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Head-Up Sleep May Cure Patients With Intractable Benign Paroxysmal Positional Vertigo: A six-Month Randomized Trial

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Objectives: The aim of the present study was to assess head-position management for intractable idiopathic benign paroxysmal positional vertigo (BPPV) when lying down. We hypothesized that head-up sleep (HUS) could prevent free-floating otoliths from entering the semicircular canals.

Study Design: A prospective two-arm multicenter randomized controlled trial.

Methods: BPPV was diagnosed in 611 patients (611/1,520; 40.2%) according to the 2015 diagnostic guidelines issued by the International Classification of Vestibular Disorders. Among them, 201 patients were intractable (201/611; 32.9%), 88 of whom were idiopathic and subsequently enrolled in the study. Patients randomly received intervention with HUS at greater than 45° (n = 44) or head-down sleep (HDS; n = 44) when lying down. Before treatment, they completed several examinations, including subjective visual vertical (SVV). The specific diagnoses for the 88 patients with BPPV included horizontal type cupula (n = 40), horizontal type canal (n = 13), posterior type (n = 26), and probable and/or atypical BPPV (n = 9).

Results: Patient backgrounds did not differ significantly between the HUS and HDS groups. Visual analog scale (VAS) scores of vertiginous sensation were significantly lower in the HUS group than in the HDS group at both the third month and sixth month post-treatment. Positional/positioning nystagmus observed just before treatment disappeared significantly more often in the HUS group than in the HDS group until the sixth post-treatment month. Further, especially in HUS group, VAS scores in SVV− group (n = 24) were significantly lower than those in the SVV+ group (n = 20) sixth month post-treatment.

Conclusions: Controlling free-floating otoliths is not easy due to aging of the otolith organs. Repeatedly returning the endless free-floating debris from the canals to the utricle through physical means is not a good strategy. Therefore, HUS when lying down at home could be recommended as an initial treatment for patients with intractable idiopathic BPPV.

Key Words: Intractable idiopathic BPPV, subjective visual vertical, head-up pillows, free-floating otolith, semicircular canals.

Level of Evidence: 1b

Abbreviations

BPPV	benign paroxysmal positional vertigo
BPPVca	canal type BPPV
BPPVcu	cupula type BPPV
BPPVsusp	suspected and/or atypical BPPV
hBPPV	horizontal type BPPV
pBPPV	posterior type BPPV

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INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is the most popular cause of vertigo, having a lifetime prevalence of 2.4%.[1] Vertigo and dizziness in BPPV is considered to result from debris that comprise small calcium crystals from the utricle that are stuck to the crista ampullaris[2] and/or floating in the ear canal.[3] BPPV is usually self-limiting, as the symptoms generally subside or disappear about 1 month after onset in posterior semicircular canal type BPPV (pBPPV), and within 2 weeks of onset in horizontal semicircular canal type BPPV (hBPPV).[4] A range of physical maneuvers and exercises including the Epley maneuver[5] and the Lempert method[6] are also usually effective for treating BPPV. However, some patients with BPPV experience intractable symptoms that frequently recur and/or are long lasting. Presumably, otolith function deteriorates with age and the number of patients with intractable BPPV is thus increasing worldwide as populations age.

Here, we propose a head-position management system for intractable idiopathic BPPV (Fig. 1) during sleep for the following reasons: 1) Controlling free-floating otoliths is not easy due to the effects of aging; 2) Repeatedly returning the free-floating otoliths from the canals to the utricle through physical maneuvers is not a good idea. Free-floating otoliths return to the canals whenever patients with intractable BPPV lie down using thin or flat

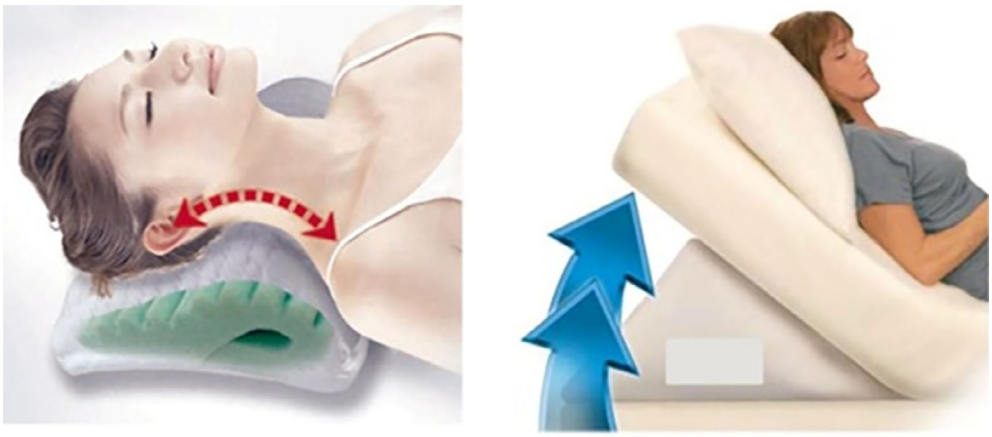

Fig. 1. Schematic representation of treatments for head-down sleep (HDS) and head-up sleep (HUS) interventions. In the present randomized controlled trial, patients with intractable idiopathic benign paroxysmal positional vertigo were divided into two groups that received different head-position management, HDS with neck pillow in group-I (G-I) and HUS with a head angle greater than 45° in group-II (G-II).

pillows.[7,8] This pilot study provides a good start for a new therapeutic strategy that uses head-position management when lying down to prevent free-floating otoliths from entering the semicircular canals.

MATERIALS AND METHODS

This clinical study was registered with UMIN (identification number: 000018399). The use of all patient data was approved by the Ethics Committee of Nara Medical University Hospital and Nara Prefecture General Medical Center (identification number: 0889) and all patients provided their informed consent.

Patients

Among 1,520 successive patients with vertigo/dizziness admitted to the Vertigo/Dizziness Center at Nara Medical University and Nara Prefecture General Medical Center between May 2014 and April 2018 (Fig. 2), 611 (40.2%) were diagnosed as BPPV according to the 2015 diagnostic guidelines of the International Classification of Vestibular Disorders.[9] In brief, these criteria were rotatory vertigo (lasting <30 seconds and precipitated by head movements), Dix-Hallpike maneuver (pBPPV; brief latency [1–5 seconds], limited duration [<30 seconds], torsional nystagmus toward the down-most ear, reversal of nystagmus upon sitting, and fatigability of the response), and lateral head turns (hBPPV; geotropic nystagmus [hBPPVca] and apogeotropic nystagmus [hBPPVcu]). Patients with other causes and disorders were excluded. A thorough medical history was obtained and neurological, neuro-otological, and magnetic resonance imaging (MRI) examinations were performed in all patients.

Patients with secondary BPPV were excluded, as were those with neck and/or waist diseases. BPPV was intractable in 201 of the 611 patients (32.9%), and was idiopathic in 88 of these cases. Through every month checking, intractable BPPV was diagnosed when medical treatments[10] and/or otolith-repositioning maneuvers[5,6] failed, and if patients experienced certain symptoms, including a motion-evoked floating sensation that lasted for at least 3–6 months. Actually, it is not so easy to determine that intractability of BPPV could be coming from "persistent" or "recurred," judged based on the interview and nystagmus at the time of patients' examination. Anyway, either will be classified into the intractability.

The final group of patients included 28 men and 60 women, with a mean age of 53.6 ± 15.0 years. The average duration from the day of disease onset to the day treatment began was 68.4 ± 82.5 months. We determined the duration of intractable idiopathic BPPV according to the patient medical history of subjective vertiginous sensation because we were unable to accurately count the number of vertigo attacks. The 88 patients were enrolled for treatment via head-down sleep (HDS) with a typical neck pillow in which the head was angled less than zero degrees or flat as control group or head-up sleep (HUS) in which the head was angled around 45° as active group, when lying down (Fig. 1). Fundamentally, neither medical treatments[10] nor otolith-repositioning maneuvers[5,6] were performed on any patient after enrollment into the present HDS/HUS study.

Examinations included the following tests: caloric test (C-test), subjective visual vertical (SVV) scores, inner ear magnetic resonance imaging (ieMRI), the Schellong test (S-test), blood tests for bone alkaline phosphatase (BAP), and the self-rating depression scale (SDS) to assess levels of depression.

Evaluations

NEURO-OTOLOGICAL TESTS. The C-test was used to assess the lateral semicircular canal and superior vestibular primary afferent neuron function. Cold water (20°C; 20 mL) was injected into the external auditory meatus over 10 seconds by turns, and the induced nystagmus was recorded using electronystagmography (ENG) in a dark, open-eyed situation. On the basis of the maximum slow-phase eye velocity, canal paresis was judged as positive when the ENG was ≤10° per second.[11]

SVV scores were used to assess otolith organ function (ie, the gravity sensitivity functioning test) with the bucket method. A clean, opaque, white, plastic trash bucket (38 cm deep, 23 cm diameter) was converted to a test device by marking a 15-cm black line on the bottom inside, and placing a protractor on the bottom outside aligned with the inside line. A small weight was hung from the center of the protractor. The bucket was placed on its side on a table (29.5 × 25 cm) atop a height-adjustable tripod to stabilize the bucket in pitch and yaw. In that position, when the bucket was rolled clockwise and counterclockwise, the string and weight rotated freely so that the investigator could read the protractor. Before testing, the tripod height was adjusted so that

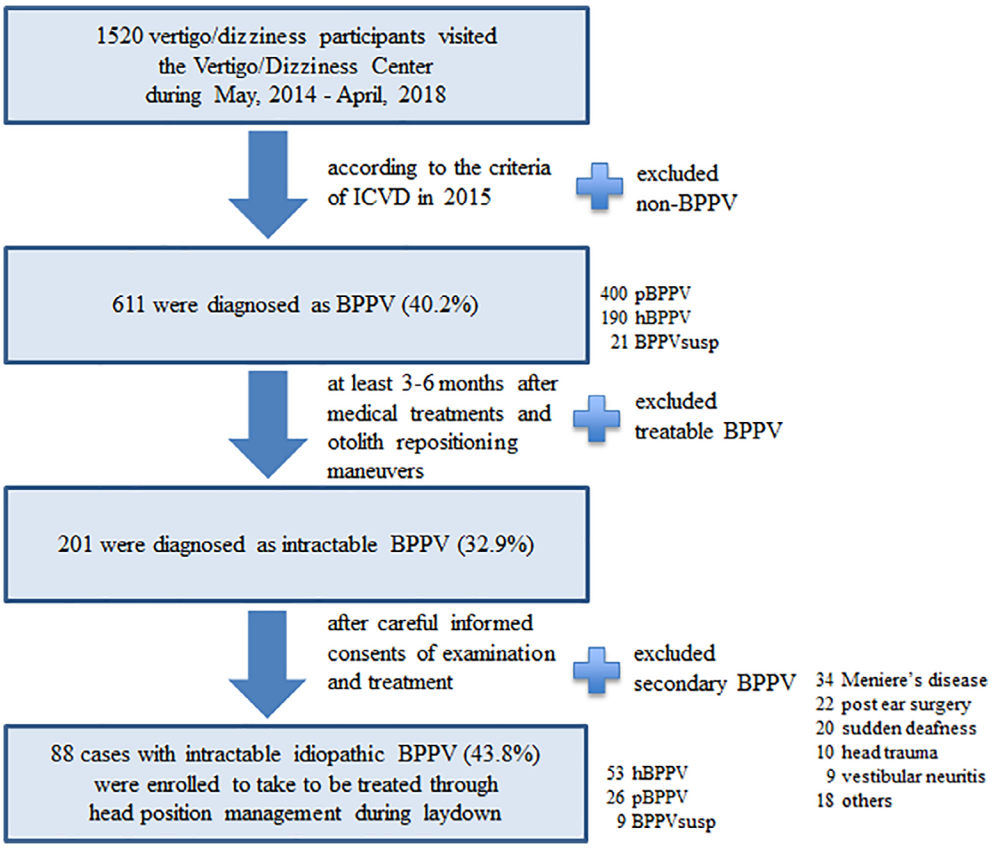

Fig. 2. Case-enrollment flow chart. Among 1,520 successive vertigo/dizziness patients admitted to the Vertigo/Dizziness Center in Nara Medical University and Nara Prefecture General Medical Center from May 2014 to April 2018, 611 were diagnosed as BPPV (40.2%) according to the 2015 ICVD diagnostic guidelines. Intractable BPPV was diagnosed in 201 patients (201/611: 32.9%), 88 of whom had idiopathic BPPV and were enrolled in the study for treatment. Patients with secondary BPPV were excluded from the study. BPPV = benign paroxysmal positional vertigo; BPPVsusp = probable and/or atypical BPPV; hBPPV = horizontal type BPPV; ICVD = international classification of vestibular disorder; pBPPV = posterior type BPPV.

each patient's face fit easily into the bucket. All measurements were taken by the examiner, monocularly, using the examiner's dominant eye. Two test conditions were used in random order: vertical roll from the upper end of the line and right and left roll of 0°. Patients were given three trials per condition. The starting point for each trial was selected randomly, and varied from 10° to 20° from the 0° line. Before each trial, the patients were instructed to state when the line was vertical while the examiner moved the bucket. The angle gaps outside of the range of −2.0° (left) to +2.0° (right) were considered positive.[12]

IMAGING. Performing ieMRI at 4 hours after intravenous administration of Gadolinium was previously reported to be useful for imaging of endolymphatic hydrops (EH).[13] In the present study, all patients received heavy T2-weighted (hT2W) MRI cisternography for an anatomical reference of the total lymph fluid, hT2W three-dimensional fluid-attenuated inversion recovery sequences with a 2,250 ms inversion time for positive perilymph images, and hT2W three-dimensional inversion recovery with a 2,050 ms inversion time for positive endolymph images. After image acquisition, and after correcting for motion by subtracting the positive endolymph images from the positive perilymph images, we obtained a hybrid image that combined the reversed positive endolymph-signal image and the negative image from the positive perilymph signal. In this protocol, pixels with a negative value were estimated as representing EH.

Two otolaryngologists blinded to the clinical progress of the patients evaluated the ieMRI findings. If their evaluations differed, a third otolaryngologist made the final decision. The degree of EH was classified as none, mild, or significant, according to criteria reported by Nakashima et al.[14] When evaluating cochlear EH, we used one axial slice near the modiolus. When evaluating vestibular EH, we used one axial slice that displayed the maximum extent of the vestibule, while the ampulla of the semicircular canal was excluded.

Patients with no EH in the vestibule had a ratio of ≤1:3, those with mild EH had a ratio of 1:3 to 1:2, and those with significant EH had a ratio >1:2. In the present study, both mild and significant EH were defined as positive.

THE SCHELLONG TEST. Daily autonomic status can easily be measured daily in the clinic using the S-test to check the changes in blood pressure (BP) or pulse rate (PR) as patients stand up from a supine position. The positive range was defined as a systolic BP decrease of more than 21 mm Hg and/or a PR increase of more than 21 beats/min before and just after standing.

BLOOD TESTS. Blood samples were collected between 08.00 A.M. and 10.00 A.M. during remission of vertigo to minimize the effects of circadian variation. Blood for the BAP assay was transferred into an ethylene-diamine-tetraacetic acid tube, centrifuged at 4°C, and the separated plasma was then stored at −80°C. BAP levels were analyzed by radioimmunoassay. In our hospital, a BAP ≥20.0 mg/L was considered positive.[15]

TEST FOR DEPRESSION. We used the SDS Japanese version to assess levels of depression. Patients with SDS scores >40 (possible range 20–80) were classified as having depression. The

SDS consists of 10 positively and 10 negatively worded items that enquire about symptoms of depression. These scores were used to define the following categories of depression: no significant depression (≤40 points), significant depression (≥41 points). The SDS has been translated into Japanese and the validity of the Japanese version previously confirmed.[16]

Background

Among the 88 patients with intractable idiopathic BPPV, 53 were diagnosed as hBPPV (60.2%; hBPPVcu, n = 40, hBPPVca, n = 13), 26 as pBPPV (29.5%), and 9 as suspected and/or atypical BPPV (BPPVsusp; 10.2%). Examination data are presented as percentages (+) of the number of BPPV patients with the data outside of the normal range as follows: C-test = 19.3% (17/88), SVV = 45.5% (40/88), ieMRI = 12.5% (11/88), S-test = 22.7% (20/88), BAP = 13.6% (12/88), and SDS = 36.4% (32/88).

Randomization

This was a randomized-controlled and open-label clinical trial study with two arms: group I (HDS, 44 cases) and group II (HUS, 44 cases) (Fig. 1). The remaining 88 patients with intractable idiopathic BPPV were randomly assigned through computer-generated block randomization organized by the clinical study section at Nara Medical University Hospital to one of the two treatment groups.[17] Patients received head-position management when lying down at home and continuous medication with antivertigo and antinausea drugs as needed.

All patients were followed up for positional/positioning nystagmus with CCD Frentzel glasses and assessment of vertiginous sensation with visual analog scale (VAS) scores at least once per 3 months until the sixth month post-treatment. At their regular check-ups, patients were excluded if they kept less than 75% compliance with the treatment rules for HDS or HUS.

Statistical Analysis

Chi square analysis and Mann–Whitney tests were used to determine any significant differences between patient groups in terms of their background information, such as gender, age, duration of disease, type of BPPV, laterality, and examination and questionnaire data (Table I). The Mann–Whitney test was performed to determine any significant changes in VAS scores between groups (Figs. 3 and 4).

All reported P values are two-sided and those under .05 were considered significant. All the statistical analyses were performed with SPSS version 14.0 (SPSS, Inc., Chicago, Illinois).

We did not do the power analysis for the appropriate sample size in the present pilot study. Therefore, we interpreted the data as feasibility/direction rather than efficacy/effectiveness.

RESULTS

The demographic data from patients with intractable idiopathic BPPV are shown in Table I. We found no significant differences in any of the variables between the two groups.

A Mann–Whitney test confirmed that VAS scores in the HUS group were significantly lower than those in the HDS group both at the third (HUS: 6.91 ± 1.42; HDS: 8.45 ± 1.26; $P = .001$) and sixth months (HUS: 4.99 ± 2.23; HDS: 7.10 ± 1.75; $P = .001$) post-treatment (Fig. 3). Obvious positional/positioning nystagmus could be seen in 21 cases from the HUS group and in 22 cases from the HDS group just before the start of treatment. By the sixth month post-treatment, nystagmus had disappeared in 18 of the 21 HUS cases (86%), but in only 11 of the 22 HDS cases (50%) (Mann–Whitney test: $P = .045$). Before treatment, 10 patients in each group were diagnosed with orthostatic dysfunction (OD) diagnosed based on S-test results. At 6 months post-treatment, S-test abnormality had disappeared in 4 out of 10 HUS cases and 3 out of 10 HDS cases (Mann–Whitney test: $P = .705$).

In the HUS group, we found that after dividing the 44 cases based on SVV status before treatment (SVV+, n = 20; SVV–, n = 24), a Mann–Whitney test revealed that

TABLE I.
Patients Demographics and Test Results for Groups I and II.

	Group-I (G-I)	Group-II (G-II)	Statistics	Total
Treatment	Head-down sleep	Head-up sleep		
Number	n = 44	n = 44		n = 88
Gender	M:F = 14:30	M:F = 14:30	n.s.	M:F = 28:60
Age	52.9 ± 10.6 yr	58.2 ± 15.7 yr	n.s.	53.6 ± 15.0 yr
Duration	65.6 ± 69.5 mo	98.3 ± 100.9 mo	n.s.	68.4 ± 82.5 mo
Type	Hcu: 21; Hca: 9; P: 11; S: 3	Hcu: 19; Hca: 4; P: 15; S: 6	n.s.	Hcu: 40; Hca: 13; P: 26; S: 9
Laterality	R: 18; L: 23; UD: 3	R: 15; L: 23; UD: 6	n.s.	R: 33; L: 46; UD: 9
Nystagmus	50.0% (n = 22)	47.7% (n = 21)	n.s.	48.9% (n = 43)
C-test	18.2% (n = 8)	20.5% (n = 9)	n.s.	19.3% (n = 17)
SVV	45.5% (n = 20)	45.5% (n = 20)	n.s.	45.5% (n = 40)
ieMRI	13.6% (n = 6)	11.4% (n = 5)	n.s.	12.5% (n = 11)
S-test	22.7% (n = 10)	22.7% (n = 10)	n.s.	22.7% (n = 20)
BAP	11.4% (n = 5)	15.9% (n = 7)	n.s.	13.6% (n = 12)
SDS	40.9% (n = 18)	31.9% (n = 14)	n.s.	36.4% (n = 32)

There were no significant differences between the two groups for any of these variables (n.s.).

M/F = male/female; Age = age (years) at start of treatment; Duration = duration of disease (months) before treatment; Type = type of BPPV; Hcu = horizontal cupula; Hca = horizontal canal; P = posterior; S = suspicious; R/L/UD = right/left/undetermined; Nystagmus = positional/positioning nystagmus observed at start of treatment; C-test = caloric test; SVV = subjective visual vertical; ieMRI = inner ear MRI; S-test = Schellong test; BAP = bone alkaline phosphatase (mg/L); SDS = self-rating depression scale score; % = percentage of patients with abnormal results at start of treatment.

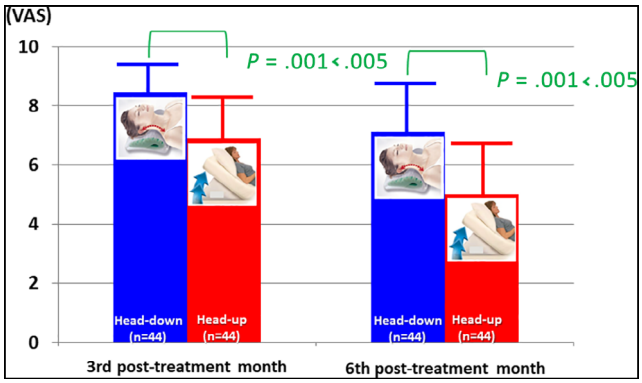

Fig. 3. Effects of head-down sleep vs. head-up sleep on vertiginous sensation for patients with intractable idiopathic benign paroxysmal positional vertigo. Paired *t* test confirmed that VAS scores of vertiginous sensation in the head-up sleep group were significantly lower than those in head-down sleep group at both the third and sixth month post-treatment. VAS = visual analog scale.

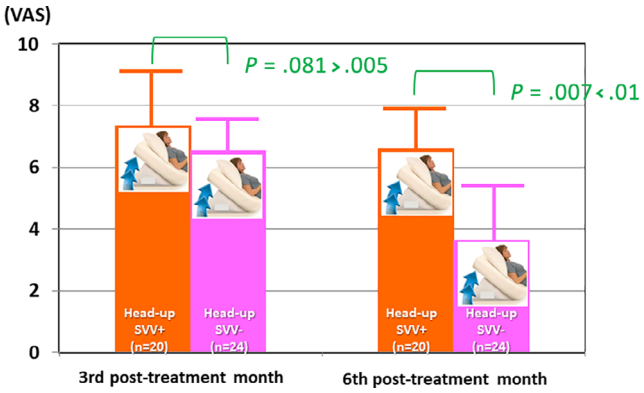

Fig. 4. Effects ad-up sleep treatment on vertiginous sensation in patients with intractable idiopathic benign paroxysmal positional vertigo and positive or negative subjective visual vertical scores. In head-up sleep group, the 44 cases were divided into SVV+ (n = 20) and SVV− (n = 24) before treatment. Paired *t* test confirmed that VAS scores of vertiginous sensation in the SVV− group were significantly lower than those in SVV+ group at 6 months post-treatment, although not significantly lower at 3 months. SVV = subjective visual vertical; VAS = visual analog scale.

VAS scores in the SVV− group were significantly lower than those in the SVV+ group at 6 months post-treatment (SVV−: 3.64 ± 1.88; SVV+: 6.60 ± 1.41; P = .007), but not at the 3 months (SVV−: 6.54 ± 1.25; SVV+: 7.35 ± 1.52; P = .081) (Fig. 4).

DISCUSSION

In the present study, we found that elevating the head to 45° when lying reduced dizziness in patients with intractable idiopathic BPPV who had poor treatment responses to medication and physical maneuvers. Vertiginous sensation was significantly more improved in the HUS group than in the HDS group by the third and sixth month post-treatment. Furthermore, we found strong evidence that the percentages of patients experiencing objective positional/positioning nystagmus and who had subjective complaints decreased significantly more in the HUS group than in the HDS group. Previous studies revealed that cupula type, canal paresis positive status, EH positive status, osteoporosis, and mental distress could be negative prognostic factors on the duration of persistent floating sensation in intractable BPPV.[18–22] There were no significant differences in such patient backgrounds between the HUS and HDS groups in this randomized controlled trial (RCT) study.

Generally, age-related damage to the utricle, head trauma, and inner ear diseases lead otolithic debris from the utricle that get stuck to the crista[2] and/or float in the canal,[3] which results in the onset of motion-evoked vertigo/dizziness. The severity of the motion-evoked vertigo/dizziness in BPPV is thought to be regulated by the amount of canal debris and the intensity of head movement. According to these mechanisms governing the onset of vertigo/dizziness in BPPV, we can consider the therapeutic strategies to combat intractable BPPV as follows: 1) Prevent debris from coming off the utricle; 2) Prevent free-floating debris from coming into the semicircular canal; 3) Return debris to the utricle; and 4) Wait for debris to diminish via turnover. The number of older people is expected to increase in the near future, and debris coming off the utricle could happen repeatedly in a great many older people. It is not so easy to prevent debris from coming off the utricle or to wait for debris to diminish via turnover. It is not a good idea return the endless free-floating debris in the canals to the utricle through repeated physical maneuvers,[7,8] although Epley and Lempert methods have already turned out to be effective are widely used worldwide.[5,6] For these reasons, here we propose keeping the head at 45° when lying down at home to prevent free-floating debris from coming into the semicircular canal. The head-up posture during sleep could be a strain on the neck and/or back. Therefore, before randomization (and after treatment) were used questionnaires to identify and exclude patients with neck and/or waist ailments.

This study has some limitations. First of all, it is not so easy to determine that intractability of BPPV before enrollment into the present HDS/HUS study could be coming from "persistent" or "recurred," judged based on the interview and nystagmus at the time of patients' examination. Anyway, either will be classified into the intractability. Second, because they were at their homes, we relied on self-reports at regular check-ups to confirm that patients were keeping the appropriate head position during sleep. Patients were excluded when they kept <75% compliance with the treatment rules for HDS or HUS. Third, only 43 out of 88 cases had typical nystagmus of BPPV when we began treatment. Therefore, treatment results were evaluated according to objective nystagmus findings in only the 43 cases who initially had nystagmus and subjective vertigo/dizziness symptoms in all 88 cases regardless of nystagmus. Fourth, HUS was reported to do a good job controlling OD in the previous study.[23] HUS might have thus reduced vertiginous sensations due to OD, rather than due to BPPV. However, judging from the results of the Schellong tests before and after treatment interventions, the influence of HUS on OD was likely limited.

It is noteworthy that all 88 patients with intractable idiopathic BPPV, including 45 cases without obvious nystagmus at the start of treatment interventions, exhibited

reduced vertigo through HUS when lying down at home. We consider patients who have no typical positional/positioning nystagmus, but who have persistent movement-evoked vertigo/dizziness, as possible BPPV. We believe that small amounts of free-floating debris in the sensitive canal can result in a persistent movement-derived floating sensation without producing obvious positional/positioning nystagmus. In a super-aging society, the number of patients with possible BPPV is increasing. It is quite regrettable that these people with possible BPPV but no typical nystagmus might be classified into psychogenic vertigo or vertigo of unknown origin. At the extreme, if people all over the world kept a vertical head-up position during sleep, BPPV might disappear. Taken together with the present RCT data, we would like to propose that no nystagmus patients with persistent motion-evoked vertigo/dizziness for 3–6 months should be diagnosed as possible BPPV based on good results from HUS of more than 45° when lying down.

CONCLUSION

Controlling age-related free-floating otoliths is difficult and continuously and repeatedly using physical maneuvers to return them from the canal to the utricle is not a good idea.[7,8] Therefore, HUS when lying down at home is recommended as the first treatment for patients with intractable idiopathic BPPV.

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AUTHOR CONTRIBUTIONS

Akira Horinaka and Tadashi Kitahara: study design, data interpretation, and writing. Tomoyuki Shiozaki and Taeko Ito: data collection and analysis. Yoshiro Wada, Toshiaki Yamanaka, and Kazuhiko Nario: data interpretation.

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