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Influence of Otoliths on the Vestibulo-Ocular Reflex in Horizontal Canal Benign Paroxysmal Positional Vertigo

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Objectives: The aim of the study was to evaluate the possible alteration of the vestibulo-ocular reflex (VOR) in patients with horizontal canal benign paroxysmal positional vertigo (h-BPPV) using the video head impulse test (vHIT).

Methods: This was a prospective case-control study of BPPV patients. We included 133 patients with h-BPPV who underwent the vHIT prior to the positioning test. The control group consisted of 76 normal subjects who also underwent the vHIT. The vHIT parameters of gain and asymmetry were assessed, and clinical parameters such as treatment duration, number of canalith reposition maneuvers executed and recurrence rates were evaluated. The VOR and clinical parameters were compared between the h-BPPV and control group. The VOR parameters of h-BPPV canalolithiasis were also compared with those of cupulolithiasis.

Results: The mean age of the patients was 56.5 years and the male to female ratio was 1:2.02. Of the patients, 75 were diagnosed as having the canalolithiasis type of h-BPPV, while the other 58 had the cupulolithiasis type. The mean vHIT gains of the ipsi-lesional horizontal canal plane were 1.13 and 1.15 in the h-BPPV and control group, respectively ($p=0.564$). However, the asymmetry of the VOR was significantly higher in the h-BPPV than the control group ($p=0.013$), while the gains and asymmetries of the vHIT in the canalolith and cupulolith types were not significantly different ($p=0.454$, $p=0.826$).

Conclusions: The asymmetry of VOR is significantly elevated in the cupulolith type of hBPPV.

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Keywords: Benign paroxysmal positional vertigo; Otolith; Vestibulo-ocular reflex

INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is a clinical disorder characterized by recurrent positional vertigo [1]. BPPV is considered the most common vestibular disease with a pre-

valence of 10.7–64.0 cases per 100,000 population. The female-to-male ratio of BPPV patients has been reported to range from 2:1 to as much as 3:1 [2].

Otoconial debris that dislodges from the utricular macula can precipitate into the semicircular canals [3], and its movement

in the endolymph produces push or pull forces on the cupula of the semicircular canal, thereby eliciting excitation or inhibition of the corresponding semicircular canals that results in the characteristic nystagmus (Fig. 1) [4]. Therefore, the diagnosis of BPPV is made by identifying the characteristic positioning nystagmus during the Dix-Hallpike and supine head roll tests [5-7].

The vestibulo-ocular reflex (VOR) is a reflex between the vestibular system and ocular movement that stabilizes images during head movements by producing exquisite eye movements. A left head turn induces excitation of the left horizontal semicircular canal, followed by excitation of the left vestibular nuclei and inhibition of the right vestibular nuclei. After that, excitation of the left oculomotor and right abducens nuclei and leading contraction of the left medial rectus and right lateral rectus muscle cause compensatory eye movement to the right side. The rotational VOR related to the plane of each semicircular canal stabilizes vision during movement.

A previous study showed that disruption of the VOR in terms

of caloric hypoexcitability was frequently identified in BPPV patients, especially in the cupulolithiasis type of horizontal canal BPPV. However, no association between symptom duration and caloric results was detected, probably due to the nonphysiologic nature of the caloric stimulation. Likewise, the authors supposed that the atypical dizziness in BPPV might result from the otolith in the endolymph affecting the flow of endolymph and disrupting the VOR. Nowadays, the video head impulse test (vHIT) allows the VOR to be easily measured objectively at physiologic stimulation speed [8].

To test this idea, we planned a prospective case-control study using vHIT to evaluate the possible alteration of the VOR in patients with horizontal canal BPPV (h-BPPV).

MATERIALS AND METHODS

1. Patients and Study Design

A prospective, case-control study was conducted in a tertiary

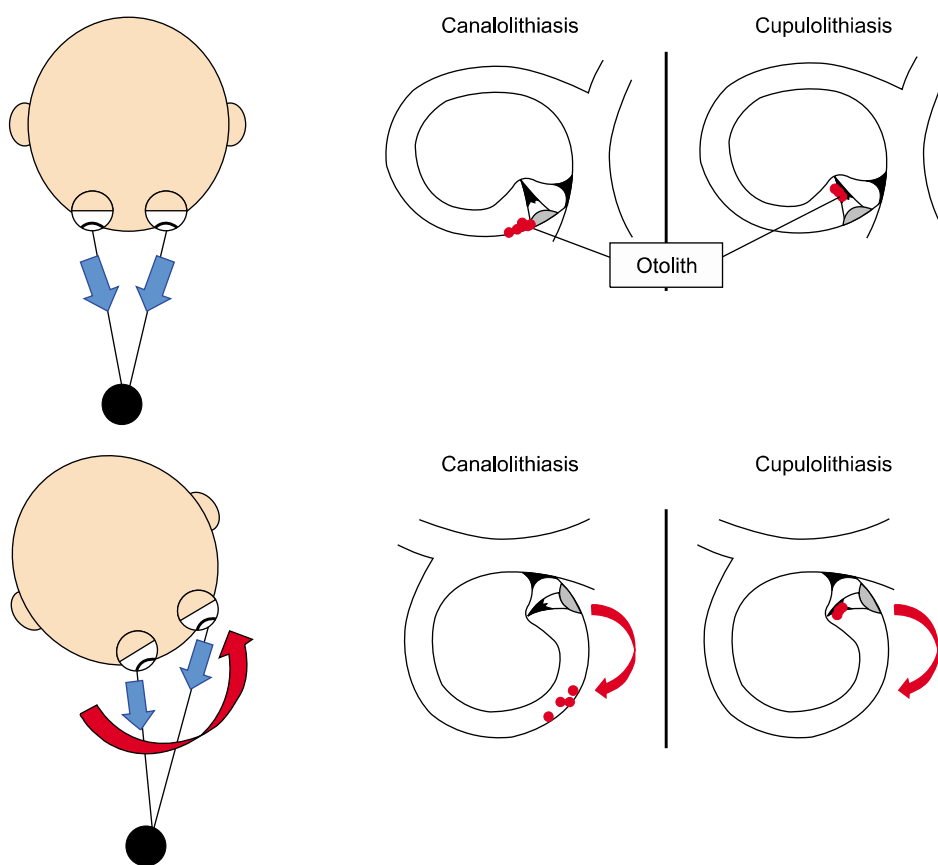


Fig. 1. Schematic diagram of the influence of an otolith on the vestibulo-ocular reflex during rapid head movement (right ear).

referral center. From January 2015 to May 2016, 387 patients with suspected BPPV from clinical history and needing positioning nystagmus tests were eligible for the study. The patients all underwent vHIT tests to evaluate the VOR prior to receiving Dix-Hallpike/Head roll tests to diagnose the specific type of BPPV. After positioning nystagmus, only h-BPPV patients were enrolled in the study and those with anterior canal or posterior canal BPPV were not included. We subdivided the patients into canalolithiasis and cupulolithiasis groups based on their characteristic nystagmus in the positioning test. The patients underwent appropriate canalith reposition maneuvers such as Barbecue maneuver or Gufoni's maneuver depending on their final diagnosis.

We excluded subjects with prior experience of vestibular disorder based on medical history. Patients with recent or chronic ear infections, acute hearing loss, inner ear diseases, and ophthalmologic problems that interfered with video nystagmography were not included. In addition, h-BPPV patients with unilateral or bilateral vestibulopathy were excluded based on the results of vHIT gain.

Finally, 133 patients diagnosed with h-BPPV were enrolled. In addition, 76 subjects who completed the vHIT without dizziness-related symptoms were assigned as the control group.

2. Ethics Statement

Written informed consent was obtained from all patients before reviewing their medical records. This investigation was approved by the local ethics review board (Hanyang University Guri Hospital: 2020-02-009) and performed in accordance with the Declaration of Helsinki and good clinical practice guidelines.

3. Diagnosing Horizontal Canal BPPV

To diagnose BPPV, spontaneous and gaze nystagmus were checked, followed by the Bow and Lean Test to detect the presence of nystagmus and to determine the affected side. The Dix-Hallpike and head roll tests were then performed to identify the affected semicircular canal. h-BPPV was confirmed by observing typical geotropic or ageotropic positional nystagmus during the head roll test. When geotropic nystagmus was

observed, the lesion side was indicated by the side showing the stronger nystagmus during the head roll test and the diagnosis was canalolithiasis. In the case of ageotropic nystagmus, the lesion was decided by the direction of the nystagmus and diagnosed as cupulolith. We rigorously enrolled only patients who showed a definite change of direction of nystagmus during the supine head roll tests. Recurrence of BPPV was defined as subjects diagnosed with a further case of BPPV after a symptom-free period of 2 weeks or more of follow-up.

4. Video Head Impulse Test

The vHIT test was done to measure the VOR in the horizontal canal plane, using an ICS impulse (vHIT GN Otometrics, Denmark). The test was conducted by applying unpredictable manual head impulses of approximately 20° with a mean velocity of 150°/sec and a mean acceleration of 1,000° to 2,500°/sec in the horizontal plane, with the patients fixing their eyes on a target placed 1 m in front of them. At least 20 adequate impulses were applied to the right and left sides for each test. Parameters such as the gain and asymmetry of the VOR were measured. All procedures were conducted by a professional examiner.

Gain is the ratio of eye movement velocity to head movement velocity. Relative gain asymmetry (%) was calculated as the difference between the lower and higher gain divided by the sum of gains multiplied by 100.

$$\text{Relative gain asymmetry ratio (\%)} = \frac{(G_c - G_i)}{(G_c + G_i)} \times 100$$

(G_i=ipsilateral gain, G_c=contralateral gain)

Abnormal vHIT was defined when vHIT was located in the gray range which indicates an inadequate VOR. Results below 0.8 were regarded as abnormal gain.

5. Statistical Analysis

The collected data were exported to IBM SPSS Statistics ver. 19.0 (IBM Co., Armonk, NY, USA) to perform statistical analyses. Data are expressed as means±standard deviation (parametric). Comparisons were made between groups using Student *t*-test (parametric). Proportions were calculated, using Student *t*-test and the chi-square test to compare vHIT values between

Table 1. Clinical characteristics of horizontal canal benign paroxysmal positional vertigo

Characteristic	Value
No. of patients	130
Age (yr)	56.8±12.4
Sex, male:female (ratio)	43:87 (1:2.02)
Side of lesion, right:left	72:58
Diagnosis	
Horizontal canal BPPV	130 (100)
Canalolithiasis	73 (56.2)
Cupulolithiasis	57 (43.8)
No. of CRM	2.1±1.9 (1–10)
Treatment duration	6.5±6.4 (1–30)
Recurrence	16 (12.3)

Values are presented as mean±standard deviation (range) or number (%).

BPPV, benign paroxysmal positional vertigo; CRM, canalith reposition maneuver.

Table 2. Comparisons of video head impulse test parameters of the horizontal semicircular canal between horizontal canal BPPV and control

	Horizontal canal BPPV (n=130)	Control (n=75)	p-value
vHIT gain	1.15±0.19	1.14±0.19	0.781
vHIT asymmetry	5.46±5.37	4.32±2.81	0.048

Values are presented as mean±standard deviation.

BPPV, benign paroxysmal positional vertigo; vHIT, video head impulse test.

groups. For each test, a statistically significant result was taken as $p < 0.05$.

RESULTS

A total of 133 patients were diagnosed as h-BPPV, 75 with canalolithiasis and 58 with cupulolithiasis. Table 1 presents their demographic characteristics. The mean age was 56.5±12.5 years old; the male to female ratio was 1:2.02, and the right side affected was in 73 patients and the left in 60. The patients underwent an average of 2.2±1.8 sessions of the canalith reposition maneuver, and 29 patients suffered recurrent BPPV (13.9%).

The VOR gain was not significantly different in the h-BPPV and control group, whereas the asymmetry on vHIT was significantly higher in the h-BPPV group ($p=0.013$). A vHIT gain below 0.8 was seen in 3 patients (2.3%) in the hBPPV group

Table 3. Comparisons of video head impulse parameters in the horizontal semicircular canal between each type of h-BPPV (canalolithiasis or cupulolithiasis) and the control group

	Canalolithiasis (n=73)	Control (n=75)	p-value
vHIT gain	1.16±0.24	1.14±0.19	0.610
vHIT asymmetry	4.87±3.41	4.32±2.81	0.328
	Cupulolithiasis (n=57)	Control (n=75)	
vHIT gain	1.14±0.19	1.14±0.19	0.377
vHIT asymmetry	5.91±6.4	4.32±2.81	0.042

Values are presented as mean±standard deviation.

h-BPPV, horizontal canal benign paroxysmal positional vertigo; vHIT, video head impulse test.

Table 4. Comparisons of vHIT parameters in the horizontal semicircular plane between canalolithiasis and cupulolithiasis

	Canalolithiasis (n=73)	Cupulolithiasis (n=57)	p-value
vHIT gain	1.16±0.24	1.14±0.19	0.555
vHIT asymmetry	4.87±3.41	5.91±6.4	0.239

Values are presented as mean±standard deviation.

vHIT, video head impulse test.

and in 1 patient (1.3%) in the control group (Table 2). In a subgroup analysis, cupulolithiasis of hBPPV showed significantly elevated asymmetry ($p=0.011$) (Table 3). Other parameters were not significantly different. There was also no significant difference in vHIT gain or vHIT asymmetry between the cupulolithiasis and canalolithiasis groups (Table 4).

DISCUSSION

This study assessed a possible alteration of the VOR in h-BPPV using vHIT. The results can be summarized as follows: (1) The asymmetry of the VOR was significantly increased in h-BPPV. (2) Cupulolithiasis of h-BPPV displayed the highest asymmetry, and (3) no decrease of VOR gain was evident in h-BPPV.

The VOR guarantees clear vision during head rotation. The rotational VOR produces a slow phase eye movement that compensates for horizontal, vertical and torsional head rotations. The ordinary rotational VOR compensates perfectly for both the direction and speed of horizontal and vertical head rotations. The eye movements remain well-aligned with the head in the direction of its rolling rotation.

BPPV can be categorized into 2 types, canalolithiasis and cupulolithiasis. “Canalolithiasis” involves free-floating particles within a semicircular canal [9]. Canalolithiasis is mostly due to free-floating debris in the endolymph, which tends to gravitate towards the posterior canal, the most gravity-affected part of the vestibular labyrinth in both upright and supine positions. Once debris enters the posterior canal, the cupula barrier at the end of the canal prevents its exit and it can only prolapse at the end at the ampulla (the common crus) [7]. “Cupulolithiasis” involves particles adherent to the cupula of a semicircular canal [10]. Since particles adhere to the cupula, the vertigo is often severe and persists while the head is in the provoking position. When the head rotates toward the affected side, the cupula undergoes an ampullofugal (inhibitory) deflection causing ageotropic nystagmus. Turning the head in the opposite side creates an ampullopetal (stimulatory) deflection, resulting in stronger ageotropic nystagmus [7]. Ageotropic nystagmus is present in about 27% of patients with h-BPPV [11].

The present study was conducted to test the possibility that the presence of otoliths can affect the VOR. Studies have pointed to canal paresis in the caloric test in patients with BPPV by showing that unilateral caloric loss occurs in up to 36% of h-BPPV patients. They also showed that the side with the decreased caloric response corresponded to the side with the highest-velocity horizontal positional nystagmus [12]. Another study demonstrated reversibility of the hypoexcitability in the caloric test after a liberatory maneuver [13,14].

It has been speculated that cupulolithiasis may affect the cupular deflection due to the weight of otoconia during the rotary chair test. However, the gain and time constant did not differ between cupulolithiasis and canalolithiasis [15]. This suggests that the otolith has little effect on the VOR. However, a recent pilot study revealed that gain in the vHIT in the plane of the posterior semicircular canal was reduced in posterior semicircular canal BPPV, suggesting a possible otolithic influence on the VOR in different angle or velocity [2].

The caloric test, rotary chair test, and vHIT can assess the functioning of the VOR in response to different stimulus frequencies. The vHIT evaluates frequencies around 2.5 Hz using rapid and short head impulses, whereas the caloric test activates lower frequency bands around 0.003Hz [16]. The rotary chair

test generally evaluates frequencies around 0.01–1 Hz. In daily life, people usually experience head rotation frequencies ranging from 1 Hz to as high as 6 Hz [17]. Since the rotatory chair test and the caloric test cannot reflect the VOR at high frequency, these tests do not directly reflect the functional changes of patients’ VORs in daily life. Thus, the vHIT test may better reflect the physiologic status of the VOR.

The present study showed that the vHIT gain was not significantly different between h-BPPV and control, whereas the asymmetry of vHIT was significantly elevated in h-BPPV patients. In addition, vHIT gain and asymmetry did not significantly differ between canalolithiasis and cupulolithiasis.

Interestingly, the asymmetry of vHIT was significantly elevated in cupulolithiasis. We assume that the otolith adhering to the cupula may influence the resting state of the cupula making it heavier, and lead to increased gain asymmetry. Accordingly, the distorted input from the semicircular canal may then affect the velocity storage system that enhances VOR performance by CNS [18]. However, in canalolithiasis, gain asymmetry is not influenced by the presence of an otolith due to physical factors such as the weight or static friction [19]. Likewise, the otolith is far from the cupula in canalolithiasis, so it probably cannot affect the VOR gain during head movement.

There are also numerous reports showing frequent occurrence of BPPV on the side of vestibular hypofunction [20,21]. Abnormal caloric results are frequently seen in BPPV patients even after performing the canalith reposition maneuver [20,22]. It has been postulated that detachment of the otolith from utricle or saccule in BPPV might also have an adverse effect on the transitional VOR [23]. Although this study did not include patients with prior experience of vestibulopathy by history, the possible coexistence of vestibulopathy might interfere with interpretation of the results.

There are a few limitations to the present study. We could not perform other vestibular function tests including the caloric test, vestibular evoked myogenic potential, and rotary test, which could provide information on the specific functional status of the vestibular system. In addition, it might have been valuable to compare the result of the vHIT before and after treatment, since this could have provided more direct evidence concerning BPPV’s influence on vHIT. In future studies, it would be ad-

visible to examine how vHIT results change after BPPV treatment.

In conclusion, the study showed that the asymmetry of vHIT gain increased in the cupulolith type of hBPPV, thus demonstrating possible alteration of the VOR.

중심 단어: 양성돌발성두위현훈, 이석, 전정안반사

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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