Does the use of betahistine dihydrochloride affect positional nystagmus?*

Betahistin dihidroklorür kullanımı pozisyonel nistagmusu etkiler mi?

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Abstract

Aim: In this study, we aimed to investigate the effect of betahistine dihydrochloride (BD) use on positional nystagmus as an objective criterion for the diagnosis of benign paroxysmal positional vertigo (BPPV).

Methods: The retrospective study included 59 patients (15 males, 44 females) who were aged between 18 and 80 years and referred with suspected BPPV to the otorhinolaryngology clinic of the Istanbul Training and Research Hospital. Only patients who had no central pathology on oculomotor tests were included. Of the patients included, those not using BD were classified as Group I and those using BD medication (24 mg/day) within the last 48 hours as Group II. The positional nystagmus latency, duration, and slow-phase velocity (SPV) values were compared using videonystagmography.

Results: There was no significant difference between the two groups in terms of oculomotor gains (p>0.05). While there was no difference between the two groups in terms of positional nystagmus latency and SPV values, nystagmus duration was found to be significantly longer in Group II.

Conclusion: Although the BD use appears to prolong the duration of nystagmus in BPPV, it does not affect the other parameters of nystagmus, including SPV, and the prolonged duration is still within normal limits. Positional nystagmus can be investigated in patients with a history of suspected BPPV and BD prescription.

Keywords: benign paroxysmal positional vertigo; betahistine; nystagmus

Öz

Amaç: Bu çalışmada betahistin dihidroklorür (BD) kullanımının benign paroksismal pozisyonel vertigo (BPPV) tanısında objektif kriter olan pozisyonel nistagmus üzerine etkisini incelemek amaçlanmıştır.

Yöntem: Retrospektif çalışmamız yaşları 18–80 yıl aralığında değişen ve BPPV şüphesiyle İstanbul Eğitim ve Araştırma Hastanesi'nin kulak–burun–boğaz polikliniğine yönlendirilen 59 (15 erkek, 44 kadın) hasta içerdi. Çalışmaya yalnızca okülomotor testlerde santral patoloji görülmeyen hastalar dahil edildi. Dahil edilen hastalardan BD kullanmayanlar Grup I, son 48 saat içinde BD grubu ilaç (24 mg/gün) kullananlar ise Grup II olarak tasnif edildi. Pozisyonel nistagmus latans, süre ve yavaş faz hızı (YFH) değerleri videonistagmografi kullanılarak karşılaştırıldı.

Bulgular: İki grup arasında okülomotor kazançlar bakımından anlamlı bir fark bulunmadı (p>0,05). Yine iki grup arasında pozisyonel nistagmus latans ve YFH değerleri açısından fark saptanmazken nistagmus süresi Grup II'de anlamlı olarak daha uzun bulundu.

Sonuç: BD kullanımı BPPV'de pozisyonel nistagmus süresini uzatıyor gibi görünse de YFH dahil diğer nistagmus parametrelerini etkilememektedir ve süredeki uzama halen normal sınırlar içindedir. BPPV şüphesi ve BD reçeteleme öyküsü olan hastalarda pozisyonel nistagmus araştırılabilir.

Anahtar sözcükler: benign paroksismal pozisyonel vertigo; betahistin; nistagmus

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INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is one of the most common peripheral vestibular disorders and usually seen in the 5th to 7th decades of life (1,2). BPPV is considered to result from migration of otoconia into the semicircular canals (canalolithiasis) or attachment of otoconia to the cupula (cupulolithiasis) (3).

The diagnosis is made by history and positional maneuvers, during which appearance of nystagmus is an important finding (3). In positioning tests, abnormal vestibulo-ocular reflexes (VORs) can manifest as nystagmus. The characteristic features depend on the affected canal and the posterior semicircular canal is the most commonly involved canal in BPPV (4).

Nystagmus is defined as involuntary, rhythmic, oscillating movement of the eyes (5), often consisting of a mixture of slow and fast movements (6). VORs, which serve to stabilize the line of sight in space during head movements, constitute the slow phase of nystagmus (6), with eye movements at almost the same speed but in the opposite direction. The direction and degree of the slow phase of nystagmus induced by positional testing are important in the diagnosis of BPPV (7).

Histamine analogues such as betahistine dihydrochloride (BD) have been widely used in the treatment of peripheral vestibular disorders (8–10). Betahistine interacts with histamine receptors to reduce histamine-induced stimuli at the level of the vestibular nuclei and reduce the discharge of hair cells in the ampulla of the semicircular canals (11,12).

Betahistine acts as a presynaptic antagonist of the H3 receptor and a weak postsynaptic agonist of the H1 receptor. It is considered to facilitate microcirculation of the labyrinth and decrease endolymphatic pressure (13,14). There have been previous reports of betahistine use despite the fact that BPPV is treated with maneuvers rather than medications (15,16). However, its effect on positional nystagmus, which is an objective criterion for the diagnosis of BPPV, remains unknown (15,16). Therefore, in this study we aimed to investigate the effect of BD use on positional nystagmus.

MATERIALS AND METHODS

The BPPV diagnosis was made based on medical history, neuro-otologic examination, and use of positional maneuvers. There was no patient with recurrent BPPV, central nervous system pathology, or peripheral vestibular disorder except BPPV.

The patients were divided into two groups. Group I (n=37) consisted of the patients not using BD and Group 2 (n=22) consisted of those treated with BD (24 mg/day) within the last 48 hours.

Anterior- and posterior-canal BPPV were diagnosed with the Dix–Hallpike maneuver while lateral-canal BPPV was diagnosed with the supine roll test. The latency, duration and maximum slow-phase velocity (SPV) values during the positional maneuvers were recorded with videonystagmography (VNG) using the VisualEyes tool (Micromedical Technologies, Chatham, IL, USA), performed on initial admission. A SPV $>4^0$/s for horizontal canals and $>7^0$/s for vertical canals was considered normal.

Statistical analysis

Statistical analysis was performed using the SPSS (v. 15.0) software (IBM Inc., USA). The independent samples t-test and one-way analysis of variance with Bonferroni corrections were used in the intergroup comparisons of VNG recordings. $p<0.05$ was considered statistically significant.

Study ethics

The study protocol was approved by the ethical committee of the Istanbul Training and Research Hospital (2017/1063). Written informed consent was obtained from all patients.

RESULTS

The mean patient age was 54±16 (range: 18–80) years. There was no statistically significant difference between the two groups in terms of age and sex ($p>0.05$). The vertical component was dominant in 71.5% and 100% of the patients with posterior- and anterior-canal BPPV, respectively. Nystagmus was geotropic in all cases of lateral-canal BPPV. No difference was found between the two groups in terms of nystagmus latency, SPV, and oculomotor test values other than nystagmus duration ($p>0.05$ for all comparisons), which was significantly longer in Group 2 ($p=0.04$) (Table 1).

Table 1. Comparison of patients with and without betahistine use (24 mg/day)

	Age (year)	Latency (sec) (mean±SD)	Duration (sec) (mean±SD)	Maximum SPV (mean±SD)
Betahistine (-)	54.8±15.9	4.3±2.5	35.6±22.4	29.1±26.7
Betahistine (+)	52.3±15.9	5.3±3.6	49.5±28.4	21.5±18.1
p	0.55	0.21	*0.04*	0.24

SD: standard deviation; sec: second; SPV: slow-phase velocity

Table 2. Canal-based comparison of the values

Canal	Number	Latency (sec) (Mean±SD)	Duration (sec) (Mean±SD)	Maximum SPV (mean±SD)
Posterior	38	5.3±3.3	41±25.5	31.3±24.4
Lateral	8	3.5±1.8	35.6±21.4	10.6±6.6
Anterior	13	3.6±1.5	43.8±28	20.8±25.1
p	0.46	0.77	*0.05*	*0.05*

SD: standard deviation; sec: second; SPV: slow-phase velocity

Unlike the latency values (p>0.05), the duration and maximum SPV values for the dominant component of nystagmus significantly differed between the affected canals (p=0.05 for both comparisons) (Table 2). Finally, a positive correlation was found between nystagmus SPV and patient age (p=0.01).

DISCUSSION AND CONCLUSION

The latency, duration, direction, and degree of nystagmus induced by positional maneuvers are helpful for recording BPPV-related parameters objectively (7). In general, nystagmus latency is 5 to 20 seconds (1), and in our study we found for the first time that betahistine use had no significant effect on nystagmus latency in BPPV. Similarly, nystagmus duration is around 60 seconds after provocation in BPPV (1), and in our study nystagmus duration was still within normal limits although it was significantly increased by betahistine use.

It is considered that betahistine facilitates vestibular compensation through upregulation of histamine turnover and H3 receptor antagonism-mediated histamine release (8,17). Also, betahistine might have a vestibular suppressant effect via histamine receptors, despite the presence of contradictory reports (17,18). It was suggested that betahistine reduced nystagmus duration in healthy people and prolonged durations were attributed to the suppression of central fixation by betahistine use (16), although those assessments were performed by caloric stimulation of the lateral semicircular canals.

Currently, SPV is considered the most reliable parameter for nystagmus assessment (7,17). A decreased VOR gain during high-frequency rotations could be attributed to the action of betahistine on H3 receptors in the vestibular nuclei (19). In contrast to the low-frequency lateral canal stimulation with caloric testing, the SPV values of the vertical canals are usually high due to the ampullopetal flow (20).

Increased SPVs were reported in patients with Meniere's disease who were treated with betahistine (17). However, it seems that there is no relation between high doses of betahistine and nystagmus duration and SPV (21). In our study, conducted on patients with BPPV, it was found that betahistine use had no significant effect on SPV.

Also, we found a positive correlation between SPV values and patient age. This might be due to age-related alterations in the structure of otoconia, which contains an organic core made of calcium carbonate and glycosylated proteins in a gelatinous matrix with filament crosslinkers (22). In the elderly, the weakening or breakdown of the connecting filaments leads to degeneration in otoconia (23). This can be supported by the increased incidence of BPPV in women with osteoporosis (14, 23).

In conclusion, although betahistine use appears to lead to longer durations of nystagmus in BPPV, it does

not affect the other parameters, including SPV, and the prolonged duration is still within normal limits. In the light of these objective data, positional nystagmus could be investigated in patients with a history of suspected BPPV and prescribed use of betahistine.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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