

Prevalence and preferred medication for vestibular migraine in Menière's disease: a multicenter retrospective cohort study in Korea

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Objectives: The aim of this study is to categorize headaches associated with definite Menière's disease (MD) according to diagnostic criteria, to determine their prevalence, and to investigate the preferred medication across participating centers.

Methods: Patients diagnosed with definite MD at 17 university hospitals in otolaryngology or neurology departments in Korea between January 1, 2021 to December 31, 2021 were retrospectively included. Data on the presence of accompanying vestibular migraine (VM), migraine or non-migraine headaches, and clinical information were collected. A survey was conducted to assess preferences for treatment drugs for vertigo and headache control in MD patients with headache.

Results: A total of 435 definite MD patients were included, with a mean age of 57.0±14.9 years. Among them, 135 (31.0%) had accompanying headaches, of whom 48 (11.0% of all definite MD patients) could be diagnosed with VM. The prevalence of comorbid VM (definite and probable) was significantly higher in females (41 of 288, 14.2%) than in males (7 of 147, 4.8%) ($p < 0.05$). There was no significant difference in the prevalence of comorbid VM between unilateral and bilateral MD patients (10.8% and 13.6%, respectively) ($p > 0.05$). Benzodiazepines, antihistamines, and antiemetics were mainly preferred for acute vertigo control, while nonsteroidal anti-inflammatory drugs, acetaminophen, and triptans were preferred for acute headache control, and topiramate, propranolol, and calcium channel blockers were mainly preferred for headache prevention.

Conclusions: VM is not uncommon in patients with definite MD in Korea. Further research is needed to understand the differences in headache prevalence and preferred medications across different centers.

Keywords: Dizziness; Menière disease; Headache; Migraine disorders; Multicenter study

INTRODUCTION

Characteristic symptoms of Menière's disease (MD) include intermittent vertigo, fluctuating hearing loss, aural fullness, and tinnitus. Although debate continues regarding the precise pathophysiology of MD, a con-

sensus exists that it is related to inner ear issues, with histopathological findings commonly showing endolymphatic hydrops [1].

Vestibular migraine is considered when patients with a history of moderate or severe migraine experience recurrent vestibular symptoms without any other identi-

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liable cause [2]. While the pathophysiology of vestibular migraine remains unclear, some patients exhibit features characteristic of MD [3-5]. Studies utilizing temporal bone magnetic resonance imaging (MRI) have reported increased incidence of endolymphatic hydrops in both MD and vestibular migraine patients [6-9], sparking interest among researchers in the relationship between the two conditions.

The pathological mechanisms of MD and vestibular migraine have been suggested to involve various factors, including genetic factors, and it is estimated that they may share some aspects of pathophysiology. Proposed pathophysiological mechanisms for vestibular migraine include the activation of meningeal nociceptors, vasospasm of the internal auditory artery [10], abnormalities in the trigemino-vascular system [11], and sensory dysfunction at the level of the vestibular system, thalamus, and cortex [12]. Meanwhile, MD has primarily been attributed to the result of endolymphatic hydrops, with impaired endolymphatic absorption by the endolymphatic sac suggested as one of the causes [13]. However, some studies have speculated that the endolymphatic duct may function as a valve regulating endolymph balance [14], and various factors such as chemical exposure, viral infections, inflammation, and ischemia have been proposed to contribute to dysfunction in endolymphatic duct function [15,16]. Thus, vascular pathological mechanisms such as ischemia may serve as common mechanisms connecting MD and vestibular migraine [17].

This study aimed to categorize headaches associated with definite MD according to diagnostic criteria, to determine their prevalence, and to investigate the preferred medication across participating centers. The goal was to advance our understanding of headache co-occurrence in Korean MD patients and facilitate future research to provide tailored treatment for each subtype.

METHODS

Ethics Statement

This study was reviewed and approved by the Institutional Review Board (IRB) of Konkuk University Medical Center (No. 2022-10-052). Due to the retrospective nature of the study, the requirement for obtaining informed consent from patients was waived by the IRB.

Study Sample

This study was a retrospective chart review of patients diagnosed with definite MD at otolaryngology or neurology departments in 17 university hospitals across Korea, from January 1, 2021 to December 31, 2021. It included both newly diagnosed patients and those with previous diagnoses who had follow-up visits during the study period. Patients with probable MD were excluded from the study. The participating institutions comprised 14 otolaryngology departments and four neurology departments.

Diagnostic Criteria and Headache Categorization

Diagnostic criteria for definite Menière's disease

The diagnostic criteria for definite MD followed the 2020 guidelines of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) [1] which is almost identical to the 2015 Bárány Society's criteria (Supplementary Table 1).

Diagnostic criteria for migraine without aura

In this study, the presence of headaches in patients with definite MD was investigated and classified as migraine or non-migraine headache. Migraine was diagnosed when all five diagnostic criteria outlined by the International Headache Society's International Classification of Headache Disorders (ICHD-3) were met [18] (Supplementary Table 2). Headaches that did not meet these criteria were classified as non-migraine headaches.

Diagnostic criteria for definite or probable vestibular migraine

The diagnostic criteria for vestibular migraine followed the consensus reached by the International Headache Society and the Bárány Society in 2012, which have remained unchanged since then [2] (Supplementary Table 3). According to the criteria established by the Bárány Society, the diagnostic criteria for vestibular migraine recognize a broader range of vestibular symptoms than those acknowledged in MD.

Accompanying headache categorization

Patients diagnosed with definite MD were classified according to headache-accompanying patterns as follows. First, they were divided into a group with headache and a group without headache. The headache group

was classified into vestibular migraine, migraine, and non-migraine headache groups, and the vestibular migraine group was further classified into definite vestibular migraine and probable vestibular migraine groups (Fig. 1). If the diagnostic criteria are strictly applied, there may be patients who do not clearly fall into either group according to the above classification criteria, but they were classified into the closest group.

Data Collection

Basic clinical information including age and sex were collected. For MD-related symptoms, data on hearing loss, aural fullness, direction of hearing loss, family history, and prior diagnosis of other auditory diseases (sudden sensorineural hearing loss, vestibular neuritis, etc.) were collected. Audiological assessments included pure-tone audiometry and speech audiometry, which were used as a basis for accurate diagnosis. Vestibular function assessments included caloric irrigation test, and unilateral semicircular canal paresis was considered abnormal if it was greater than 25%.

Survey on Preferred Treatment Drugs for Menière's Disease Patients with Headache

To investigate which treatment drugs are preferred for controlling vertigo and headache in patients with definite MD accompanied by headache, a survey was conducted via email with 16 otolaryngology specialists and four neurology specialists participating in the study (Supplementary Table 4). The survey was divided into preferred drugs for acute vertigo control, acute headache control, and headache prevention, allowing multiple selections.

RESULTS

Demographic Characteristics of Menière's Disease Patients

A total of 435 patients were diagnosed with definite MD, of which 147 were males (33.8%). The mean age of all patients was 57.0 ± 14.9 years, with males having a mean age of 55.3 ± 14.6 years and females having a mean age of 57.8 ± 15.0 years. Among the diagnosed patients, 407 had unilateral MD (93.6%). Of those with unilateral MD, 166 cases were right-sided (40.8%). Out of the 327 patients whose family history of MD was investigated, only eight had a positive family history.

Prevalence of Accompanying Headache in Menière's Disease Patients

Among the 435 patients diagnosed with definite MD, 135 (31.0%) had accompanying headaches, of whom 48 (11.0% of all definite MD patients) patients could be diagnosed with vestibular migraine. Among 48 vestibular migraine patients, 26 patients (6.0% of all definite MD patients) could be diagnosed with definite vestibular migraine (Table 1). The accompanying headache patterns were analyzed using the above-mentioned categorization: vestibular migraine, migraine, non-migraine headache, and no headache group. The prevalence of comorbid headaches, including the vestibular migraine, migraine, and non-migraine headache group, varied across hospitals. In 12 of the 16 surveyed university hospital clinics, the combined prevalence of all comorbid headaches (vestibular migraine, migraine, and non-migraine headaches) did not exceed 50%, and in 13 clinics, the prevalence of comorbid vestibular migraine was

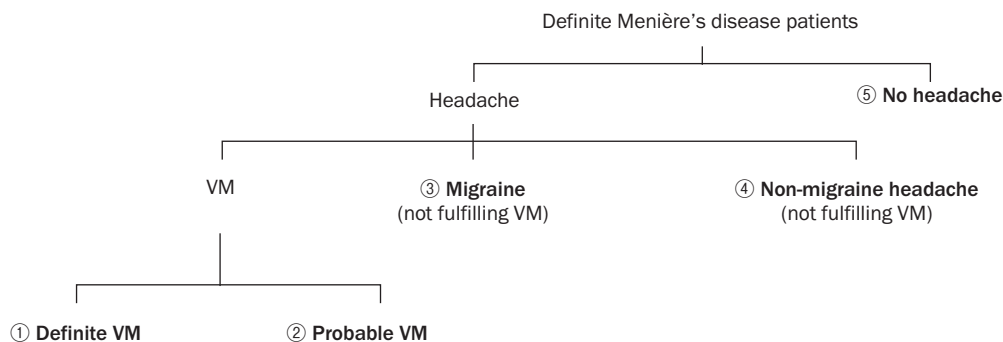


Fig. 1. Headache categorization in patients with definite Menière disease. VM, vestibular migraine.

Table 1. Incidence of accompanying headache in patients with definite Menière disease

Variable	Definite Menière disease (n=435)
No headache	297 (68.3)
Headache	135 (31.0)
Vestibular migraine	48
Definite	26
Probable	22
Migraine	11
Non-migraine	76
Unknown	3 (0.7)

Values are presented as number (%) or number only.

below 20%. The accompanying headache patterns in patients with definite MD investigated in 12 otolaryngology departments and four neurology departments are summarized in Fig. 2, summed by the department.

Among all 435 patients with definite MD, the prevalence of comorbid vestibular migraine (including both definite and probable vestibular migraine) was significantly higher in females (41 of 288, 14.2%) than in males (7 of 147, 4.8%) ($p < 0.05$, Pearson chi-square test). There was no significant difference in the prevalence of comorbid vestibular migraine (including both definite and probable vestibular migraine) between unilateral and bilateral MD patients (10.8% and 13.6%, respectively) ($p > 0.05$, Pearson chi-square test).

Results of Caloric Irrigation Testing according to the Presence of Headache in Menière's Disease Patients

Among the 435 patients diagnosed with definite MD, 301 patients who underwent caloric irrigation testing were included. Approximately half of the patients showed abnormalities in the caloric irrigation test.

We investigated the relationship between the presence of headaches and abnormalities in the caloric irrigation test, comparing various combinations of headache groups and headache-free group. The rate of caloric test abnormality was slightly higher in the group without headaches than in the group with headaches, but there was no statistical significance (Pearson chi-square test) (Fig. 3).

Preferred Treatment Drugs for Menière's Disease Patients with Headaches

The results of the survey on preferred treatment drugs for MD patients with headaches (multiple selections

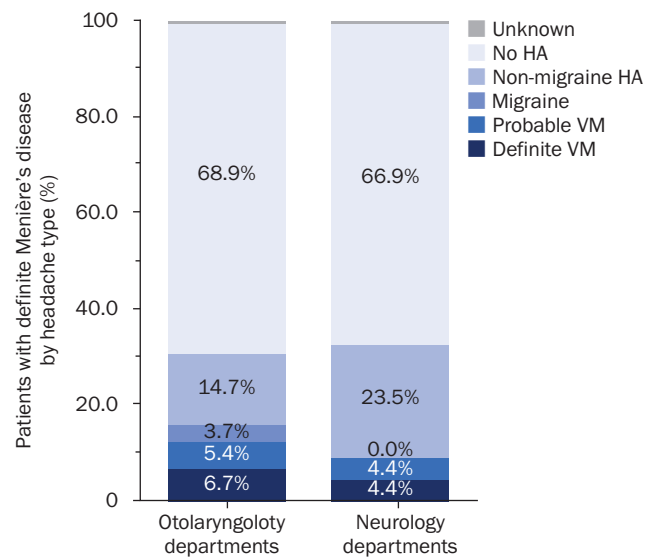


Fig. 2. Accompanying headache (HA) patterns in patients with definite Menière's disease according to department. VM, vestibular migraine.

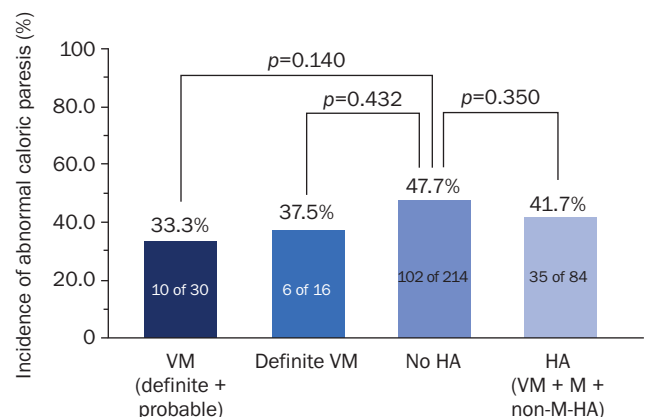


Fig. 3. Incidence of abnormal caloric paresis (≥25%) in patients with definite Menière's disease. VM, vestibular migraine; HA, headache; M, migraine; non-M-HA, non migraine headache.

allowed) were compiled based on responses provided by 10 otolaryngology specialists and four neurology specialists from university hospitals (Fig. 4). For the control of acute vertigo, benzodiazepines, antihistamines, and antiemetics were the most preferred drugs by otolaryngology specialists. Neurology specialists preferred antiemetics, benzodiazepines, and antihistamines, and the use of anticholinergics, systemic steroids, and beta-histidine was reported by one specialist each.

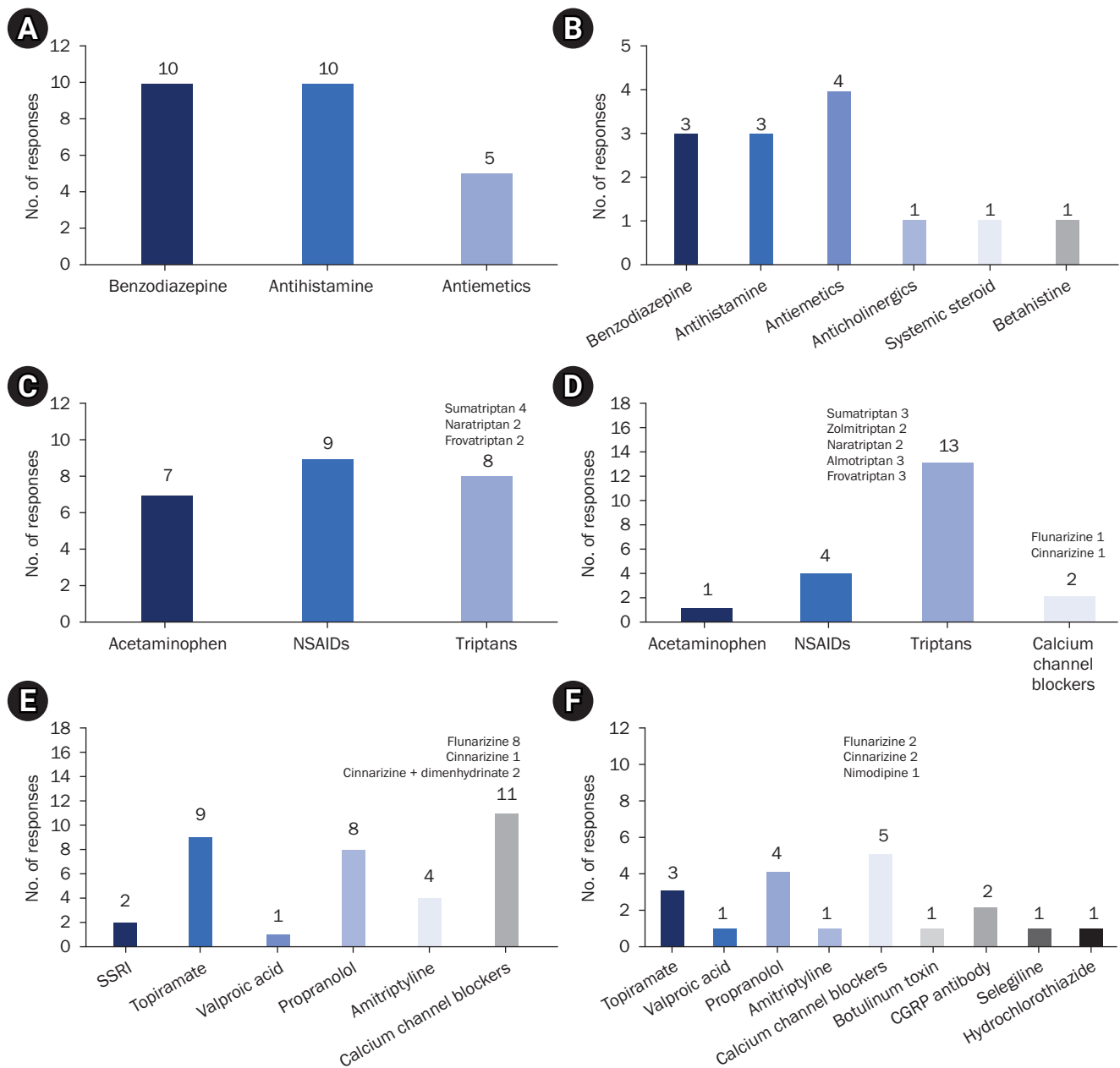


Fig. 4. Preferred medication for controlling vertigo and headaches. Data collected from 10 otolaryngology (OL) professors (A, C, E) and four neurology (NR) professors (B, D, F). (A, B) For acute vertigo. (C, D) For acute headache. (E, F) For prophylaxis. OL, otolaryngology; NR, neurology; NSAIDs, nonsteroidal anti-inflammatory drugs; SSRI, selective serotonin reuptake inhibitor; CGRP, calcitonin gene-related peptide.

For the control of acute headaches, among otolaryngology specialists, nonsteroidal anti-inflammatory drugs were the most preferred, followed by acetaminophen, and triptans. Among neurologists, nonsteroidal anti-inflammatory drugs were the most preferred, followed by triptans, as well as acetaminophen and calcium channel blockers.

To prevent recurrent headache symptoms, otolaryngology specialists preferred topiramate, propranolol, calcium channel blockers, amitriptyline, selective serotonin reuptake inhibitors, and valproic acid. Neurology specialists preferred propranolol, topiramate, calcium channel blockers, calcitonin gene-related peptide an-

tibodies, as well as valproic acid, amitriptyline, botulinum toxin, selegiline, and hydrochlorothiazide.

DISCUSSION

MD and vestibular migraine pose diagnostic challenges, as they cannot be solely diagnosed through a physical examination or laboratory tests, leading to difficulties even with established diagnostic criteria. The diagnostic criteria for MD have evolved over time, with the AAO-HNS developing criteria from 1972 to 1995, classifying it into four categories (certain, definite, probable, and possible). Similarly, in Japan, the Japanese Society for Equilibrium Research developed criteria from 1974 to 2008. Then, in 2015, the Bárány Society agreed upon the latest diagnostic criteria for MD, classifying it into two categories: definite and probable ([Supplementary Table 1](#)) [19]. Furthermore, the Menière's Disease Clinical Practice Guideline released by the AAO-HNS in 2020 closely follows these diagnostic criteria [1]. Regarding vestibular migraine, since Neuhauser et al. [20] first proposed diagnostic criteria in 2001, the International Headache Society and the Bárány Society agreed upon diagnostic criteria for vestibular migraine for the first time in 2012. Subsequently, in 2018, the International Headache Society included these diagnostic criteria for vestibular migraine in the new appendix of the ICHD-3, and in 2021, the Bárány Society announced an update that maintained the diagnostic criteria from the original 2012 consensus document while incorporating the latest insights ([Supplementary Table 3](#)) [2].

Upon closer examination of the mentioned criteria, it is evident that the latest diagnostic criteria for MD acknowledge a broader range of vestibular symptoms, including rotational and sensation of movement, whereas for vestibular migraine, the range of vestibular symptoms is more broadly recognized. While the duration of vestibular symptoms in definite MD is defined as 20 minutes to 12 hours (up to 24 hours for probable MD), and the number of attacks is stipulated as two or more, for vestibular migraine, the duration of vestibular symptoms is defined as 5 minutes to 72 hours, with a requirement of five or more attacks. Efforts to enhance the discriminative criteria between the two diagnoses are evident. This is believed to be because ambiguous diag-

nostic criteria make it challenging to conduct research and analysis on both MD and vestibular migraine, given their high comorbidity rates.

The diagnostic criteria for MD do not include any consideration of headaches, and likewise, the diagnostic criteria for vestibular migraine do not include any consideration of ear symptoms (hearing loss, tinnitus, or ear fullness). However, since the two diagnoses are not mutually exclusive, patients who meet the diagnostic criteria for MD may experience headaches, and patients who meet the diagnostic criteria for vestibular migraine may experience ear symptoms. Additionally, there may be patients who meet the criteria for both diagnoses. In this study, we confirmed that approximately 6% (26 out of 435) of all definite MD patients met the diagnostic criteria for vestibular migraine, and when including probable vestibular migraine, this number increased to approximately 11% (48 out of 435). It is well known from previous reports that the prevalence of headaches in MD patients is higher than in the general population. Furthermore, it is also known that MD patients may experience accompanying symptoms such as migraine, phonophobia, and photophobia [3,17,21]. Although reports vary, generally, approximately up to half of MD patients exhibit characteristics of migraine headaches, while up to 40% of vestibular migraine patients exhibit auditory-related symptoms such as ear fullness, tinnitus, and hearing loss [3,17,21,22]. In this study, the prevalence of accompanying headaches in patients with definite MD was 31.0% (135 out of 435) when combining vestibular migraine, migraine, and non-migraine headaches, and 13.6% (59 out of 435) for vestibular migraine and migraine, which were within a similar range to that reported in previous literature. The 2020 AAO-HNS clinical practice guideline for MD recommends evaluating the presence of vestibular migraine in MD patients because it can increase diagnostic accuracy, avoid unnecessary treatment or testing, potentially lead to more precise treatment and patient education, and facilitate multidisciplinary treatment approaches. Regarding the prevalence of accompanying headaches in definite MD patients examined in this study, there was a tendency for the prevalence of headaches to be similarly reported in neurology departments (four hospitals). In contrast, in otolaryngology departments (12 hospitals), where

more data were collected, the prevalence of headaches varied widely, ranging from around 10% to as high as 80%. This variation can be attributed to the unique characteristics of each hospital's patient population and patterns of hospital utilization, individual differences in medical history collection patterns by clinicians, and the greater number of hospitals contributing data in otolaryngology departments.

Due to the limited data, we cannot draw definitive conclusions regarding the causes of differences in headache prevalence across each hospital or specialty. However, considering reports indicating the ongoing underdiagnosis of vestibular migraine [23], we believe that these observed variations can prompt discussions on improving interdisciplinary communication, refining diagnostic criteria, and tailoring treatment strategies for MD patients with diverse symptom profiles.

In this study, we compared the results of caloric testing according to the presence of headaches in MD patients. However, no statistically significant differences in the presence of abnormalities on caloric testing were observed among various comparing combinations, including groups with definite or probable vestibular migraine, migraine, non-migraine headaches, a combined group of all types of headaches, and a group without headaches. According to a review published in 2017, the rate of abnormalities on caloric testing was higher in MD patients than in vestibular migraine patients in six out of seven studies [17]. In this study, the rate of abnormal caloric test results in the group without a headache was higher than in the definite vestibular migraine group, which was consistent with this tendency. Meanwhile, a study comparing caloric testing results among MD patients, vestibular migraine patients, and patients satisfying both criteria found that caloric testing alone could not distinguish MD patients from those satisfying the criteria for both MD and vestibular migraine [24]. This aligns with the current understanding that vestibular function tests play a supportive rather than essential role in the diagnosis of both MD and vestibular migraine. Until recently, several studies have reported how vestibular evoked myogenic potential tests, endolymphatic hydrops-suggesting MRI findings, and electrocochleography results appear in both groups of disorders [25], which can be used as a reference in dif-

ferentiating the two conditions. When interpreting the results of these studies, it is necessary to consider the diagnostic criteria for MD and vestibular migraine used in the respective study.

The pharmacological treatment for migraine associated with MD includes a wide range of medications both for acute attacks and preventive therapy. Clinicians need to carefully consider the characteristics and side effects of each medication to make individualized treatment decisions for patients. This study found that neurologists tended to consider a more diverse range of medications than otolaryngologists when selecting drugs for the management of acute vertigo and headaches. Additionally, there appeared to be a wide variety of medications used for the prevention of migraine symptoms among different clinicians.

In conclusion, This study holds significance as the first nationwide investigation into the prevalence of comorbid vestibular migraine among patients with MD in South Korea. Efforts were made to apply the latest diagnostic criteria considering the high comorbidity rate of these two conditions. Unfortunately, due to the retrospective nature of our study, we were unable to draw significant conclusions regarding clinical differences according to the presence or absence of headaches in patients with MD. However, we did observe variations in headache prevalence among different university hospitals. We also confirmed differences among clinicians in their preferred medications for managing headaches or vertigo in patients with MD. Considering these variations, it is essential to conduct well-planned prospective studies to uncover meaningful clinical characteristics regarding the relationship between MD and vestibular migraine and to determine optimal and tailored treatments in the future.

ADDITIONAL INFORMATION

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Conflicts of Interest

Minbum Kim and Hyun Ah Kim are a member of the Editorial Board of *Research in Vestibular Science* and were not involved in the review process of this article. All authors have no other conflicts of interest to declare.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article. For other data, these may be requested through the corresponding author.

Authors' Contributions

Conceptualization, Methodology, Project administration, Resources, Supervision: HJP, KSK, CHK; Data curation, Formal analysis, Investigation, Validation: All authors; Software: LDH; Visualization: LDH, HJP, KSK, CHK; Writing-Original Draft: LDH, HJP, KSK, CHK; Writing-Review & Editing: All authors.

All authors read and approved the final manuscript.

Supplementary Materials

Supplementary materials can be found via <https://doi.org/10.21790/rvs.2024.005/>

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