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Vestibular and Auditory Manifestations of Migraine

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Abstract

Purpose: The purpose of this narrative review is to discuss current literature about vestibular migraine and other cochleovestibular symptoms related to migraine.

Recent findings: Vestibular migraine affects 2.7% of the United States population. Misdiagnosis is common. The pathophysiology is currently unknown but new research shows that CGRP, which is implicated in migraine headaches, is expressed in the audiovestibular periphery. A recent large-scale placebo controlled trial looking at metoprolol for vestibular migraine was terminated early due to poor recruitment; however, at study completion, no differences were seen between treatment arms. Many other audiovestibular symptoms have been shown to be associated with migraine, including tinnitus, hearing loss, aural fullness, otalgia and sinus symptoms. Migraine is also associated with risk for developing numerous otologic conditions, including Meniere's disease, vestibular loss, BPPV, and sudden sensorineural hearing loss. There is now some evidence that patients may experience fluctuating hearing loss and aural fullness without vertigo in association with migraine, which is called cochlear migraine.

Summary: Migraine can cause a variety of audiologic and vestibular symptoms, and further research is required to understand how migraine affects the inner ear.

Keywords

vestibular migraine; vertigo; headache; audiovestibular symptoms

Introduction

Vestibular migraine (VM) is a distinct variant of migraine that causes vestibular symptoms, with or without an accompanying migrainous headache. Patients frequently also experience phonophobia, photophobia, head pressure, and motion sensitivity. Aural symptoms, including tinnitus and aural pressure, are common as well. Furthermore, there's emerging evidence that hearing loss (HL) may be associated with migraine, without vestibular

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symptoms, and this has been termed cochlear migraine.[1,2] Migraine is a common culprit for many otolaryngologic symptoms, including sinus pressure, facial pain, and facial numbness. Finally, migraine is statistically associated with several other vestibulopathies, including benign paroxysmal positional vertigo, bilateral vestibular loss, Meniere's disease, and benign paroxysmal vertigo in childhood and adulthood.[3–8] In this manuscript, we will review how migraine causes auditory and vestibular symptoms, focusing on recent developments with VM.

Vestibular Migraine

Epidemiology—The overall prevalence of VM in the United States is estimated to be 2.7%, and it may be the most common cause of episodic vertigo in adults.[9,10] Underdiagnosis appears to be common. In a study assessing VM prevalence, two thirds of patients with VM were evaluated by a physician but only 20% were diagnosed with VM.[11] More women than men are affected, with a 3 to 1 ratio.[12] At the senior author's (JDS) institution, a personal history of migraine is present 78% of the time, a family history of migraine in a first degree family member is present 46% of the time, and a personal history of motion sickness is present 59% of the time (unpublished data).

Presentation—Diagnostic criteria are available from the Barany Society for both probable VM and VM, the latter of which has been added to the appendix of the International Criteria for Headache Disorders (ICHD-3).[13] Patients with probable VM present with vestibular symptoms and have a history of migraine with or without aura or migrainous symptoms (photophobia, phonophobia, migraine headache) during attacks, while those with definite VM, have both. However, a recent study showed that a large proportion of vertigo patients with migrainous features did not meet the ICHD criteria for VM, most likely as a result of diagnostic criteria rather than intrinsic features unique to the VM cohort.[14]

Vestibular symptoms which are required for diagnosis include vertigo, postural imbalance, head motion-induced dizziness, and visually-induced vertigo. The most commonly associated vestibular symptom is spontaneous rotational vertigo, with an estimated prevalence of 67%.[11] In a cohort of 54 patients from the senior author's institution (unpublished data), the most common triggers for vertigo were motion (83%), stress (76%), busy visual scenes (72%), scrolling on a screen (67%), and impaired sleep (61%). In that cohort, 63% of patients experienced ear pressure with VM attacks. Furthermore, patients with a history of VM are at higher risk of cochlear disorders (tinnitus, sudden deafness, and sensorineural hearing loss), with a nearly three-fold increase in likelihood.[15] Interestingly, about half of Meniere's patients, who suffer from tinnitus, HL, and aural fullness also have a history of migraine, making it likely that Meniere's disease is in fact a migraine-related phenomenon.[4,16]

Recently, VM-PATHI (Vestibular Migraine Patient Assessment Tool and Handicap Inventory) was developed and validated as a disease specific outcome measure for VM. Symptom specific measures, like the Dizziness Handicap Inventory (DHI), are certainly helpful in quantifying disease severity but may not capture the full spectrum of symptomatology. VM-PATHI was developed using a panel of experts, including

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audiologists, neurologists, and neurotologists, along with patient input. Over several iterations involving 95 patients, the item bank was refined and tested. The final questionnaire was found to have internal consistency (Cronbach's alpha 0.92), test-retest reliability, responsiveness, discriminative validity, and both face and content validity. It is freely available online at the UCSF Balance and Falls Center website (https://ohns.ucsf.edu/balance-falls/). Exploratory factor analysis uncovered six groupings within the items, covering the following themes: cognition, emotion, disequilibrium, headache equivalents, motion sensitivity, and anxiety. Of note, ear pressure had a mean score of 1.6 (0 = no problem, 1= mild problem, 2= moderate problem, 3 = severe problem, 4= as bad as it can be), and clustered together with headache and head pressure.

Pathogenesis—The pathogenesis of VM remains largely unknown, but there are several theories, related to sensory hypersensitivity, altered multisensory processing, and trigemino-vascular and calcitonin gene-related peptide (CGRP) effects on the vestibular system.

Migraine is believed to be caused by neuroinflammation of the trigemino-vascular system. The trigemino-vascular system is thought to be composed of peripheral trigeminal nerve endings innervating the pia, dura mater, and cranial blood vessels. The trigeminal nerve is responsible for pain sensation from the anterior two-thirds of the head, and it mediates pain signaling through the release of neuropeptides such as CGRP, substance P, neurokinin A, and nitrous oxide.[17] This process leads to vasodilation, mast cell degranulation, and neurogenic inflammation. CGRP, a neuropeptide involved in the efferent synapses of hair cell organs, such as the cochlea, semicircular canal, and the lateral line, has also been investigated in the pathogenesis of VM. CGRP deletion in transgenic mice has been associated with reduced suprathreshold cochlear nerve activity and decreased vestibulo-ocular reflex (VOR) gain. CGRP deficient mice also show impaired otolith activity and decreased balance.[18]

While a family history of migraine is common with VM, not much is known about specific genetic alterations. An autosomal-dominant inheritance pattern has previously been described.[11] However, specific genetic loci have yet to be validated in VM. Most recently, a mutation in the transient receptor potential (TRP) channel, a cation channel mediating pain, touch, hearing, and thermal sensation, has been associated with the development VM in a single family.[19]

Management—The management of VM is similar to that of traditional migraine. Data is lacking regarding treatment effectiveness, and a 2015 Cochrane review found no high quality studies available for VM.[20] Management involves conservative options, symptomatic and abortive treatment during acute attacks and prophylactic therapies. Non-medical therapies include stress reduction, sleep hygiene, treatment of anxiety, avoiding dietary triggers, avoiding visual triggers and stabilizing hormone fluctuations.[21] Acute VM attacks can be treated with anti-emetics to treat nausea and vestibular suppressants to treat the vestibular symptoms.

A variety of classical migraine prophylactics have been studied for the treatment of VM. Multiple medication classes have shown efficacy in retrospective reviews including

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tricyclic antidepressants, mixed reuptake inhibitors, anti-epileptics, beta-blockers and calcium channel blockers.[22] The PROVEMIG trial, a recently completed placebo-controlled randomized controlled trial, investigated the efficacy of metoprolol in the treatment of VM. There was no significant difference between the incidence of acute vertigo episodes between placebo and control groups. However, it is important to note that the trial was discontinued early due to poor patient accrual, but even so, the final analysis included 114 subjects, making it unlikely that there is a large, beneficial effort that was not observed.[23]

Another promising treatment option for aborting an acute VM attack is non-invasive vagus nerve stimulation. The non-invasive vagus nerve stimulator, a device in which a patient places electrodes on their neck that stimulate the vagus nerve, has recently been approved by the Food and Drug Administration (FDA) for the treatment of episodic classical migraine. There is preliminary evidence that vagal nerve stimulation improves acute vertigo as well as headache during an acute attack in individuals with VM.[24]

Other Audiovestibular Symptoms Associated with Migraine

Tinnitus and Hyperacusis—Tinnitus may be associated with a migraine phenomenon, as both are similarly elusive in etiology but possibly share a pathophysiology linked by the central nervous system, specifically the activation of the trigeminal nerve and likely central hypersensitivity.[25,26] Tinnitus has been reported to be more prevalent in different types of migraine.[27–29] Pulsatile tinnitus is another symptom which can be seen in the context of migraine and may be resolved with migraine treatment with avoidance of dietary triggers with or without medication.[30] In a study examining the rate of tinnitus in patients with a definite diagnosis of migraine versus healthy subjects, 36.4% were found to have tinnitus while there were no patients with tinnitus among the healthy subjects ($p<0.05$). Patients with migraine had over a three-fold increase in likelihood of having tinnitus.[15] Similarly, in a survey assessing cochleovestibular symptoms of migraine, 20% reported tinnitus.[31] This association has been found to be stronger in young individuals with migraine with aura.[27] The association of hyperacusis with chronic migraine is well described and is typically called “phonophobia” in the migraine literature. It is a symptom strongly associated with the severity of headache and has been shown to be improved from migraine prophylaxis therapy.[32,33]

Cochlear Migraine—While the relationship between migraine and vestibular symptoms has been assessed more carefully since formal diagnostic criteria were introduced in 2012, the relationship between migraine and cochlear symptoms is less recognized. Cochlear symptoms (e.g., fluctuating or sudden hearing loss) with or between headache attacks affect a smaller percentage of patients.[31] The concept of cochlear migraine was first described in 2018, with an aim to assess the relationship between migraine and auditory dysfunction. The major criteria for diagnosis include recurrent or fluctuating unilateral sensorineural hearing loss (low frequency or all frequencies) without vertigo or mild dizziness that does not meet the criteria for VM or migraine disorder along with aural fullness in the affected ear. Minor clinical features include aura before HL; concurrent tinnitus; family history of migraine-related disorders; history of migraine or chronic headaches, or unilateral neck stiffness (ipsilateral to HL); photophobia or phonophobia; motion sickness; visual motion

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intolerance; and sensitivity to atmospheric pressure changes.[1,34] Prior to this, research was performed to assess a correlation between migraine and otoacoustic emissions to carefully assess cochlear function. Despite normal hearing, patients with migraine have demonstrated lowering of otoacoustic emissions (TEAOEs) at various frequencies, along with central auditory dysfunction as evidenced by prolonged wave III latency and I-V IPL of auditory brainstem response[17]. Additional case reports have described patients with unilateral or bilateral, transient and reversible mild HL during a migraine attack.[35]

Hearing Loss—Subjective hearing change during VM attacks is common as well, although it is unclear if that is a peripheral or perceptual process. A national database study revealed that migraine was independently associated with an increased likelihood of subjective tinnitus and HL. This study of approximately 13,000 U.S. adults demonstrated that migraineurs were more likely to have subjective HL (25.0% *vs.* 16.6%, $p<0.001$) and tinnitus (34.6% *vs.* 16.9%, $p<0.001$) compared to the non-migraineurs. Among migraineurs, a higher proportion of those with tinnitus also had HL compared to those without tinnitus (40.0% *vs.* 15.3%, $p<0.001$), and a higher proportion of those with HL also had tinnitus compared to those without HL (58.1% *vs.* 27.3%, $p<0.001$).[36] Additionally, a recent meta-analysis concluded that a history of migraine is a risk factor for sudden sensorineural hearing loss, with a pooled hazard ratio of 1.84 (95% CI: 1.11–2.57; P < .001).[30] Other large database analyses have also found that a history of migraine was 35–80% more likely in developing sudden HL.[37] Finally, treatment of patients with sudden HL using migraine prophylactic medications in addition to standard oral and intratympanic steroid has been found to improve lower frequency hearing.[38] A large portion of patients with chronic, sudden HL (>3 months) have also been found to improve with migraine prophylactic therapy combined with intratympanic steroid injections.[39]

Sinus Pressure—The International Headache Society (IHS) has published criteria for headache that is attributed to rhinosinusitis. However, it is important to note that this entity is only in conjunction with an acute exacerbation of rhinosinusitis, and the IHS does not recognize chronic rhinosinusitis as a form of headache. It is common for patients with supposed chronic rhinosinusitis to have normal computed tomography findings or to fail standard antibiotic therapies. These patients often present with midfacial pain and pressure with rhinorrhea without evidence of infection or inflammation of the sinuses or nasal cavities. Many practitioners are now considering viewing this as a migraine variant instead of a manifestation of sinus or nasal pathology.[8] Patients with migraine are known to exhibit lacrimation, conjunctival injection, eyelid edema or nasal congestion.[40]

Many patients with “sinus” headache are now recognized to really have migraine. In a study of 100 people who believed they had sinus headache, 86% of participants met the definition of migraine with or without aura or probable migraine. A majority of patients in this study also presented with bilateral forehead and maxillary pain or pain in the distribution of the second division of the trigeminal nerve.[7] In addition to sinus pain, misdiagnosed patients often also present with sinus pressure and nasal congestion.[41] Overall, the literature supports that these patients respond to treatment with classical migraine medications, further supporting this entity as a form of migraine. A systematic review of the literature in 2013

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shows that triptans are effective for the treatment of chronic facial pain without evidence of acute rhinosinusitis.[42] In 2007, a randomized, double-blind, placebo-controlled study assessing the efficacy of sumatriptan for patients with “sinus headache” found significant improvement in headache.[43]

Aural Fullness—Aural fullness (AF) is a symptom that can result from a number of different conditions, but most commonly presents with Eustachian tube dysfunction (ETD). Idiopathic AF is the second most common classification after ETD. The relationship between AF and migraine is understudied. In a study assessing patients with AF and migraine symptoms, 54% of patients with AF met IHS criteria for migraine and all patients had symptomatic improvement with migraine prophylactics: verapamil (82%) or nortriptyline (18%). Migraine features that were commonly associated with AF included visual motion sensitivity (91%), head motion sensitivity (81%), sinus/facial pressure (72%), and phonophobia (72%).[44] Another study showed that 74% of patients with migraine related AF fulfilled a majority of the migraine headache criteria. Aural fullness in patients without ETD and normal imaging studies (no mass or third window) is most likely related to migraine.[45]

Otalgia—Sensation to the ear is controlled by multiple nerves including afferents from the trigeminal nerve, which is implicated in migraine pathophysiology. Patients with classic migraine are more likely to report ear pain than patients with other types of headache and patients with otalgia are more likely to report headache than patients who do not have otalgia.[46,47] In a retrospective review of patients presenting with otalgia without another identifiable cause in a single otolaryngology practice, more than half had a prior history of headache and 65% met IHS criteria for migraine with or without aura. Otalgia was triggered by classical migraine triggers in the majority of patients. The majority of these patients had improvement in otalgia with classical migraine therapies.[48] Migraine patients with otalgia often present with other otologic symptoms including sinus pressure, aural pressure or vertigo. Otalgia can also be seen as an otologic manifestation in patients with VM.

Key Bullet Points

- Migraine is involved in a wide variety of otologic symptoms, including tinnitus, hearing loss, vertigo, hyperacusis, otalgia, and ear pressure.
- Vestibular migraine is a common and disabling cause of vertigo.
- Otolaryngologists should be familiar with migraine, and always ask about a personal and family history of migraine when evaluating new patients.

Conclusion

Migraine is clearly involved in the generation of numerous otologic symptoms, including vertigo, tinnitus, aural pressure, otalgia, and HL. A supplemental video abstract reviewing this is available for viewing. It seems likely to the authors that a clear understanding of how migraine affects the peripheral and central audiovestibular structures is required for an advancement in the conceptualization of otologic disease. Given its prevalence

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and myriad presentations, migraine should be on the differential diagnosis for almost any audiovestibular complaint.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of Interest:

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2. Jeffrey D. Sharon, MD - consultant for Spiral Therapeutics, and research support from Eli Lilly and Advanced Bionics.

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