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Efficacy of medical therapy in the prevention of residual dizziness after successful repositioning maneuvers for Benign Paroxysmal Positional Vertigo (BPPV)

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Abstract. *Efficacy of medical therapy in the prevention of residual dizziness after successful repositioning maneuvers for Benign Paroxysmal Positional Vertigo (BPPV). Objectives*: The aim of this study was to investigate the efficacy of trimetazidine, betahistine, and ginkgo biloba extract in the treatment of residual dizziness after successful repositioning maneuvers for benign paroxysmal positional vertigo.
Methodology: This was a randomized controlled clinical trial. Complete clinical data were analyzed from 100 patients (27 men and 73 women; mean age 52.16 ± 13.2 years, range 11-80 years) with BPPV who underwent succcessful repositioning maneuvers and then received betahistine, trimetazidine, gingko biloba extract, or no medication ($n = 25$ for each group) for 1 week. On days 1, 3, and 5 after the repositioning maneuver, scores obtained from the Dizziness Handicap Inventory (DHI) questionnaire were compared.
Results: There were no statistically significant differences in the premedication DHI scores of patients with residual dizziness among the four groups ($p > 0.005$). After 3 and 5 days of treatment, the mean DHI scores of the groups receiving medication did not differ significantly from the the mean DHI score of the control group ($p > 0.005$).
Conclusions: Our study results suggest that betahistine, trimetazidine, and gingko biloba extract do not alleviate residual dizziness after successful repositioning maneuvers.

Introduction

Residual dizziness is a commonly experienced and persistent imbalance that may last for days after successful repositioning maneuvers. Previous authors have explained "residual dizziness after successful repositioning" as follows: Residual dizziness is the sensation of unsteadiness or lightheadedness without rotational and/or positional vertigo even after successful repositioning maneuvers have improved positional vertigo.[1]

These symptoms of unknown origin may affect the quality of life of patients by decreasing postural control, which can contribute to falling and psychological problems (e.g., anxiety, panic, agoraphobia, and depression).[2] Furthermore, these patients may perceive the sensation as a recurrence of vertigo; this can lead to recurrent consultation, particle repositioning maneuvers, and prescriptions.[3]
Antivertiginous drugs (e.g., betahistine) that improve labyrinthine microcirculation are still being administered by many clinicians to treat residual dizziness.[3,4] However, there is no good evidence that these medications provide relief for residual dizziness compared to placebo.

To the best of our knowledge, the therapeutic efficacy of adjuvant antivertiginous medication in addition to the canalith repositioning procedure has not been documented previously. Therefore, the aim of this study was to compare the efficacy of three different antivertiginous drugs versus no medication in the treatment of residual dizziness. Another objective of the study was to investigate the necessity of vestibular medication in the treatment of residual dizziness after successful repositioning maneuvers.

Patients and methods

The study was approved by the Institutional Review Board of Kecioren Training and Research Hospital. Patients included in the study were recruited for assessment between January 2013 and April 2013 and were prospectively followed by the same interviewer for at least 1 week. An interviewer blinded to groups evaluated the patients 1, 3, and 5

days after the repositioning maneuver. A total of 100 patients (27 men and 73 women) suffering from posterior semicircular canal (PSC) BPPV were enrolled in the study.

The diagnosis of BPPV was based on a history of brief episodes of vertigo and the results of the Dix–Hallpike test, which was performed by physicians. The Dix–Hallpike test was considered positive if fatigable nystagmus was recorded with appropriate positioning, typical features presented with brief latency (1-5 seconds) and duration (<1 min), and symptoms were reversed upon assuming an upright position The same consultant applied the Epley maneuver to the patients.[5,6]

Patients who reported no residual dizziness were not included in the study. In addition, patients diagnosed with BPPV-like central nervous system disorders; bilateral BPPV; cardiopulmonary, musculoskeletal, neurological, or psychological disorders; or a history of drug or alcohol abuse were excluded from the study.

After the repositioning maneuver, patients were randomly divided by means of computerized rapid number generation into four groups according to the antivertiginous drugs administered. The groups received the following treatments for 1 week: group 1, two doses/day of 24 mg of betahistine; group 2, three doses/day of 20 mg of trimetazidine; group 3, two doses/day of 80 mg of gingko biloba; and group 4, no medication.

Dizziness assessment follow-up was conducted on days 3 and 5 day after the repositioning maneuver; at this time, diagnostic maneuvers were repeated. Dizziness Handicap Inventory (DHI) questionnaires were completed on days 1, 3, and 5 of medication administration. None of the patients included in this sample presented residual positional nystagmus upon follow-up examination.

Statistical analysis

Data obtained from the study are presented as mean ± standard deviation (SD) for normally distributed continuous variables, median (minimum-maximum) for continuous variables with a skewed distribution, and frequencies for categorical variables. Pearson's chi-square test was used for comparisons of categorical variables. Means of normally distributed continuous variables were compared with the analysis of variance (ANOVA) test, and continuous variables with a skewed distribution were compared by Mann-Whitney U test. Tukey's test was used for post-hoc analysis. The Statistical Package for Social Sciences (SPSS) for Windows version 10.0 (SPSS Inc., Chicago) was used for the analyses, and a two-sided P value of <0.05 was considered significant.

Results

There were no significant differences among the three study groups and the control group with respect to age or gender distribution (Table 1). The mean age of all of the patients was 52.16±13.2 years (range 11-80 years).

Scores from the DHI obtained at the initial interview (day 1) and on follow-up days 3 and 5 are listed in Table 2 ($P>0.05$). At the end of the first week, none of the patients felt unsteady while standing or walking. The mean duration of dizziness was 4.3 days for group 1, 4.6 days for group 2, 4.7 days for group 3, and 4.9 days for group 4. The scores for the DHI obtained after the repositioning maneuver did not differ significantly among the groups ($P>0.05$). The distributions of the DHI scores for each group are shown in Figure 1. There was also no significant difference between the

Table 1

Mean ages and percentages of women and men by treatment group. There were no significant differences among control and treatment groups with respect to age or gender

Characteristics	Group 1	Group 2	Group 3	Group 4
Age, years; mean ± SD	52.2±11.1	51.8±13.2	56±10.9	48.64±16.4
Women, *n* (%)	17 (68)	20 (80)	19 (76)	17 (68)
Men, *n* (%)	8 (32)	5 (20)	6 (24)	8 (32)

Group 1: betahistine; group 2: trimetazidine; group 3: gingko biloba; and group 4: no medication.

Table 2
Mean and SD of Dizziness Handicap Index (DHI) scores for each group on days 1, 3, and 5 after successful repositioning maneuvers ($n=25$ in each group)

Group	DHI score, mean ± SD		
	Day 1	Day 3	Day 5
1	61.44 ± 22.09	42.08 ± 23.22	23.68 ± 18.24
2	62.16 ± 16.91	37.76 ± 18.96	20.4 ± 19.68
3	68.08 ± 14.3	43.28 ± 21.4	19.12 ± 16.19
4	69.04 ± 17.28	32.48 ± 23.32	13.52 ± 11.06

Group 1: betahistine; group 2: trimetazidine; group 3: gingko biloba; and group 4: no medication.

means of DHI scores obtained 3 and 5 days after repositioning maneuvers ($P>0.05$; Table 2).

Discussion

BPPV is popularly believed to be due to small cupular deposits that cause endolymph to deflect the cupula and stimulate the hair cells. This faulty stimulation causes the sensation of vertigo in BPPV. However, some temporal bone samples from patients with BPPV do not contain these deposits.[7] In 2003, Gacek suggested an alternative theory, whereby BPPV includes loss of the inhibitory effect of otolith organs on canal sense organs.[8]

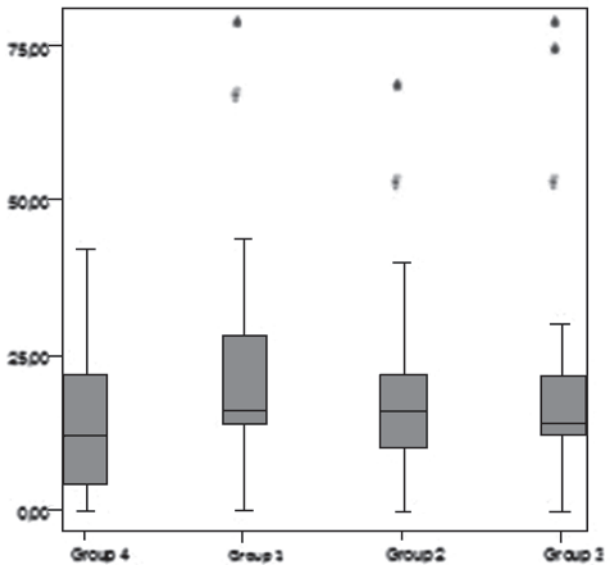

Figure 1
Box-plot graphs of DHI scores for groups 1-4. Black lines within boxes indicate median, edges of boxes are 25th and 75th percentiles, and lines extend to the maximum and minimum values.

Although dizziness caused by BPPV can be treated with repositioning maneuvers, some patients complain of imbalance that is independent of position for several days after successful repositioning maneuvers.[1,9] The prevalence of residual dizziness in adults was found to be 61-74% in some studies.[10,11]

The pathophysiology of residual dizziness has yet to be clarified and remains subject to controversy. The strongest theory put forward to explain this phenomenon is the existence and persistence of otoconial debris in the semicircular canal.[1] These small particles of debris do not cause severe vertigo and nystagmus, but they can cause dizziness. Another idea is the utricular dysfunction theory, as suggested by von Brevern and colleagues. According to this theory, in patients with BPPV, there is degeneration at the secondary utricular macula. As a result, during prolonged post-repositioning maneuvers, mild imbalance and dizziness occurs.[12] There have also been some reports of indirect observations of neuronal damage in the macula.[13] Inagaki *et al*. stated that otoconial debris between the posterior semicircular canal and the utricular macula causes transient utricular potentials, as observed during their experiments with an animal model.[14] Another possibility is that patients may have a coexisting, undiagnosed vestibular disorder or an incomplete central adaptation period, since BPVV usually occurs after the fifth decade of life.[15] Additionally, some studies have shown that prolonged periods of BPVV are associated with an increased occurrence of residual dizziness.[10]

Dizziness has adverse physical and psychological consequences. It increases the risk of falls or fear of falling, disturbs daily life, and results in restriction of social activities.[16,17] In order to prevent these

conseqences, which can have a significant negative impact on daily life, antivertiginous drugs that increase labyrinthine microcirculation and suppress excessive neuronal activities in vestibular receptor cells, afferent neurons, and vestibular nuclei are included in the treatment plan from time to time. However, it is uncertain how effective these drugs are against residual dizziness. BPVV patients continuously use many drugs, because of comorbid chronic diseases associated with advanced age. Antivertiginous drugs taken on a daily basis by patients after repositioning maneuvers often cause side effects and thus are sometimes not taken as prescribed.

There are several tests and surveys to evaluate patient perception of dizziness. The most commonly used survey is the DHI, which was the first self-assessment inventory to identify precipitating factors associated with dizziness in daily life. This dizziness disability survey was developed by Jacobson and colleagues[18] and translated into Turkish by Karapolat and colleagues.[19] It has been shown that the Turkish version of this survey can be used to consistently and reliably evaluate the symptoms of patients with dizziness. In the present study, the DHI was used to evaluate the effect on residual dizziness of three different antivertiginous drugs plus a control, no-treatment group.

Several medical agents are used to treat dizziness. Betahistine is thought to work by relaxing the precapillary sphincters, thereby increasing blood flow to the inner ear.[20] Ginkgo biloba extract is a neuroprotective agent that has antioxidant and free radical scavenger characteristics and inhibits platelet activating factor.[21,22] Trimetazidine, betahistine, and ginkgo biloba extract use a common mechanism of action to decrease the hemostatic disorders caused by ischemia and limit the damage caused by free radicals.

To the best of our knowledge, there are no previously published studies of the effect of trimetazidine and ginkgo biloba extract on residual dizziness. A placebo-controlled study conducted by Guneri and colleagues did not focus on residual dizziness, but it can be compared with our study method since betahistine treatment was administered together with repositioning maneuvers.[3] In their study, the effect of betahistine on BPVV was examined. Betahistine was found to be more effective than placebo; however, in line with the results of our study, the mean scores of vertigo symptom scales obtained after treatment did not differ among the groups treated with the Epley maneuver alone compared to the maneuver combined with placebo or betahistine.

Sundararajan *et al.*[4] claimed that sedatives that increase labyrinthine microcirculation do not have any effect on relieving residual dizziness; on the contrary, they may delay recovery by prolonging central compensation. The most important limitation of this previous study was the lack of a control group. In our study, inclusion of a control group allowed us to conclude that treatment with medication was not more effective than treatment in which no medication was administered, either during the follow-up period after successful maneuvers or at the end of the treatment period.

Conclusions

BPVV can be effectively treated with repositioning maneuvers. The results of our study indicate that antivertiginous drugs are not effective in the treatment of residual dizziness following successful maneuvers. Moreover, the claim that these drugs may delay recovery by prolonging central compensation should not be ignored; thus, we conclude that antivertiginous drugs administered after repositioning maneuvers unnecessarily increase the daily drug load of patients with BPVV. More advanced multicenter studies, in which systemic diseases are excluded, are required to augment the results of the present study, since the majority of patients with BPVV are of advanced age and thus likely to have concomitant conditions.

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