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### To compare the safety and effectiveness of Betahistine dihydrochloride vs a fixed combination of Cinnarizine and dimenhydrinate in vertigo patients in Tertiary Care Hospital

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#### ABSTRACT

**Objectives:** The aim of the current study was to examine the comparison of efficacy and safety of cinnarizine and dimenhydrinate vs Betahistine dihydrochloride and evaluate the psychological distress of vertigo patients. **Material and Methods:** Over the course of six months, this observational research was conducted at Adesh Hospital in Bathinda on over 160 patients who visited the otorhinolaryngology department, Adesh Institute of Medical Sciences and Research, Adesh Hospital, Bathinda. **Results:** The patients taking cinnarizine and dimenhydrinate have reduced symptoms than patients taking betahistine dihydrochloride, combination therapy is more efficient. In terms of safety both drugs are equally safe and patients have mild to moderate psychological distress due to vertigo. **Conclusion:** This study concluded that the patients taking combination therapy has less moderate symptom of vertigo than the patient taking monotherapy which shows that the efficacy of the Cinnarizine and Dimenhydrinate is more than the Betahistine dihydrochloride.

**KEYWORDS:** Cinnarizine, Dimenhydrinate, Betahistine, Vertigo, safety

## INTRODUCTION

Vertigo is characterized by a sense of movement, such as swaying or rotating, in one's own body, in the environment, or in both and it can also cause symptoms such as cold, sweating, nausea, and vomiting. Vertigo has a variety of underlying causes, some of which include psychogenic factors as well as peripheral or central vestibular system dysfunction. Primary symptoms of illnesses affecting the vestibular system include vertigo and dizziness. Their clinical characteristics are diverse since these can be brought on by each of two chronic or transient illnesses. The most prevalent kind is called benign paroxysmal vertigo, and it consists of brief acute bouts that don't interfere with daily activities. Conversely, vestibular neuritis and the Meniere's disease, and other types of recurrent vertigo are characterised by symptoms that last more and reoccur with varying frequency and unpredictability (like vertigo followed by dizziness). (Benecke et al. 2013)

The relocation of deteriorated otoconia into the semicircular canals, which makes their sensitivity to head movements, is the explanation for BPPV. BPPV is frequently described by patients as a brief impression of a spinning environment. It is a personal experience brought on by adjustments to head position. Otoconia move from the utricular macula to the semicircular canals, causing BPPV. Patients with BPPV are significantly restricted in their everyday activities. BPPV's cause is mainly unclear. In fact, an analysis indicated that the following determinants for BPPV recurrences: gender, high blood pressure, diabetes, dyslipidaemia, and vitamin D insufficiency. The result that older women who don't exercise regularly have a higher chance of developing BPPV than those who do is related to this. (Kim et al. 2020)

The most often prescribed anti-vertigo medication in the world is likely betahistine, which is typically prescribed as betahistine dihydrochloride with dose of 16 mg thrice a day. Although its precise mode of action on the vestibular system is still unclear, it is a histamine analogue that functions as a strong H3 antagonist and a weak H1 agonist. The main symptoms of Menière's disease may include vertigo. Betahistine is a widely used and approved medication for vertigo associated with Menière's disease. In cases with somewhat vague symptomatology and aetiology, primary care doctors routinely prescribe betahistine.

Since more than three decades ago, vertigo from diverse causes has been successfully treated with a constant combination medication made of cinnarizine and dimenhydrinate. Its anti-vertiginous effectiveness is because of the twofold mode of action. One of the actions is that Cinnarizine, which is a calcium channel blocker, primarily affects the peripheral vestibular system by preventing calcium from entering vestibular cells and so regulating consequential vestibular transmission. The other is the vestibular nuclei and vomiting centre's which is regulated by histamine- and cholinergic-receptor activities are inhibited by the antihistamine dimenhydrinate to produce its antivertigo and antiemetic effects. (Scholtz AW et al. 2019)

A histamine-like medication called betahistine works as both a partial H1 receptor agonist and an H3 receptor antagonist. The effectiveness of betahistine is thought to be due to its vascular actions, which cause a surge in blood flow to the internal ear. However, betahistine was also successful in treating vestibular disorders unrelated to vascular deficiency of the internal ear, suggesting that it may possibly have some outcome on the central vestibular system. Histamine mimics boost the synthesis of the chemical mostly via blocking the H3 auto receptors. (Molnar et al. 2019)

There are at least three psychologically incapacitating symptoms associated with vertigo. First of all, because it is difficult to recognize and/or perceive visually, patients frequently fail to pinpoint its cause and may develop somatization. This is because vertigo arousal is frequently unpredictable. Thirdly, it causes intense bodily and mental sensations to be involved. Even though there hasn't been much research to evaluate these components in controlled trials, it is believed that the co-occurring conditions of psychopathological factors and vestibular diseases is implicated in the feeling of vertigo. (Monzani, D et al. 2001)

## **MATERIALS AND METHODS**

### **Study design**

This observational study was approved by AIPBS College Research Committee and Ethics Committee for Biomedical and Health Research, Adesh University. It was carried out at the Department of Otorhinolaryngology, Adesh Institute of Medical Sciences and Research, Adesh Hospital Bathinda,

### **Study criteria**

Information was gathered from individuals experiencing vertigo via a data collection form that includes details on the factors that contribute to the vertigo. The patients who meet the inclusion criteria are the patients who were suffering from vertigo in the Out-patient department and the exclusion criteria involves patients having underlying complications such as labyrinthitis and patients having hypersensitivity to the study medications were also excluded.

### **Method of data collection**

The information gathered using the pre-made structured data questionnaire form. Interviews were scheduled at the institute with experts and other specialists' aid, serving as the data questionnaire method for the study. Before circulating the data questionnaire form, the chosen subjects received a thorough explanation of the study's objectives and the information contained in the data collecting form, along with assurances of data confidentiality. The individuals that visited the Department of Otorhinolaryngology at Adesh Hospital were the chosen subjects. Signing a signed consent form was required of those who consented to take part in the research.

### **Statistical Analysis of data**

IBM SPSS version 26.0<sup>®</sup> was used for all data recording and analysis where a p-value of less than 0.05 was used for the Chi-square test.

## **RESULTS**

The entire 160 patients who visited the Department of Otorhinolaryngology, Adesh Hospital, Bathinda were examined to compare the efficacy and safety of the drugs given to the vertigo patients and to evaluate the psychological distress of vertigo patients. The outcomes were explained using both the analytical and descriptive analyses. Test which was used to calculate the results was Pearson's Chi-Square, with a p-value of less than 0.05 being deemed significant for an association.

### **Age in years**

It was discovered that vertigo was more common in the age range of 31-60 years [130 (81.3%)] followed by 61 & above [26 (16.3%)] and then 18-30 years [4 (2.5%)]. Thus, The age range that vertigo most commonly affects is 31-60 years.

**Table 1: Distribution according to age in years**

S No.	Age in years	Frequency	Percent	Valid Percent	Cumulative Percent
1.	18-30 years	4	2.5	2.5	2.5
2.	31-60 years	130	81.3	81.3	83.8
3.	61 &above	26	16.3	16.3	100.0
4.	Total	160	100.0	100.0	

### Gender of the patients

The prevalence of the vertigo is higher in males [120(75.0%)] than in females [40(25.0%)], according to the degree of exposure to the disease's risk factors.

**Table 2: Distribution according to the gender of the patients**

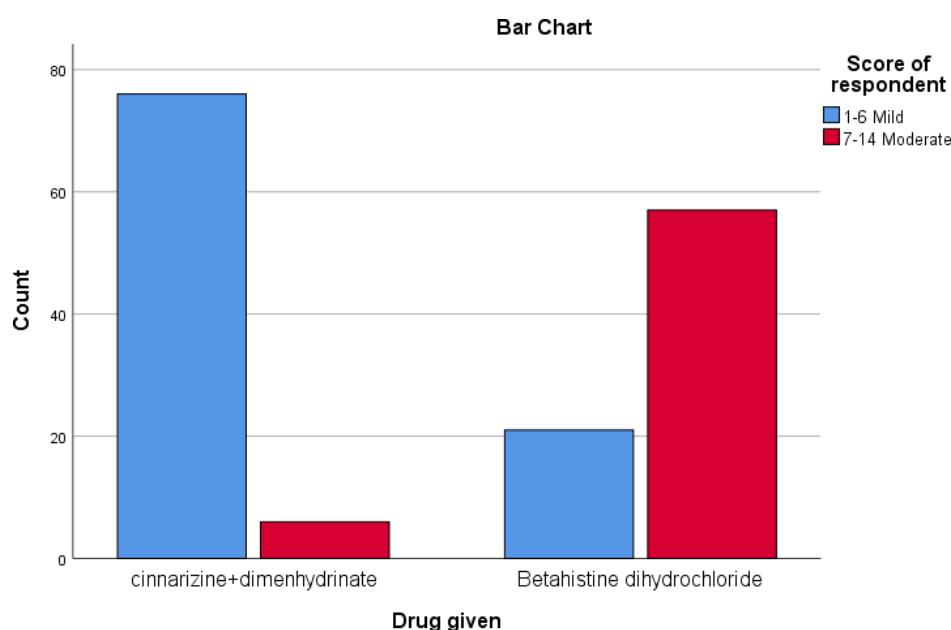
S No.	Gender	Frequency of patients	Percent	Valid Percent	Cumulative Percent
1.	Male	120	75.0	75.0	75.0
2.	Female	40	22.0	25.0	100.0
3.	Total	160	100.0	100.0	

### Efficacy of the combination therapy (Cinnarizine+Dimenhydrinate) with monotherapy (Betahistine dihydrochloride)

According to the symptom severity among the patients, the moderate symptoms in the patients taking Betahistine dihydrochloride was observed to be high [57(35.6%) out of total 78(48.8%)] than the mild symptoms [21(13.1%) out of total 78(48.8%) patients] whereas in patients taking Cinnarizine+Dimenhydrinate the moderate symptom was low [6(3.8%) out of total 82(51.2%)] than the mild symptom [76(47.5%) out of total 82(51.2%)]. Hence, the patients taking combination therapy has less moderate symptom than the patient taking monotherapy which shows that the efficacy of the Cinnarizine+Dimenhydrinate is more than the Betahistine dihydrochloride.

**Table 13: Comparison of the efficacy of the combination therapy with monotherapy**

Symptom severity	Cinnarizine+Dimenhydrinate		Betahistine dihydrochloride	
	Number of patients	Percentage of total patient	Number of patients	Percentage of total patient
Mild symptom	76	47.5%	21	13.1%
Moderate symptom	6	3.8%	57	35.6%
Total	82	51.2%	78	48.8%

**Figure 1: Association of symptom severity with drug**

### **Safety of the combination therapy (Cinnarizine+Dimenhydrinate) with monotherapy (Betahistine dihydrochloride)**

According to the complaints given by patients after taking cinnarizine+dimenhydrinate there were only 2(1.3%) patients with headache complaint, 5(3.1%) patients with indigestion complaint and patients with no complaint were 75(46.9%) out of total 82(51.2%). The complaints of patientstaking betahistinedihydrochloride were only indigestion 4(2.5%) and the patients with no complaints were 74(46.3%) out of total 78(48.8%) patients. This shows that both therapies which were combination therapy and monotherapyare safe.

**Table 14: Comparison of the safety of the Cinnarizine+Dimenhydrinate with Betahistine dihydrochloride**

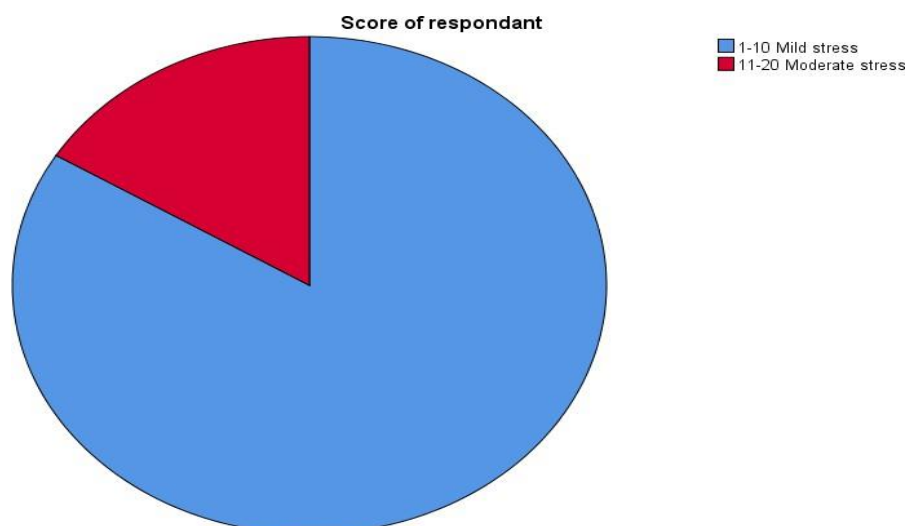
Complaints by patients after taking the drug	Cinnarizine+Dimenhydrinate		Betahistine dihydrochloride	
	Number of patients	Percentage of total patient	Number of patients	Percentage of total patient
Headache	2	1.3%	0	0.0%
Indigestion	5	3.1%	4	2.5%
None	75	46.9%	74	46.3%
Total	82	51.2%	78	48.8%

**Evaluation of psychological distress in vertigo patients**

In vertigo patients it was observed that the patients have mild distress of 134(83.8) and moderate distress of 26(16.3) due to vertigo.

**Table 30: Distribution of psychological distress in vertigo patients**

S No.	Psychological Distress	Frequency	Percent	Valid Percent	Cumulative Percent
1.	Mild distress	134	83.8	83.8	83.8
2.	Moderate distress	26	16.3	16.3	100.0
3.	Total	160	100.0	100.0	



### Association of the symptom severity with the therapy

The symptom severity in the patients who had vertigo had more moderate to severe problem with Betahistine as compared to those who have given Cinnarizine + Dimenhydrinate.

76(47.5%) patients were having mild symptom who had taken Cinnarizine+Dimenhydrinate whereas 21(13.1%) patients were recorded to have mild symptom with Betahistine. 6(3.8%) patients were founded to have moderate problem as compared to 57(35.6%) patient who were given Betahistine.

The association of the mild symptom with the Cinnarizine+Dimenhydrinate is found to be highly significant with the p value (0.000). The association of the moderate symptom with the Betahistine is highly significant with the p value (0.001).

The association of the safety of the patients with both drug use is highly significant with the p value of (0.002).

The association of the moderate stress with the vertigo is found to be highly significant with p value of (0.000).

## DISCUSSION

The purpose of the research was to compare the effectiveness and safety of a fixed combination of cinnarizine and dimenhydrinate vs betahistine dihydrochloride. It was a hospital-based study in which symptoms were observed. Data was collected from patients experiencing vertigo via a data collection form that includes details on the factors that



contribute to the vertigo. Test which was used to calculate the results was Pearson's Chi-Square, with a p-value of less than 0.05 to assess the effectiveness and safety of cinnarizine and dimenhydrinate vs Betahistine dihydrochloride and to evaluate the psychological distress of vertigo patients. After assessing the symptoms in vertigo patients it was noted that the patients taking cinnarizine and dimenhydrinate have no severe vertigo symptoms and have very less moderate symptoms [6(3.8%) out of total 82(51.2%)] compared to the patients taking betahistine dihydrochloride [57(35.6%) out of total 78(48.8%)] which shows the efficacy of cinnarizine and dimenhydrinate is more than betahistine dihydrochloride and by observing the complaints of the patients after taking medicines it shows that there were only 2-4 complaints of headache and indigestion which showed that both the therapies (combination therapy and monotherapy) are safe.

## **CONCLUSION**

This study concluded that the patients taking combination therapy has less moderate symptom than the patient taking monotherapy which shows that the efficacy of the Cinnarizine+Dimenhydrinate is more than the Betahistine dihydrochloride. Based on the findings and observations, it can be said that both the therapies are safe. The efficacy of the combination therapy and the monotherapy were determined by the symptoms during the second visit. In vertigo patients, after the evaluation it was observed that the patients have mild distress due to vertigo as vertigo affect the daily life of the patients.

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