Vestibular Migraine has Higher Correlation with Carsickness than Non-vestibular Migraine and Meniere's Disease

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Abstract

Purpose: To investigate whether patients with vestibular migraine (VM) are more susceptible to carsickness than patients with non-vestibular migraine (NVM) or Meniere's disease (MD).

Methods: Consecutive patients with a diagnosis of definite VM, probable VM, NVM, or MD at our Headache and Dizziness clinics were interviewed using the same three questions to investigate the history of carsickness. The patients who had experienced carsickness in their lifetime and those who had still experienced carsickness in the past ten years were identified. The rates of carsickness were compared between groups.

Results: 78.4% of the VM patients had experienced carsickness in their lifetime, which was significantly higher than the patients with NVM (43.6%) and MD (18.2%). Both the lifetime rate of carsickness and the rate in the past ten years were highest in the patients with definite VM, followed by probable VM, NVM, and MD ($p<0.05$, chi-square test). The odds ratio of lifetime carsickness for VM versus MD was high (8.7).

Conclusion: Both patients with definite VM and probable VM were more susceptible to carsickness than the patients with NVM or MD. This reinforces the theory of vestibular hypersensitivity in VM. We suggest that a past history of carsickness may help in the diagnosis of VM, and especially in distinguishing VM from MD.

Key Words: vestibular migraine, migrainous vertigo, carsickness, motion sickness, Meniere's disease

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INTRODUCTION

A close relationship between migraine and vertigo has been postulated for decades[1,2], however, it has only been studied extensively in the last 10 years. Since Neuhauser et al. established an uniform diagnostic criteria for vertigo associated with migraine[3,4], vestibular migraine (VM, or migrainous vertigo) has been considered to

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Table 1A. Neuhauser's criteria of vestibular migraine

Definite vestibular migraine:

(1) Recurrent episodic vestibular symptoms of at least moderate severity;
(2) Current or previous history of migraine according to the criteria of the International Headache Society;
(3) One of the following migrainous symptoms during at least two vertiginous attacks: migrainous headache, photophobia, phonophobia,
visual or other auras;
(4) Other causes ruled out by appropriate investigations.

Probable vestibular migraine:

(1) Recurrent episodic vestibular symptoms of at least moderate severity;
(2) One of the following:
(a) Current or previous history of migraine according to the criteria of the International Headache Society,
(b) Migrainous symptoms during 2 attacks of vertigo,
(c) Migraine-precipitants before vertigo in more than 50% of attacks: food triggers, sleep irregularities, hormonal changes,
(d) Response to migraine medications in more than 50% of attacks;
(3) Other causes ruled out by appropriate investigations.

Table 1B. AAO-HNS criteria of definite Meniere's disease

Definite Meniere's disease

(1) Two or more definitive spontaneous episodes of vertigo lasting 20 minutes or longer;
(2) Audiometrically documented hearing loss on at least one occasion;
(3) Tinnitus or aural fullness in the treated ear;
(4) Other causes excluded.

AAO-HNS: American Academy of Otolaryngology-Head and Neck Surgery

be one of the most common vestibular disorders in the general population[5]. However, VM remains a diagnostic challenge for most clinicians under Neuhauser's criteria (Table 1) because of the following reasons:

1. VM is a clinical diagnosis. It cannot be verified by any biomarkers, imaging studies, or electrophysiological examinations.
2. Both the vestibular symptoms and signs of VM are nonspecific. The duration and frequency of vestibular episodes are highly variable between individuals[6].
3. The clinical diagnosis of VM mostly relies on comorbid migrainous headache. Both vertigo and headache have a high prevalence in the general population. It is sometimes difficult to distinguish whether migraine coexists with other dizziness or truly with VM. Therefore, it is necessary to seek other diagnostic clues beside migrainous headaches to support the diagnosis of VM.
4. Many patients fitting the criteria of probable VM have vertigo and migraine without a temporal relationship[3]. In clinical practice, it is difficult to make a diagnosis if the patients complain about recent vertigo but cannot remember their headache history in detail. Moreover, some patients have rare migrainous symptoms but their vertigo responds to prophylactic migraine drugs.
5. Since some clinical features of VM and Meniere's disease (MD) overlap, VM is often misdiagnosed as MD[7].

Motion sickness is a common physiological condition. The prevalence of motion sickness is about 28% in the general population, however there are differences between carsickness, seasickness, and airsickness[8]. The prevalence of carsickness is unknown, however it is known to be much lower than that of seasickness. It has been recognized for many years that motion sickness is linked to migraine, and about 50% of migraineurs report motion sickness, which is much higher than in the general population[2]. In addition, motion sickness and migraine share some common features including female-predominance, similar symptoms, and the same triggers (such as menstrual cycle and sleep)[9]. Vestibular[10,11] or gastrointestinal hyperexcitability[12] has been proposed to be the cause, however the true pathophysiology of this association is still uncertain.

In this study, we compared the rates of carsickness in patients with VM, non-vestibular migraine (NVM), and MD. Evidence that VM is related to hypersensitivity of the vestibular system has recently been reported[13-15]. If true, the patients with VM may be more susceptible to motion sickness than patients with migraine without vestibular symptoms and other disorders.

METHODS

Subjects

Consecutive patients with a diagnosis of VM, NVM, or MD were recruited from our Dizziness and Headache Special Clinics from September 2010 to April 2011. All patients underwent comprehensive history taking and neurological examinations. The diagnosis of migraine was made based upon the criteria of the International Classification of Headache Disorder-II[16]. The diagnosis of VM was in accordance with Neuhauser's criteria[3] (Table 1A) following the diagnostic algorithm proposed by Furman et al[17]. On the basis of Neuhauser's criteria, the patients with VM were further classified into two groups; definite VM (dVM) and probable VM (pVM). The patients who fit the criteria of migraine but not the criteria of dVM or pVM were classified as NVM. The diagnosis of MD was based on the criteria of definite MD established by the American Academy of Otolaryngology-Head and Neck Surgery[18] (Table 1B). Because the VM criteria partially overlap the MD criteria, the MD patients who had a migraine history may also have met the VM criteria and were thus excluded from the MD group.

Patients with intracranial lesions were excluded by brain computed tomography (CT) or magnetic resonance imaging (MRI). The patients whose vestibular symptoms resulted from other vestibular disorders were excluded by detailed clinical history, neurotological examinations, videonystagmography, or caloric test. The patients who were unable to describe their headache or vertigo well, those with mixed-type headache, and those with major central nervous system diseases were also excluded from the study.

This study was performed in accordance with the declaration of Helsinki and was approved by the hospital's Institutional Review Committee on Human Research.

Assessment of carsickness

All of the recruited patients were interviewed by two neurologists specializing in vestibular disorders and headache. Carsickness was defined as dizziness, nausea, and/or vomiting provoked by riding in an automobile or a bus. We investigated the history of carsickness using the same three questions for each patient:

1. Have you ever experienced carsickness?
2. When did you start to experience carsickness?
3. When was the most recent experience of carsickness?

The subjects were then classified into: (1) those who had experienced carsickness in their lifetime; and (2) those who had never experienced carsickness. For those who had experienced carsickness in their lifetime, the patients who had still experienced carsickness in the past ten years were identified.

Statistical analysis

ANOVA was used to analyze age between the groups. Comparisons of gender and rate of carsickness between the groups of dVM, pVM, NVM, and MD were analyzed by the chi-square test using SPSS version 16 (SPSS Inc., Chicago, IL, USA). We also calculated the odds ratios of carsickness among each group.

RESULTS

A total of 149 patients were recruited into this study (Figure 1). Eighty-eight patients had VM, 39 had NVM, and 22 had MD. The VM group was further divided into those with dVM (37 patients) and those with pVM (51 patients). Table 2 shows the demographic data and carsickness rates among the different groups. Compared with the dVM (89.2%), pVM (92.2%) and NVM (79.5%)

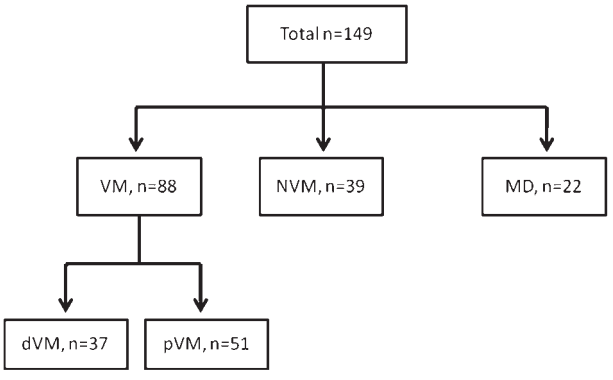

Figure 1. Algorithm of the classification of migraine and Meniere's disease in this study.
VM: vestibular migraine; dVM: definite vestibular migraine; pVM: probable vestibular migraine; NVM: non-vestibular migraine; MD: Meniere's disease

Table 2. Demographic Data and Carsickness Rates in the Patients with VM, NVM, and MD

	Case Number, n	Women, n (%)	Mean Age± SD, years	CS, n (%)	CS10, n (%)
VM	88	80 (90.9)	46.2 ± 12.9	69 (78.4)	47 (53.4)
dVM	37	33 (89.2)	43.1 ± 12.¬8	33 (89.2)	27 (73.0)
pVM	51	47 (92.2)	48.4 ± 12.6	36 (70.5)	20 (39.2)
NVM	39	31(79.5)	34.7 ± 16.0	17 (43.6)	12 (30.8)
MD	22	11(50.0)	66.6 ± 10.9	4 (18.2)	2 (9.1)

VM: vestibular migraine, dVM: definite VM, pVM: probable VM

NVM: non-vestibular migraine, MD: Meniere's disease, CS: lifetime carsickness rate, CS10: carsickness rate in the past ten years

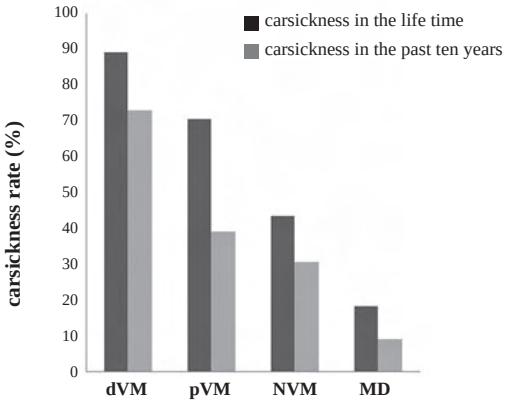

Figure 2. Lifetime rate of carsickness (CS) and carsickness in the past ten years (CS10) were highest in the patients with dVM, followed by those with pVM, NVM, and lowest in the MD group (all $p<0.05$, chi-square test).
VM: vestibular migraine; dVM: definite vestibular migraine; pVM: probable vestibular migraine; NVM: non-vestibular migraine; MD: Meniere's disease

Table 3A. Adjusted odds ratio of lifetime carsickness between different migraine groups

	OR	95% CI		P-value
NVM	Ref.			
VM	6.73	2.57	17.63	<0.001
dVM	13.90	3.77	51.34	<0.001
pVM	4.31	1.52	12.17	0.006

All ORs were adjusted for age and gender.

Table 3B. Adjusted odds ratio of lifetime carsickness between different vertigo groups

	OR	95% CI		P-value
MD	Ref.			
VM	8.67	2.10	35.84	0.003
dVM	20.94	3.71	118.37	0.001
pVM	6.38	1.49	27.34	0.013

All ORs were adjusted for age and gender.
NVM= non-vestibular migraine,VM= vestibular migraine,
dVM= definite VM, pVM= probable VM,
MD= Meniere's disease,
OR= odds ratio, CI= confidence interval

groups, there were fewer women in the MD group (50.0%, $p<0.001$ chi-square test). The patients in the MD group (66.6 ± 10.9 years) were the oldest, and those in the NVM group the youngest (34.7 ± 16.0 years, $p<0.001$, ANOVA following post hoc Bonferroni correction).

Overall, 78.4% of the VM patients had experienced carsickness in their lifetime. In subgroup analysis, 89.2% (33/37) of the dVM patients and 70.5% (36/51) of the pVM patients had a history of carsickness compared to 43.6% (17/39) of the NVM patients and 18.2% (4/22) of the MD patients (Table 2). The carsickness rates were significantly different between any two groups of dVM, pVM, NVM, and MD (all $p<0.05$, chi-square test; Figure 2).

Among the patients who had experienced carsickness, most (88/90) had experienced carsickness in childhood before the onset of VM, NVM, or MD. Only 2 patients (one dVM patient and one NVM patient) had begun to suffer carsickness in the past ten years. With regards to habituation to carsickness, 20 patients had experienced carsickness until adolescence, and 7 patients had experienced carsickness until early adulthood. Sixty-one patients had still experienced carsickness in the past 10 years, including 27 dVM, 20 pVM, 12 NVM, and 2 MD

patients (Table 2).

Figure 2 illustrates the rate of still having carsickness in the recent ten years among each subgroup (gray bars), ranked in the order of 73.0% dVM, 39.2% pVM, 30.8% NVM, and 9.1% MD. These results showed a similar trend ($p<0.001$, chi-square test) but no obvious differences between groups compared with the lifetime carsickness rate (black bars).

Table 3A compares the adjusted odds ratios of lifetime carsickness between migraineurs with and without vertigo (odds ratio=6.73, $p<0.001$). We further classified the patients into definite and probable VM to compare with the NVM patients, and the odds ratios were 13.90 ($p<0.001$) and 4.31 ($p=0.006$), respectively. Table 3B shows the adjusted odds ratios of lifetime carsickness between the patients with different kinds of vertigo which may be difficult to distinguish when making a differential diagnosis. We compared VM versus MD, and the odds ratio was 8.67 ($p=0.003$). We further compared definite and probable VM to MD, and the odds ratios were 20.94 ($p=0.001$) and 6.38 ($p=0.013$), respectively.

DISCUSSION

In the current study, the carsickness rate was highest in those with dVM, followed by pVM and NVM, and lowest in those with MD. The high percentage of lifetime carsickness in the dVM (89.2%) and pVM (70.5%) groups implies that motion sickness is a characteristic of vestibular migraineurs. The high odds ratios of carsickness rate comparing VM to NVM or MD further advocates this viewpoint.

Although the comorbidity of migraine and motion sickness has been widely documented in the literature[12], the association between VM and motion sickness has rarely been investigated. In the study by Jeong et al., the VM group was most susceptible to motion sickness, followed by migraine with dizziness, migraine only, and the control group[13]. In another study by Boldingh et al., patients with VM reported more motion sickness than common migraineurs[19]. These findings are similar to our study. However, our study differs from these two studies in that it is the first motion sickness study comparing VM with MD. In addition, it is the first study to use Neuhauser's criteria to stratify VM into definite VM and probable VM, and to investigate carsickness in these patients.

Distinguishing VM from MD can be difficult, especially when auditory symptoms are not noticed by the patients. Recently, several studies have attempted to differentiate these two disorders by vestibular-evoked myogenic potentials, however the results have not been conclusive[20,21]. In our study, the carsickness rates were significantly different between the VM and MD groups, with the rate in the VM patients being four times higher than that in the MD patients without migraine. Therefore, a history of carsickness may be useful in the differential diagnosis between VM and MD.

While the criteria for dVM have been extensively accepted in clinical diagnosis and research, the value of the criteria for pVM, which defines a loose link between vestibular symptoms and migraine, is still under debate. It is known that motion sickness is not a comorbidity in other vestibular disorders such as MD, benign paroxysmal positional vertigo, or vestibular neuritis[22]. If pVM is just a coincidence of migraine and another vestibular disorder, the prevalence of motion sickness in the patients with pVM should be equal to the prevalence in patients with NVM. In our study, however, following the patients with dVM, the patients with pVM were much more susceptible to carsickness than the patients with NVM or MD. Therefore, the higher rate of carsickness in pVM not only discloses the VM nature of pVM, but may also support the validity of the criteria of pVM.

Hypersensitivity of the vestibular system is one of the most accepted hypotheses to explain the co-existence of migraine and motion sickness. Serotonin has been proven to be a possible mediator[23]. In a study on rotary chair testing, the subjects with VM were more sensitive to vestibular stimuli than the subjects with migraine only[12]. This may explain why the patients with VM are more susceptible to motion sickness than the patients with migraine only.

In our study, 30.7% of the patients gradually adapted to carsickness after adolescence or early adulthood. These patients seemed to be innately susceptible to carsickness, however, as they grew older they gradually adapted to travelling in vehicles. This condition was especially apparent in the patients with pVM, of whom 70.5% had experienced carsickness in their lives but only 39.2% had

still experienced carsickness in the past ten years. As a result, the differences in carsickness rates in the past ten years between groups were still significant, but not as obvious as the lifetime carsickness rates (Figure 2). To the best of our knowledge, habituation to motion sickness is affected by repetitive vestibular or optokinetic stimuli[24,25], and these stimuli depend on the acquired environment of individuals. Therefore, in the assessment of VM, we suggest that lifetime experience of carsickness is more valuable than recent experience of carsickness in order to investigate innate vestibular hypersensitivity.

Our VM group had a higher proportion of women and younger patients than the MD group. A previous study showed a higher rate of motion sickness in women[8], so gender may have led to bias. Nevertheless, after adjusting for age and gender, the adjusted odds ratios still demonstrated that the patients with VM were much more susceptible to carsickness than the patients with MD. Age and gender did not affect the results in the current study.

There are several limitations to this study. First, recall bias did exist. Second, we did not investigate other types of motion sickness such as seasickness or airsickness. Third, the severity of carsickness in this study was not measured quantitatively. Further community-based prospective studies with a formal questionnaire and larger sample size are warranted. In addition, inverse research exploring the prevalence of vestibular migraine in people with motion sickness would be worthwhile.

In conclusion, our study demonstrates that patients with VM, including both dVM and pVM, are more susceptible to carsickness than patients with NVM or MD. This finding reinforces the theory of hypersensitivity of the vestibular system in VM. We suggest that a history of carsickness may be helpful in the diagnosis of VM, and especially in differentiating VM from MD. In addition, a lifetime history of carsickness, which is not affected by habituation, may be more valuable in the assessment of innate vestibular hypersensitivity than a recent history of carsickness.

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