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The relationship between vasomotor symptoms and menopause-associated dizziness

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Running title: Dizziness and vasomotor symptoms

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Abstract

Conclusion: Vasomotor symptoms (VMS) and especially hot flushes are negatively associated with recovery from menopause-related dizziness. A further study is justified in order to determine whether hormone replacement therapy (HRT) can shorten this recovery time. *Objectives:* This study aimed to compare the rate of recovery from dizziness between patients who had VMS and those who did not. We also evaluated the effect of HRT on recovery from dizziness. *Methods:* The medical records of 85 women aged between 40 and 59 years were analyzed retrospectively. The patients were asked detailed questions about their menopausal symptoms as well as any episodes of dizziness, which were diagnosed based on neuro-otological examinations and were treated appropriately. All patients were followed up until dizziness improved. *Results:* Over a 2-month period, the rate of recovery from vertigo was significantly higher in patients without VMS (no-VMS group, n = 38) than in those with VMS (VMS group, n = 29). In the VMS group, patients treated with HRT (n = 7) recovered from dizziness more quickly than those who were not treated with HRT (n = 22), although this difference was not statistically significant.

Keywords: hot flushes, hormone replacement therapy

Introduction

Data from the National Institutes of Health (NIH) suggest that in the United States, most women experience menopause between 40 and 58 years of age, with a median age of 52 years [1]. Other studies have reported a universal age of menopause of approximately 50 years [2-5]. The World Health Organization and the Stage of Reproductive Aging Workshop (STRAW) working group have defined menopause as the permanent cessation of menstrual periods that occurs naturally or is induced by surgery, chemotherapy, or radiation. Menopausal transition often begins with a variation in the length of the menstrual cycle [1].

Some women who transit menopause have no symptoms at all, but most experience some symptoms, often beginning several years before the final menstrual period [1]. Menopausal symptoms include vasomotor symptoms (VMS; hot flashes and night sweats), dizziness, palpitation, headache, stiff shoulder, insomnia, depression, nervousness, anxiety, fatigue, and irritability [5, 6]. Of the many symptoms of menopause that may affect a women's quality of life, the most common are those related to thermoregulation, specifically hot flashes and night sweats [2]. Hot flashes (a sudden sensation of intense heat with sweating and flushing, typically lasting 5–10 minutes) and night sweats are reported to occur frequently in perimenopausal women (i.e., those in menstrual transition and in the first year after their last menses) [3]. Longitudinal and cross-sectional observational studies have provided strong evidence showing that the

menopausal transition causes VMS [1], of which dizziness is one of the most common manifestations during perimenopause and especially during the late stage of menopausal transition [7]. Previous studies have suggested a causal relationship between VMS and balance disturbances on the basis of epidemiologic investigations of the general population conducted using a questionnaire [8].

The present study aimed to assess whether there is an association between VMS and menopause-related dizziness. In addition, we compared the period required to recover from dizziness between patients who had VMS and those who did not. Hormone replacement therapy (HRT), using estrogen alone or estrogen combined with progestin, is the most consistently effective therapy for hot flushes and night sweats [1, 4]. Therefore, we also investigated whether HRT is effective in reducing dizziness in patients with VMS symptoms, including hot flushes.

Subjects and methods

We retrospectively analyzed the outpatient and inpatient records of 85 women aged 40–59 years who had both menopausal symptoms and dizziness between April 2008 and March 2012. In our department, dizziness in each patient was treated with medication including betahistine and steroid therapy or physical exercise. In addition, 52 of the 85 patients visited the gynecology department for treatment of menopausal symptoms. The patients were asked detailed questions about their menopausal symptoms as well as

dizziness, and were diagnosed based on clinical symptoms and neuro-otological examinations. The latter consisted of a pure tone audiogram and vestibular functional tests, including gaze nystagmus, positional and positioning nystagmus using an infrared CCD camera, and/or electronystagmography (ENG). In addition, eye tracking, optokinetic nystagmus, and caloric tests (with a cold air temperature of 24°C and a warm air temperature of 46°C, for 1 minute) were recorded using ENG. Magnetic resonance imaging (MRI) was performed to rule out intracranial lesions such as infarction, hemorrhage, or vestibular schwannoma.

We checked for menopausal symptoms, especially VMS such as hot flushes and night sweats, in each patient. We first subjectively compared the time to recover from dizziness between patients who had VMS and those who did not. Seven patients in the VMS group were administered HRT orally or with transdermal patches or a gel. We compared the time taken to recover from dizziness between patients who received HRT (HRT group) and those who did not (no HRT group).

We obtained informed consent from all patients. This study was approved by the Institutional Review Board of Toho University Sakura Medical Center (No. 2012-080 on January 9, 2013) and was conducted in full accordance with the Declaration of Helsinki. A statistical analysis was performed using Fisher's exact test. A value of $p < 0.05$ was considered statistically significant.

Results

Neuro-otological diagnoses

Neuro-otological examinations revealed 44 cases (51.8%) of benign paroxysmal positional vertigo (BPPV), 15 cases (17.6%) of peripheral vestibulopathy, and 14 cases (16.5%) of Meniere's disease. In addition, 2 patients were diagnosed as sudden deafness with vertigo, and there was a single case each of vestibular schwannoma, vasomotor angina, and mitochondrial encephalomyopathy.

Neuro-otological diagnoses in the VMS and no-VMS groups

The presence or absence of VMS was not recorded in the medical records of 6 of the 85 patients. Furthermore, 12 patients did not come back to our hospital for the 1-month follow-up; therefore, we were able to compare 29 cases in the VMS group with 38 cases in the no-VMS group. No significant difference was found between the 2 groups with respect to disease distribution, as diagnosed by neuro-otological examination (Table 1).

Comparison of the VMS and no-VMS groups

The rate of recovery from dizziness was significantly higher in the no-VMS group than in the VMS group, when measured at the end of a 2-month period (Fig. 1). However, no significant differences were found if this rate was measured after only 1 month, or beyond 2 months.

Comparison of the HRT and no-HRT groups

Seven patients in the VMS group received HRT. These patients recovered more quickly from dizziness than patients who were not treated with HRT; however, this difference was not statistically significant (Fig 2).

Discussion

In this study, we found a negative association between the time needed to recover from dizziness and the presence of VMS in middle-aged women considered to be in menopausal transition. These women recovered from dizziness more slowly compared to those who did not have VMS. When assessed after 2 months, the rate of recovery from dizziness was significantly higher in the no-VMS group than in the VMS group ; however, no significant difference was observed between the 2 groups beyond 2 months (Fig. 1).

Although the occurrence of VMS may be associated with an early recovery from menopause-related dizziness, it may not affect the final rate of recovery. Another possibility is that the therapeutic effect of VMS treatment may occur over a 3-month period.

Vertigo, dizziness, unsteadiness, and a fainting sensation are common menopausal symptoms. A study conducted in Nagano, Japan found that 41.7% of the female population aged between 45 and 60 years had felt dizzy or faint at some point [9]. In general, middle-aged women visit their gynecologist for bothersome symptoms, including dizziness, when they think that these symptoms may be related to menopause [3]. Dizziness and vertigo, which occur during perimenopause, are frequently misclassified as

nonspecific climacteric symptoms or are mistakenly thought to have a psychological cause [7]. In the present study, 75 of the 85 patients who reported menopause-related vertigo or dizziness also had peripheral vestibular symptoms. Therefore, we suggest that middle-aged women suffering from dizziness should be assessed by both a gynecologist and an otolaryngologist.

We found that 44 of 85 patients who experienced menopausal-related dizziness were also diagnosed with benign paroxysmal positional vertigo (BPPV) during neuro-otological examinations. Studies using mice have demonstrated that the rapid decline of estrogen during menopause causes a reduction in the number of estrogen receptors, inducing a disturbance in otoconial metabolism; this may explain the high prevalence of BPPV [10]. We did not find a significant difference in the prevalence of BPPV between the VMS and no-VMS groups. This finding suggests the occurrence of VMS in BPPV may not be associated with disturbed otoconial metabolism. Physical activity may improve VMS through increased production of endogenous opioids [11]. Given that BPPV can be cured with vestibular rehabilitation [12], physical rehabilitation may be useful for treating menopausal women suffering from both dizziness and VMS.

Menopausal signs and symptoms are generally attributed to 3 main causes: reduced estrogen production (giving rise to VMS and vaginitis), sociocultural changes, and psychological changes [6]. Sociocultural factors include a lack of support by intimate friends and a low socioeconomic status

[13]. Psychological factors include a feeling of poor health, low self-esteem, a perceived lack of respect from people, dissatisfaction with present life, anxiety about the future, and a feeling of being a burden to one's family and/or community [13]. In the current study, 14 of 85 patients with menopause-related dizziness also had Meniere's disease. Because vertiginous attacks in Meniere's disease may also be influenced by psychological and sociocultural factors [14], a psychological approach using anxiolytic and antidepressants drugs may be an effective strategy for treating menopause-related dizziness.

An additional finding in this study was that significantly more patients recovered from vertigo within 2 months in the no-VMS group compared to the VMS group. Ekblad et al. also described a relationship between balance disturbances and hot flashes [8]. In agreement with their observation, we found that the recovery period for dizziness was greater in the VMS group than in the no-VMS group. Among women with VMS who were also experiencing postural imbalance, hot flashes and sweating may affect the quality of nighttime sleep, which would in turn may influence concentration and balance function [8]. In addition, VMS may negatively affect the central integration of balance impulses in the central nervous system [8].

Recently, the incidence of hot flashes has increased in Japanese menopausal women and is approaching that for menopausal women in Europe and America [9]. Estrogen therapy is one of the most effective

treatments for VMS [2, 15], and postural balance in postmenopausal women with VMS is significantly improved by HRT [16]. In addition, older women who are prescribed estrogen over a prolonged period have better postural balance than that of women of a similar age who are not prescribed estrogen [17]. However, several studies have reported results that conflict with these findings; in these studies, HRT did not reduce vertigo and balance disturbances [8, 15, 18]. Estrogen is thought to act on the hearing and vestibular functions of the inner ear [10]. Menopausal women receiving HRT have slightly better hearing compared to those not being treated with HRT [19]. In Japan, middle-aged women with menopausal symptoms are often treated not only with HRT but also with a traditional herbal medicine known as kampo [20]. In the current study, HRT was associated with an earlier recovery from dizziness, although this association was not statistically significant. However, as this study only included 7 patients who received HRT, a further study that includes more patients receiving HRT is needed to assess the effectiveness of HRT in reducing menopausal-related dizziness.

In conclusion, VMS, especially hot flushes, are negatively associated with an early recovery from menopause-related dizziness. HRT was ineffective in reducing the recovery time after dizziness.

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Figure legends

Figure 1. The rate of recovery from dizziness was significantly higher in patients without vasomotor symptoms (VMS) (no-VMS group, n = 38) than in patients with VMS (VMS group, n = 29), over 2 months.

Figure 2. There was no significant difference in the time needed to recover from dizziness between patients treated with hormone replacement therapy (HRT group, n = 7) and those who did not receive HRT (no-HRT group, n = 22) among patients with VMS.

Figure 1.

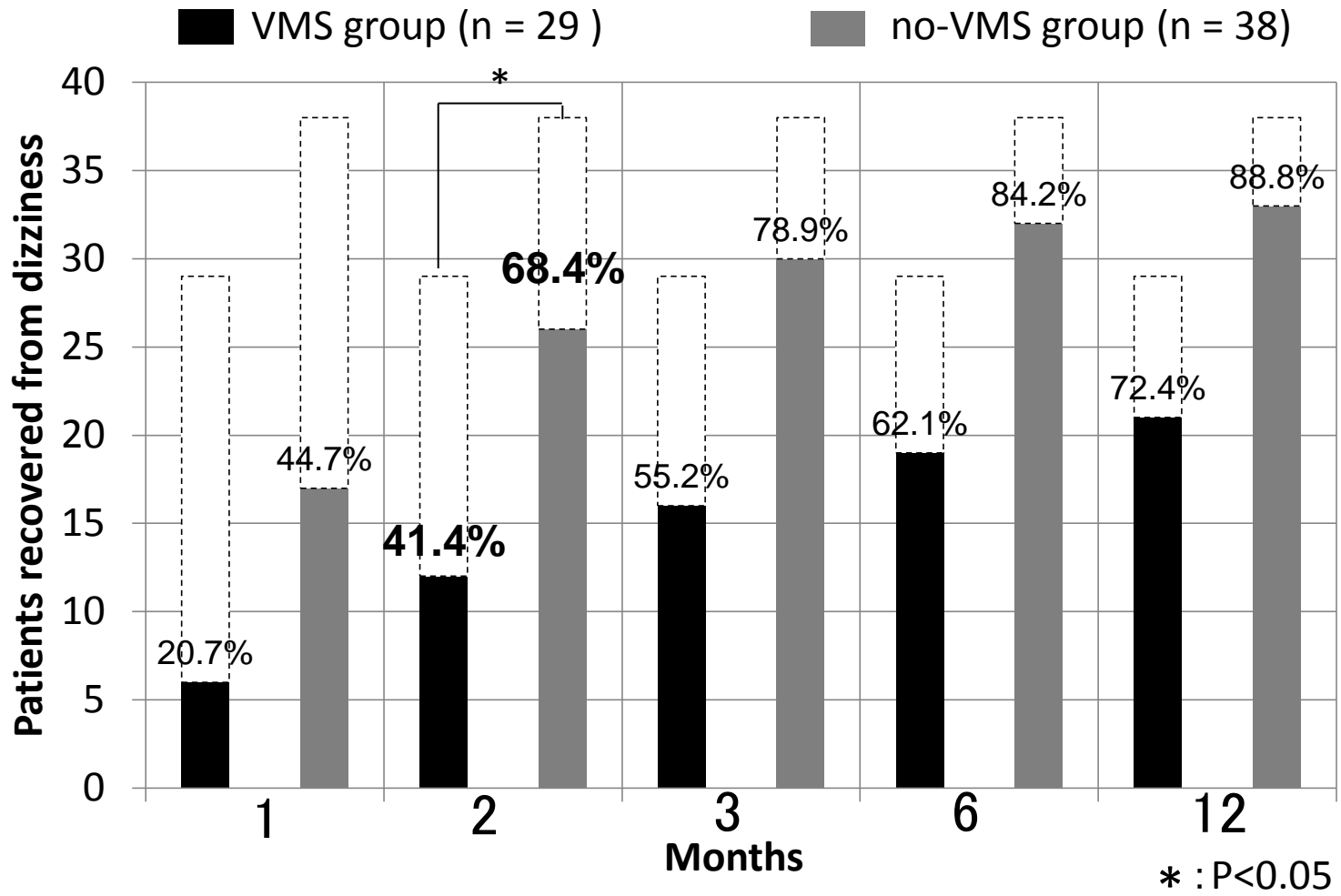


Figure 2.

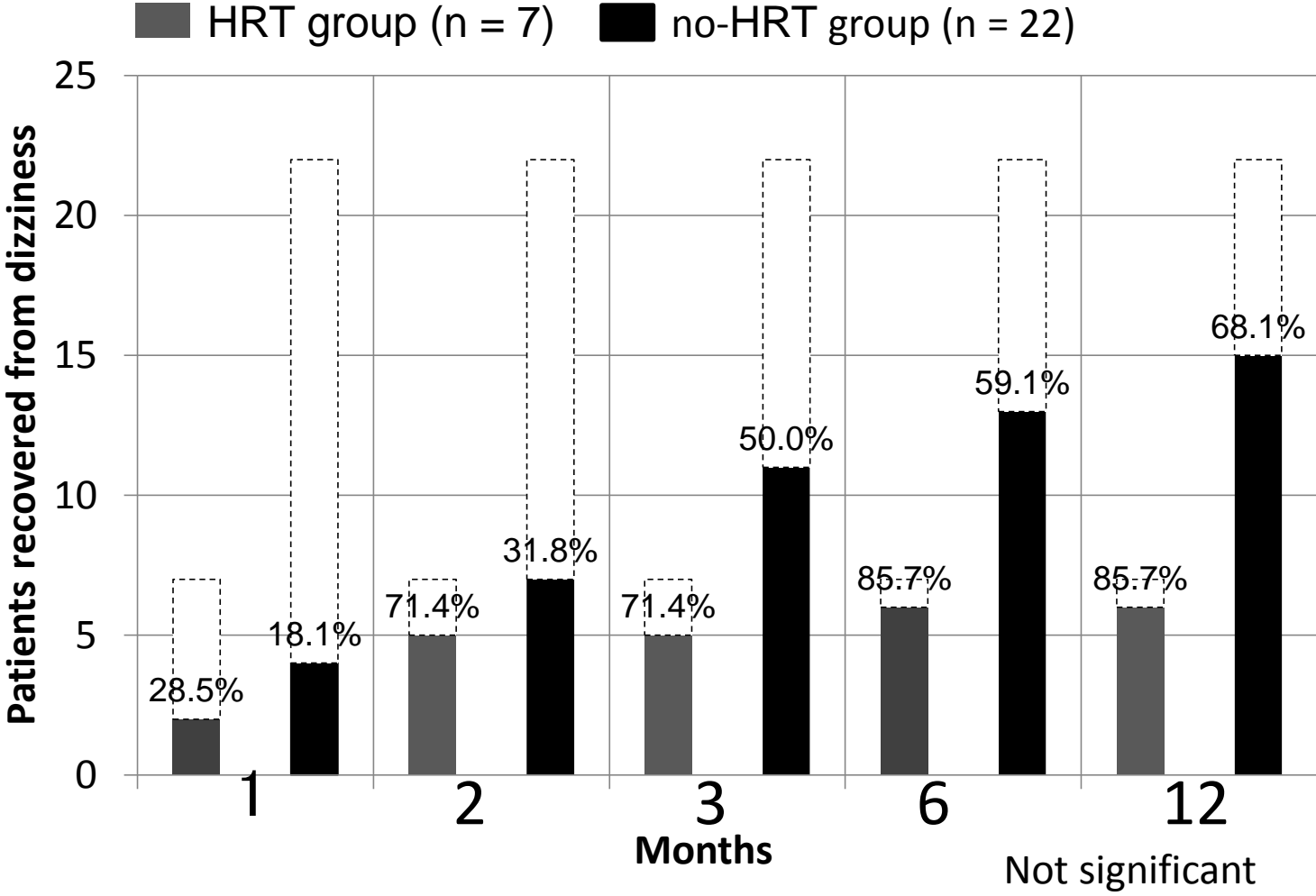


Table 1. Neuro-otological diagnoses for patients with or without vasomotor symptoms (VMS)

Diagnosis	VMS (n = 29)	No-VMS (n = 38)	P Value
BPPV	13 (44.8%)	19 (50.0%)	NS
Peripheral vestibulopathy	7 (24.1%)	8 (21.1%)	NS
Meniere's disease	5 (17.2%)	7 (18.4%)	NS
Sudden deafness	0 (0.0%)	2 (5.3%)	NS
Vestibular schwannoma	1 (3.4%)	0 (0.0%)	NS
Cardiac disorder	1 (3.4%)	0 (0.0%)	NS
Unknown etiology	2 (6.9%)	2 (5.3%)	NS

NS, not significant; BPPV, benign paroxysmal positional vertigo