess the effectiveness of the combination of cinnarizine and dimenhydrinate in your patients?

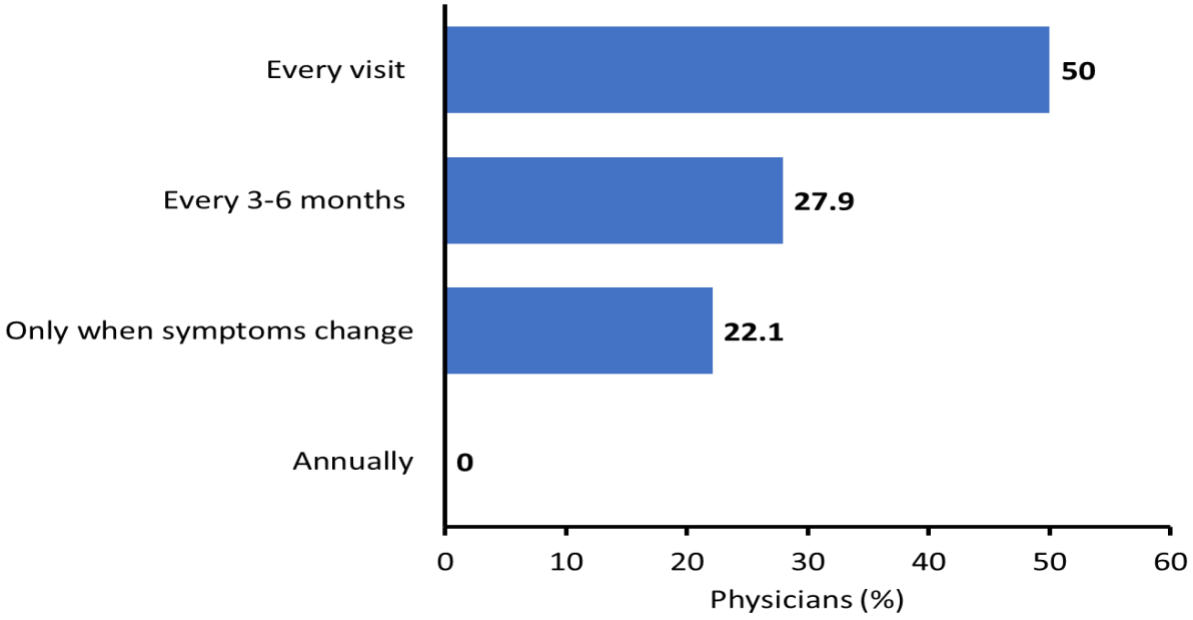
Options	Number of Physicians (N=85)
Clinical examination	18 (21.4)
Patient-reported outcomes	12 (14.3)
Both	54 (64.3)
Data Presented as n (%).	



- Majority of physicians, (64.3%) assessed the effectiveness of the combination of cinnarizine and dimenhydrinate in their patients through both the way clinical examination as well as patient reported outcomes in their clinical practices.
- Around 21.4% (18 physicians) assessed the effectiveness of the combination of cinnarizine and dimenhydrinate in their patients through clinical examination in their clinical practices.
- Around 14.3% (12 physicians) assessed the effectiveness of the combination of cinnarizine and dimenhydrinate in their patients through patient reported outcomes in their clinical practices.

Question 13: In your clinical practice, how often do you review the treatment plan of patients taking the combination of cinnarizine and dimenhydrinate for vertigo?

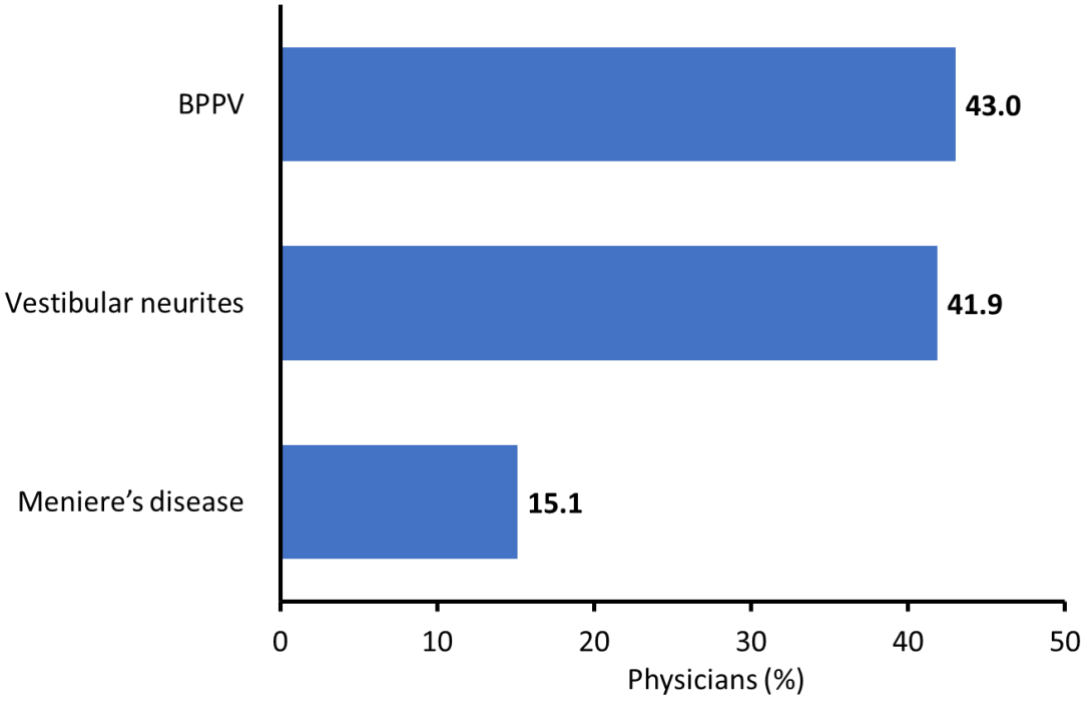
Options	Number of Physicians (N=86)
Every visit	43 (50)
Every 3-6 months	24 (27.9)
Only when symptoms change	19 (22.1)
Annually	0
Data Presented as n (%).	



- Around 50% of physicians review the treatment plan of patients in every visit for taking the combination of cinnarizine and dimenhydrinate for vertigo during their clinical practice.
- This was followed by the 27.9% review the treatment plan of patients in every 3-6 months, 22.1% review it in only when symptoms change for taking the combination of cinnarizine and dimenhydrinate for vertigo during their clinical practice. No physician review it annually.

Question 14: In your clinical practice, what type of vertigo patients you prefer to use Cinnarizine & Dimenhydrinate combination ?

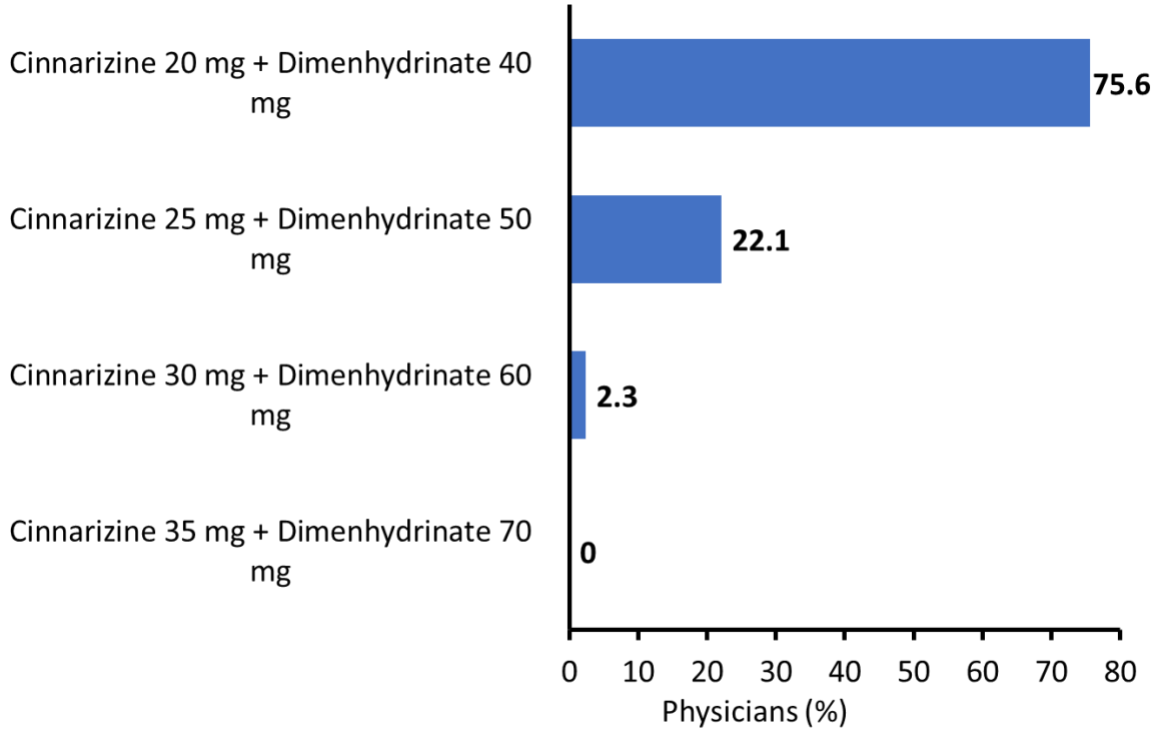
Options	Number of Physicians (N=85)
BPPV	37 (43.0)
Vestibular neurites	36 (41.9)
Meniere's disease	13 (15.1)
Data Presented as n (%).	



- Around 43% of physicians preferred Cinnarizine & Dimenhydrinate combination in BPPV type of vertigo patients during their clinical practices.
- Additionally, 41.9% of physicians preferred Cinnarizine & Dimenhydrinate combination in Vestibular Neurites type of vertigo patients during their clinical practices.
- Small group of physicians (15.1%) preferred Cinnarizine & Dimenhydrinate combination in Meniere's disease type of vertigo patients during their clinical practices.

Question 15: In your clinical practice, what dose of Cinnarizine & Dimenhydrinate combination do you use in your Vertigo patients?

Options	Number of Physicians (N=85)
Cinnarizine 20 mg + Dimenhydrinate 40 mg	65 (75.6)
Cinnarizine 25 mg + Dimenhydrinate 50 mg	19 (22.1)
Cinnarizine 30 mg + Dimenhydrinate 60 mg	2 (2.3)
Cinnarizine 35 mg + Dimenhydrinate 70 mg	0
Data Presented as n (%).	



- Majority of the physicians preferred Cinnarizine 20 mg + Dimenhydrinate 40 mg as dose combination for treatment of vertigo patients in their clinical practice.
- Approximately 22.1% of the physicians preferred Cinnarizine 25 mg + Dimenhydrinate 50 mg as dose combination for treatment of Vertigo patients in their clinical practice.

- Small group of physicians 2.3% preferred Cinnarizine 30 mg + Dimenhydrinate 60 mg as dose combination for treatment of Vertigo patients in their clinical practice. Whereas no physicians preferred Cinnarizine 35 mg + Dimenhydrinate 70 mg dose combination for treatment of Vertigo patients in their clinical practice.

6 SUMMARY

This survey of physicians revealed that in clinical practice, a majority of physicians encountered 26-50% of their total patients presenting with vertigo, with 32.6% encountering 25% and 16.3% encountering 51-75%. Almost all physicians (91.9%) considered the combination of cinnarizine and dimenhydrinate as a treatment option for vertigo, citing efficacy (54.7%) as the primary factor influencing their prescribing decisions, followed by safety concerns (32.6%). Patient response varied, with 57% observing 26-50% receiving treatment and varying degrees of symptom reduction: 39.5% saw 26-50% improvement, 36% noted 51-75% improvement, and 14% reported 76-100% improvement. Adverse effects, primarily drowsiness and dry mouth (each 32.6%), were monitored occasionally (38.4%) or regularly (31.4%) by physicians. Relief from vertigo symptoms was typically observed within 1-2 days by 56.1% of physicians. The combination was widely regarded (89%) as a first-line treatment, with cinnarizine (78.8%) preferred over other medications like promethazine, meclizine, or alternative doses. Effectiveness assessments were commonly conducted through clinical examination and patient-reported outcomes (64.3%), with treatment plans reviewed frequently during visits (50%) or every 3-6 months (27.9%). Specific preferences for BPPV (43%) and Vestibular Neuritis (41.9%) were noted, while 15.1% favored its use in Meniere's disease.

7 DISCUSSION

The survey findings highlight several key insights into physicians' practices and perspectives regarding the combination of cinnarizine and dimenhydrinate for treating vertigo. A significant majority of physicians (54.7%) reported encountering 26-50% of their patients with vertigo, with smaller percentages encountering either

fewer or more severe cases. Nearly all physicians (91.9%) considered this combination therapy as a viable treatment option for vertigo, citing efficacy (54.7%) as the primary determinant in their prescribing decisions, followed by considerations of safety (32.6%). Responses varied regarding patient uptake, with 57% of physicians estimating that 26-50% of eligible patients received the treatment, while 26.7% believed 51-75% received it, and 16.3% reported lower uptake rates.

Regarding treatment outcomes, a significant proportion of physicians observed varying degrees of symptom reduction: 39.5% noted 26-50%, 36% observed 51-75%, and 14% reported 76-100% improvement among treated patients. Adverse effects were monitored with varying frequency, with approximately half of physicians rarely encountering them, and 9.3% frequently noting adverse effects such as drowsiness and dry mouth (each 32.6%). Relief from vertigo symptoms was typically experienced within 1-2 days by a majority (56.1%) of physicians, with smaller percentages noting quicker or longer onset times.

The combination was widely regarded (89%) as a first-line treatment for vertigo, with cinnarizine (78.8%) being the preferred choice among physicians. Assessment of treatment effectiveness commonly involved both clinical examination and patient-reported outcomes (64.3%), while smaller percentages relied solely on clinical examination (21.4%) or patient reports (14.3%).

Treatment plans were regularly reviewed by physicians during visits (50%) or every 3-6 months (27.9%), with specific preferences noted for different types of vertigo: BPPV (43%), Vestibular Neuritis (41.9%), and Meniere's disease (15.1%). Dosing preferences centered on cinnarizine 20 mg + dimenhydrinate 40 mg (majority), with some variability in preferred dosages observed among a smaller group of physicians.

In conclusion, the survey underscores a consensus among physicians regarding the efficacy and safety considerations of the cinnarizine and dimenhydrinate combination for vertigo treatment, alongside varied practices in patient management and treatment evaluation across different types of vertigo.

8 CLINICAL RECOMMENDATIONS

- Consideration of Efficacy and Safety: Given that efficacy (54.7%) and safety (32.6%) were primary factors influencing prescribing decisions, clinicians should prioritize these aspects when selecting treatment options for vertigo.
- Patient Uptake and Treatment Initiation: Since only 57% of physicians reported that 26-50% of eligible patients received the combination therapy, efforts should focus on improving patient education and adherence strategies to enhance uptake rates.
- Monitoring of Treatment Outcomes: Regular assessment of treatment outcomes, including symptom reduction and adverse effects, is crucial. Physicians observed varying degrees of symptom improvement (39.5% to 76-100%) and monitored adverse effects such as drowsiness and dry mouth (32.6%). Monitoring should be tailored to individual patient needs and treatment responses.
- Timely Onset of Symptom Relief: Majority of physicians (56.1%) noted that relief from vertigo symptoms typically occurred within 1-2 days of starting treatment. Clinicians should inform patients about expected timelines for symptom relief and manage expectations accordingly.
- First-Line Treatment Consideration: With 89% of physicians regarding the combination as a first-line treatment for vertigo, it should be considered early in the treatment algorithm. This approach aligns with the consensus on its efficacy and safety profile.
- Individualized Treatment Plans: Tailoring treatment plans based on specific vertigo types (e.g., BPPV, Vestibular Neuritis, Meniere's disease) and patient preferences is essential. Dosing preferences centered around cinnarizine 20 mg + dimenhydrinate 40 mg, although some variability was observed, suggesting flexibility in dosing based on patient response.
- Regular Review and Assessment: Establishing regular follow-up visits (every 3-6 months or as needed) for reviewing treatment efficacy, adjusting doses if necessary, and monitoring adverse effects is recommended. This approach ensures ongoing management and optimization of treatment outcomes.
- Overall, these recommendations aim to guide clinicians in optimizing the use of cinnarizine and dimenhydrinate for vertigo management, emphasizing

personalized care based on efficacy, safety considerations, and patient-specific factors.

9 CONSULTANT OPINION

Based on the survey findings, the combination of cinnarizine and dimenhydrinate emerges as a preferred and effective treatment option for vertigo among physicians. Its high efficacy rating (54.7%) and minimal adverse effects, predominantly drowsiness and dry mouth (32.6%), underscore its suitability as a first-line therapy (89%). Physicians commonly monitor treatment outcomes through both clinical examination and patient-reported outcomes (64.3%), adapting dosing and follow-up intervals based on vertigo type and individual patient response. This comprehensive approach ensures tailored care and optimized symptom management, reinforcing the combination's role in addressing vertigo effectively with a favorable safety profile.

10 MARKET OPPORTUNITIES

- Expanded Patient Education: Develop targeted educational materials to increase patient awareness and acceptance of the combination therapy.
- Enhanced Adherence Strategies: Innovate adherence tools and technologies to improve patient compliance with prescribed treatments.
- Tailored Dosing Options: Introduce more flexible dosing options to accommodate individual patient needs and optimize treatment outcomes.
- Specialized Vertigo Management Programs: Establish specialized clinics or programs focusing on comprehensive vertigo management using the combination therapy.
- Clinical Trials and Research: Invest in further clinical research to validate and expand the use of the combination in different types and severities of vertigo.

11 MARKET POSITIONING

Physicians universally recognize the combination of cinnarizine and dimenhydrinate as highly effective, with significant proportions reporting symptom reduction rates between 26% to 100% among treated patients. Despite concerns over adverse effects like drowsiness and dry mouth, encountered by 9.3% of physicians, the majority rarely experienced these issues, affirming the combination's overall safety profile.

Widely accepted as a first-line treatment (89%), particularly favored for its efficacy in managing vertigo across different types, including BPPV, Vestibular Neuritis, and Meniere’s disease. While uptake rates varied, efforts to enhance patient education and adherence could potentially optimize treatment outcomes.

Standard dosing of cinnarizine 20 mg + dimenhydrinate 40 mg is preferred, though some variability exists, suggesting flexibility in dosing strategies based on individual patient needs. Regular review of treatment plans (50% during visits, 27.9% every 3-6 months) underscores the importance of ongoing assessment to tailor treatments and manage outcomes effectively.

Combination of clinical examination and patient-reported outcomes (64.3%) provides a comprehensive approach to evaluating treatment effectiveness, ensuring a holistic patient care approach. Cinnarizine emerges as the preferred medication (78.8%), reflecting its established efficacy and familiarity among clinicians.

Positioned as a reliable and effective therapeutic option in vertigo management, based on robust clinical support and widespread physician acceptance. Rapid relief from vertigo symptoms within 1-2 days for a majority of patients (56.1%) highlights the treatment's quick onset of action and patient satisfaction.

Continued emphasis on optimizing efficacy, minimizing adverse effects, and enhancing patient adherence can further solidify the combination's role in vertigo treatment protocols.

12 REFERENCES

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