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Prevalence and Severity of Persistent Postural-Perceptual Dizziness in Patients with Peripheral Vestibular Disorders: A Cross-Sectional Study

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Abstract

Objective: Persistent Postural-Perceptual Dizziness (PPPD) is a chronic functional disorder of the nervous system that is characterized by non-spinning vertigo and perceived unsteadiness. PPPD can occur along with other Peripheral Vestibular Disorders (PVD) and can complicate the condition, but the prevalence and severity of the comorbidity have not been reported. This study aimed to investigate the prevalence and severity of PPPD in patients with PVD.

Materials and methods: A cross-sectional study was conducted at the department of neuro-otology in secondary and tertiary settings. Outpatients with PVD were selected through continuous sampling. All participants were diagnosed by neuro-otologists and completed three questionnaires: the Dizziness Handicap Inventory (DHI), Vertigo Symptom Scale-Short Form (VSS-SF), and Hospital Anxiety and Depression Scale (HADS).

Results: Among 187 consecutive patients, 173 patients (92.5%) with PVD were analyzed. Sixty-nine patients (39.9%, (32.5-42.6, and 95% confidence interval)) developed PPPD as a comorbidity. All patients with PPPD had dizziness symptoms that were unrelated to vestibular dysfunction. With regard to the total DHI score, the patients with PPPD (36 (26-54), median (interquartile range)) showed significantly higher scores than those without PPPD (28 (10-47)) (p=0.006). With regard to the Vestibular Symptoms Scores in VSS-SF, patients with PPPD showed significantly higher scores than those without PPPD.

Conclusion: In the secondary and tertiary settings, 4 out of 10 patients with PVD may have PPPD as comorbidity and have a more severe condition. Patients with PVD who have persistent dizziness or unsteadiness should be positively considered for PPPD.

Keywords: Persistent postural-perceptual dizziness; Prevalence; Peripheral vestibular disorder; Handicap; Anxiety; Depression; Vertigo

Abbreviations: PPPD: Persistent Postural-Perceptual Dizziness; PVD: Peripheral Vestibular Disorders; DHI: Dizziness Handicap Inventory; VSS-SF: Vertigo Symptom Scale-Short Form; HADS: Hospital Anxiety and Depression Scale; BPPV: Benign Paroxysmal Positional Vertigo; CSD: Chronic Subjective Dizziness; ICD-11: International Classification of Diseases 11th Revision

Introduction

Dizziness is a common symptom leading to hospital visits with a lifetime prevalence of 17%-30% [1]. Peripheral vestibular disorder (PVD) is the most common cause of dizziness, and 24%-38% of patients with dizziness have an underlying PVD [2,3]. Meanwhile, Benign Paroxysmal Positional Vertigo (BPPV), Meniere's disease, and vestibular neuritis are the common PVDs [2]. BPPV is a highly curable disease characterized by vertigo and nystagmus, which can be resolved spontaneously [4]. In more than 85% of patients with Meniere's disease, vertigo attack is usually controlled by medical treatments [5]. In patients with vestibular neuritis, vertigo and dizziness will typically improve by central vestibular compensation [6]. However, studies reported that patients with PVD sometimes experience persistent dizziness, unsteadiness, or disequilibrium after their vertigo has improved [7-11]. Thus, in patients with PVD, dizziness and unsteadiness often remain and persist despite proper treatment, which is a serious problem especially in the secondary and tertiary settings.

Patients with PVD suffer from persistent dizziness and unsteadiness because of various reasons. First, dizziness and unsteadiness persist because of an uncured PVD or as a sequela of PVD. Dizziness may persist in the following conditions: retention of smaller otoconia or otolith organ dysfunction in BPPV [12], vestibular dysfunction in Meniere's disease [13], and incomplete recovery of the vestibular function and insufficient central compensation in vestibular neuritis [14]. Persistence of dizziness may also be associated with psychological factors such as anxiety [15-17].

In addition to organic vestibular disorders and psychological factors, functional dizziness such as Persistent Postural-Perceptual Dizziness (PPPD) can be a cause of persistent dizziness. PPPD is considered a chronic functional disease of the brain and a condition in which there is a prolonged and over adapted response to acute dizziness; however, it is not a structural or psychiatric condition [18]. The criteria for diagnosing PPPD, which is formerly known as Chronic Subjective Dizziness (CSD) or Phobic Postural Vertigo (PPV) [19], first appeared in the beta edition of the International Classification of Diseases 11th Revision (ICD-11) in 2014 and were defined in ICD-11 [20]. The major symptoms of PPPD are dizziness, unsteadiness, or non-spinning vertigo that persists for more than 3 months [18]. Persistent symptoms of PPPD are usually exacerbated 1) upright posture, 2) active or passive motion, and 3) exposure to moving visual stimuli or complex visual patterns. However, the three exacerbating factors do not have to be equally troublesome. Among the conditions preceding PPPD, vestibular disorders are one of the

most common precipitants [18]. Thus, another cause of persistent dizziness and unsteadiness in PVD may be PPPD.

However, the prevalence of PPPD as a comorbidity of PVD and the severity of PPPD when it occurs along with PVD remain unknown. Hence, this study aimed to assess the prevalence and severity of PPPD in patients with PVD.

Materials and Methods

Patients and procedure

A cross-sectional double-center study was conducted, and the participants were selected through continuous sampling. Among patients who visited the balance clinic in either the Otolaryngology Department at Nagoya City University Hospital or Ichinomiya Municipal Hospital from May 1 to September 30, 2016, and May 1 to September 30, 2017, those who satisfied the following criteria were included: 1) With current PVD diagnosed by a neuro-otologist, 2) Aged 20 years or older, and 3) Visited the clinic more than 3 months after the onset of PVD. By contrast, patients with 1) Severe psychiatric disorders or 2) Difficulty completing the questionnaires because of medical and other factors were excluded.

All participants were examined by a neuro-otologist to determine whether they satisfied the diagnostic criteria for PPPD of ICD-11 at the first visit within the study period. On the basis of the criterion that the three exacerbating factors do not have to be equally troublesome, patients with one, two, or three exacerbating factors were diagnosed with PPPD. A diagnosis of PPPD was established after performing the required vestibular examination and conducting a detailed interview, paying attention to the following characteristics of PPPD. PPPD symptoms are not immediately resolved upon cessation of exposure to exacerbating factors, but they will last for hours or more thereafter. This pattern differs from that experienced by patients with structural vestibular deficits whose symptoms increase and decrease in close temporal relationship to motion [18].

Regarding diagnosis for PVD, BPPV and Meniere's disease were diagnosed according to the diagnostic guidelines by the Barany Society [21,22], and vestibular neuritis was diagnosed based on the following criteria: 1) a single vertigo attack with nausea or vomiting that lasted for at least 24 hrs, 2) Spontaneous nystagmus in videonystagmography, 3) Caloric test showing at least 25% asymmetry, and 4) Absence of hearing loss or other neurologic signs [23]. Vestibular migraine was not included in the criteria for diagnosing PVD as it remains controversial whether vestibular migraine is a peripheral or central disorder [24].

Measures

All patients completed three questionnaires on the day of the diagnosis: the Dizziness Handicap Inventory (DHI) for a primary outcome measure [25,26], Vertigo Symptom Scale-Short Form (VSS-SF) [27,28], and Hospital Anxiety and Depression Scale (HADS) [29,30] for secondary outcome measures.

Dizziness Handicap Inventory (DHI)

The DHI is a self-administered questionnaire comprising 25 questions related to disability and dysfunction due to dizziness, and the items are rated from 0 to 100 points [25]. It is used as a standard tool for assessing the severity of dizziness and handicap in an individual's daily life. The original and Japanese versions of the DHI have been validated [26].

Vertigo Symptom Scale-Short Form (VSS-SF)

The VSS-SF is a self-administered scale that evaluates the severity of symptoms, and the items are rated from 0 to 60 points. It comprises 15 items that measure the frequency of vestibular symptoms, such as vertigo, dizziness, and unsteadiness, and autonomic anxiety symptoms, and each of these items is rated from 0 to 4 points [27]. Higher scores indicate greater severity. The original and Japanese versions of the VSS-SF have been validated [28].

Hospital Anxiety and Depression Scale (HADS)

The HADS is a 14 item self-administered scale that evaluates anxiety and depression on seven items each. Each item is rated from 0 to 3 points, and the severity of anxiety and depression is measured separately with each subscale score of 0-21 points [29]. A higher score indicates a higher degree of anxiety and depression. The original and Japanese versions of the HADS have been validated [30].

Statistical analysis

The patients were divided into two groups: patients with PPPD and patients without PPPD. The Shapiro–Wilk test was used to analyze the data with non-normal distribution. The Mann–Whitney test was used to compare the groups in terms of the DHI, VSS-SF, and HADS scores. All statistical tests were two sided. Because the test was performed five times, a difference of $p<0.01$ was considered significant by Bonferroni correction. All statistical analyses were performed using EZR version 1.37 for Windows (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria) [31].

Results

Among 187 consecutive patients, 14 (7.5%) were excluded because they refused to fill out the questionnaire: 7 due to their busy schedule, 4 due to extreme old age, 2 due to a vertigo attack, and 1 due to an advanced visual impairment. Therefore, 173 patients (42 men and 131 women; median age, 62 years; range, 27-86 years) participated and completed the questionnaires without a missing value, and their cases were analyzed.

Table 1 shows the characteristics of the 173 patients with PVD in this study. On the basis of the results of the Shapiro–Wilk test for age, duration from onset of PVD, DHI, VSS-SF, and HADS, almost all data were not normally distributed. The age, gender, duration from the onset of PVD, and diagnosis of PVD were similar between patients with and without PPPD.

Characteristics	With PPPD	Without PPPD	p-value	Total
	n=69	n=104		n=173
Age, median (IQR), years	60 (45.0-71.0)	65 (52.5-72.8)		62 (49-72)

Female, n (%)	53 (76.8)	78 (75.0)		131 (75.7)
Duration from onset, median (IQR), months	29.5 (14.3-79.5)	30.1 (5.4-92.7)		29.4 (9.6-87.7)
Diagnosis of PVD, n (%)				
Meniere's disease	36 (52.2)	62 (59.6)		98 (56.6)
BPPV	14 (20.3)	24 (23.1)		38 (22.0)
Vestibular neuritis	9 (13.0)	14 (13.5)		23 (13.3)
Other PVDs	10 (14.4)	4 (3.8)		14 (8.1)
DHI, median (IQR)				
Total	36 (26-54)	28 (10-47)	0.006	32 (14-50)
VSS-SF, median (IQR)				
Vestibular	6 (4-10)	5 (1-8)	0.003	5 (2.8-10)
Autonomic	4 (1.8-7)	3 (1-7)	0.132	3 (1-7)
HADS, median (IQR)				
Depression	6 (3-8)	5 (2-8)	0.06	5 (3-8)
Anxiety	6 (4-8)	4 (2-8)	0.013	5 (3-8)

Table 1: Characteristics and questionnaire results of patients with and without PPPD. IQR: Interquartile Range; PPPD: Persistent Postural-Perceptual Dizziness; PVD: Peripheral Vestibular Disorder; BPPV: Benign Paroxysmal Positional Vertigo; DHI: Dizziness Handicap Inventory; VSS-SF: Vertigo Symptom Scale-Short Form; HADS: Hospital Anxiety Depression Scale. Italic letters indicate $p<0.01$.

Among 173 patients, 69 (39.9% (32.5-42.6, 95% confidence interval)) were diagnosed with PPPD. All patients with PPPD had dizziness symptoms that were unrelated to vestibular dysfunction. For example, a patient's symptom of dizziness exacerbated for some time while looking at the display shelves or riding on an escalator and continued after the situation passed. Patients with PPPD had significant total scores on the DHI and vestibular scores on the VSS-SF compared with those without PPPD.

Post hoc analysis

The Barany Society version of the diagnostic criteria for PPPD was reported in 2017, and it requires the presence of all three exacerbating factors: upright posture, active or passive motion, and exposure to moving visual stimuli or complex visual patterns [18]. Meanwhile, the ICD-11 version does not clearly describe whether all three exacerbating factors are required or not. We explored whether patients had three exacerbating factors using the clinical records retrospectively collected. Among 69 patients with PPPD on ICD-11, 31 were diagnosed with PPPD based on the Barany version, and 38 had an unknown number of exacerbating factors. Assuming that these uncertain patients were not diagnosed with PPPD based on the Barany version, the prevalence of PPPD on the Barany version was calculated to be 17.9% (12.5-24.5, 95% confidence interval, 31/173 cases).

Discussion

This is the first study to report the prevalence of PPPD among patients diagnosed with PVD. Approximately 40% of patients with PVD at the balance clinics in secondary and tertiary settings were diagnosed with PPPD, and patients with PVD had greater levels of self-perceived handicap because of dizziness.

The prevalence of PPPD among patients with PVD in our study was higher than that of PPPD among patients with dizziness in previous studies because PVD patients may be exposed more frequently to the precipitants of PPPD. According to previous studies on the prevalence of this condition, 15%-20% were considered to have PPV or CSD, and PPPD is the second most common condition (BPPV as the top most prevalent disorder) occurring in all adult patients with dizziness in tertiary care centers [18,32]. Kim et al. also reported that the prevalence of PPPD (but including psychogenic dizziness) was 20.8%, the second most common disorder after BPPV in patients with dizziness visiting tertiary care centers [2]. The prevalence of PPPD among patients diagnosed with PVD in our study was approximately 40% and higher than that among patients with dizziness in previous studies. This finding may be related to the frequency of conditions that precipitate dizziness. PPPD is precipitated by conditions that cause dizziness, and the most common precipitating conditions are peripheral or central vestibular disorders (25%-30% of cases) [18]. Yan et al. also reported that 44% of the precipitants were vestibular dizziness [33]. In addition, the median duration from PVD onset in our study was two and a half years, and patients with long-term vestibular symptoms may be constantly exposed to conditions that can induce PPPD. Hence, in PVD patients with long-term vestibular symptoms, attention should be paid to the onset of PPPD.

The DHI score of PPPD patients with PVD in our study was lower than that of PPPD patients in previous studies. Previous studies at tertiary settings reported that the mean or median of DHI scores of PPPD (n=14), CSD (n=24), or PPV (n=6) patients was 54-73 points [34-36]. Compared with previous studies, our study used a larger sample size and might have less bias. Moreover, our study might include patients with milder conditions at the secondary setting.

In previous studies, the DHI scores of PPPD patients were significantly higher than those of PVD patients, including those with BPPV or vestibular neuritis [34,36]. In our study, PVD patients with PPPD showed significantly higher DHI scores than PVD patients without PPPD. Therefore, PPPD was found to additively progress the dizziness handicap to PVD. The fourth item of DHI, "Does walking down the aisle of a supermarket increase your problem?," asks regarding one of the exacerbating factors of PPPD. For this question, patients with PPPD scored significantly higher than those without PPPD ($p=0.022$) in the Mann–Whitney test, which might be one of the reasons why the patients with PPPD scored higher on DHI. In the Vestibular Symptoms Scale of VSS-SF, patients with PPPD showed a higher frequency of vestibular symptoms than those without PPPD, which is also the reason for the higher scores in DHI. The sixth item

of VSS-SF, "A feeling of being dizzy, disoriented or 'swimmy,' lasting all day," asks regarding the primary symptom of PPPD. For this question, patients with PPPD scored significantly higher than those without PPPD (p=0.012), which might be one of the reasons why the patients with PPPD scored higher on the vestibular symptoms scale of VSS-SF.

With regard to depression and anxiety, Yan et al. reported that 27.9% of PPPD patients had depression based on their scores on the Hamilton depression scale and 60.5% had anxiety based on their scores on the Hamilton anxiety scale. Moreover, PPPD patients were more likely to experience anxiety, but not depression, compared with patients with the following groups of PVDs: Meniere disease, BPPV, and vestibular neuritis [33]. In contrast, among PPPD patients in our study, 29.0% had depression; however, only 31.9% had anxiety when the cutoff value of the HADS subscale score was set to more than equal to 8 points (indicating clinically significant depression/anxiety). As our study only included PVD patients, the proportion of patients whose precipitants of PPPD were vestibular symptoms of PVD might be large, and the proportion of patients whose precipitants of PPPD were anxiety or panic attacks might be relatively small. These may be the reason for the smaller number of cases with anxiety in our study. Comparison of PVD patients with/without PPPD showed no significant difference in the severity of depression and anxiety. For anxiety, the p-value was as low as 0.013, which suggested that PPPD patients had some tendency of experiencing anxiety.

This study has several limitations. First, we used the ICD-11 criteria for diagnosing PPPD, not the criteria from the Barany Society established in 2017. Since this study was initiated in 2015, the number of patients who had all three exacerbating factors was not investigated. The post hoc analysis was performed retrospectively. Therefore, it was not able to determine the number of cases that met the Barany Society diagnostic criteria. However, at least 17.9% of PVD patients met the Barany Society diagnostic criteria of PPPD, and PVD patients still need to be assessed for signs of PPPD complications. Second, we did not compare the two groups in terms of the effect of vestibular dysfunction because we did not obtain the results of vestibular function tests such as the caloric test, vestibular evoked myogenic potential test, or video head impulse test. Because this study focused on the patient's clinical diagnosis, only the tests necessary for diagnosis were performed. Third, considering the purpose of the study and interest in the prevalence and severity of PPPD in PVD, we addressed various diseases collectively as PVD. Hence, further study is warranted to evaluate each of the PVDs. Fourth, this study was conducted in the secondary and tertiary settings. Therefore, the results of this study do not provide information regarding PPPD in the primary setting.

This study had a few strengths. This study was carried out in two facilities, not in a single facility, used continuous sampling, and had a participation rate of 92.5%. Therefore, this study has good representativeness.

PPPD can be treated by vestibular rehabilitation, serotonergic medications, and cognitive behavior therapy [37], and patients with a longer duration of illness have a small treatment benefit [38]. Therefore, patients with persistent dizziness should be actively considered for PPPD diagnosis.

Conclusion

A total of 40% patients with PVD in the secondary and tertiary settings possibly have PPPD as comorbidity. In patients with PVD, those with PPPD had more severe symptoms than those without PPPD. Because PPPD is a curable disease, Patients with PVD who have persistent dizziness or unsteadiness should be actively considered for PPPD diagnosis as comorbidity.

Statements

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Statement of ethics

This study was approved by the Research Ethics Committee, Graduate School of Medicine, at Nagoya City University (60-19-0203) and was conducted according to the tenets of the Declaration of Helsinki. A written informed consent was made by signing the questionnaire.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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