Epidemiology of Vestibular Migraine and Related Syndromes

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5.1 Epidemiological Aspects

A causal link between vertigo and migraine has been suspected, based on epidemiological observations indicating a more than chance association of migraine with vertigo and dizziness. Dizziness and vertigo rank among the most common complaints in the general population and are frequently reported by patients with migraine. The prevalence of migraine has been shown to be increased in patients with dizziness [1] and, in particular, among patients with unclassified recurrent vertigo [2, 3]. Conversely, patients with migraine reported more frequently vertigo than patients with tension-type headache (27 % vs. 8 %) [4]. Vertigo was also more common in migraine patients than in headache-free controls in a case-control study [5]. However, the interrelations of migraine and vertigo are complex as different causes may account for an association. First, since both dizziness/vertigo and migraine are very common in the general population, they may coincide simply by chance. The lifetime prevalence of migraine in industrialized countries has quite consistently been estimated at 13–16 % [6], and dizziness and vertigo affect approximately 20–30 % of the general population [7, 8]. In a large population-based neurotological survey, the lifetime prevalence of dizziness/vertigo was estimated at nearly 30 %. Vertigo of vestibular origin accounted for 7.4 % of all dizziness/vertigo symptoms [9]. Thus, assuming a lifetime prevalence of 14 % for migraine [6] and 7.4 % for vertigo, one can expect a chance coincidence of 1 %. However, the actual prevalence of participants reporting both migraine and vertigo of vestibular origin in the neurotological survey was three times higher (3.2 %), suggesting a more than

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chance concurrence [9]. In addition, other vestibular disorders such as benign paroxysmal positional vertigo [10, 11] and Menière's disease [12] show a statistical link with migraine, the basis of this association still remaining uncertain. In an individual patient with dizziness/vertigo and migraine, clinicians must, therefore, determine if vertigo symptoms are causally related to migraine, if they are caused by another vestibular disorder that is statistically associated with migraine or if vertigo and migraine are unrelated.

5.1.1 Prevalence of Vestibular Migraine

The prevalence of vestibular migraine was 7 % in a group of 200 consecutive patients of a specialized dizziness clinic and 9 % in a group of 200 unselected migraine clinic patients [1]. In a large, two-stage population-based study ($n = 4{,}869$ adults) with screening interviews followed by expert telephone interviews, the lifetime prevalence of VM was estimated at 0.98 % (95 % CI 0.7–1.37) [13]. Of note, VM accounted for only a third of vertigo symptoms in migraine patients, which underlines the importance to also consider other *vestibular diagnoses* in these patients [13]. In a community-based sample of middle-aged women in Taiwan, VM was identified in 5 % and in 30 % of those with migraine [14].

5.1.2 Demographic Aspects

VM may occur at any age [15, 16]. It shows a marked female preponderance with a reported female to male ratio between 1.5 and 5 to 1 [15–17]. Familial occurrence is not uncommon and probably based on an autosomal dominant pattern of inheritance with decreased penetrance in men [18]. In most patients, migraine begins earlier in life than VM [1, 16]. However, vertigo may precede the onset of migraine headaches by several years, and some patients have been free from migraine headaches for years when vertigo attacks first occur, which may obscure the link between the two [16]. In women, vertigo attacks may replace migraine around menopause.

VM typically first manifests in young and mid-adulthood but may already begin in childhood or, rarely, in older age [16]. Early manifestation of vertigo attacks related to migraine has long been recognized by the ICHD (International Classification of Headache Disorders) as benign paroxysmal vertigo of childhood. The syndrome is characterized by brief attacks of vertigo or disequilibrium, anxiety and often nystagmus or vomiting, recurring for months or years in otherwise healthy young children [19]. Many of these children later develop migraine, often many years after vertigo attacks have ceased. A family history of migraine in first-degree relatives is twofold increased compared to controls [20]. In a population-based study, the prevalence of recurrent vertigo probably related to migraine was estimated at 2.8 % in children between 6 and 12 years [20].

5.1.3 Epidemiological and Clinical Link of Migraine with Other Disorders Causing Vertigo and Dizziness

Prevalence of migraine is increased in some well-defined vestibular disorders such as Menière's disease [12] and benign paroxysmal positional vertigo (BPPV) [10, 11]. In addition, there is a more than chance association of migraine with several other dizziness syndromes including motion sickness [4, 5, 21, 22], orthostatic hypotension and syncope [23, 24], panic disorder [25] and depression [26]. These disorders may be the sole cause for vertigo and dizziness in a patient with migraine or may coexist with VM.

5.2 Migraine and Menière's Disease

The interrelations of migraine and Menière's disease are complex. Vestibular migraine and Menière's disease share many clinical features [4, 27], and prevalence of migraine is increased in patients with Menière's disease [12]. Fluctuating hearing loss, tinnitus and aural pressure may occur in vestibular migraine, but hearing loss does not progress to profound levels [17, 27]. Similarly, migraine headaches, photophobia and even migraine auras frequently occur during Menière attacks [12]. An association of Menière's disease and migraine has already been suggested by Prosper Menière in his first description of the disorder in 1861 [28]. A case-control study in 78 patients with idiopathic unilateral or bilateral Menière's disease according to the criteria of the American Academy of Otolaryngology [29] found a twofold increased prevalence of migraine according to the ICDH-2 criteria compared to age- and sex-matched controls (56 % vs. 25 %). Nearly half of the Menière patients always experienced at least one migrainous symptom (migrainous headache, photophobia, aura symptoms) along with their Menière attacks, suggesting a pathophysiological link between the two disorders or reflecting an unsolved overlap of clinical symptoms and current diagnostic criteria [12, 30]. Patients with features of both Menière's disease and vestibular migraine have been repeatedly reported [31]. Migraine, episodic vertigo and Menière's disease may occur in familial clusters, suggesting genetic inheritance [32]. Comorbidity with migraine was found to be associated with a more severe clinical phenotype of Menière's disease, with an earlier age of onset and higher incidence of bilateral cochlear involvement [31]. Common pathophysiological mechanisms that may cause a variable phenotype of vertiginous, cochlear and migrainous symptoms include neurotransmitter imbalances [15, 33] or defunct ion channels which are expressed both in the inner ear and brain [34].

In the first few years after onset of symptoms, differentiation of vestibular migraine from Menière's disease may be challenging, as Menière's disease can be monosymptomatic with vestibular symptoms only in the early stages of the disease. As a rule, the two disorders can be distinguished when a pronounced sensorineural hearing loss becomes evident in Menière's disease within a few years, while cochlear impairment in VM, if present, remains mild even at longer follow-up [27].

5.3 Migraine and Benign Paroxysmal Positional Vertigo (BPPV)

Recurrent episodes of positionally induced, short-lasting vertigo attacks in VM may closely resemble benign paroxysmal positional vertigo (BPPV) [35]. Although clinically two separate entities, there is clinical evidence for a link between migraine and BPPV. Migraine is three times more common in patients presenting with idiopathic BPPV compared to patients with BPPV secondary to trauma or surgical procedures [10]. Similarly, the prevalence of migraine was two times higher in patients with idiopathic BPPV compared to age- and sex-matched controls [11]. Genetic factors and vascular damage to the labyrinth have been proposed as potential pathophysiological mechanisms linking the two disorders [10].

In a patient with migraine and episodic positional vertigo, the clinician must, therefore, determine if positional vertigo is due to vestibular migraine or if BPPV exists as a comorbid condition. When patients present during the acute episode, BPPV is easily diagnosed by the typical nystagmus beating in the plane of the affected semicircular canal, which is elicited on positional testing [36]. In patients with VM, most often a central-type positional nystagmus can be observed during the acute attack [37, 38]. In the vertigo-free interval, episodic positional vertigo in VM may be distinguished from BPPV by its shorter episode duration and greater episode frequency [35].

5.4 Migraine and Motion Sickness

Migraineurs are more susceptible to motion sickness (30–50 %) than patients with tension headache or headache-free controls (about 20 %) [4, 5, 21]. Susceptibility to vestibular stimuli may be most marked in patients with VM who were four times more likely to become nauseous during caloric testing compared to patients with other causes of dizziness [39] and showed the highest motion sickness scores among patients with different types of migraine [22].

Conversely, vestibular stimulation by caloric testing induced migraine attacks in half of 39 migraineurs within 24 h, the effect being most pronounced in migraineurs with VM. Interestingly, migraine headaches were also triggered by caloric stimulation in 12 % of non-migraineurs [40]. Migraineurs also report more ‘visual vertigo’ while looking at spinning objects [5]. Headache, scalp tenderness and photophobia could be provoked by optokinetic stimulation in a recent study. Migraineurs were more nauseated and had longer-lasting headache and photophobia than controls [41]. Recently, *rizatriptan*, a serotonin agonist effective in treatment of migraine headaches, has been shown to reduce vestibular-induced motion sickness in migraineurs [42]. Pathophysiological models explaining the concurrence of headache, vertigo and motion sickness in migraineurs include common neurotransmitters such as *serotonin* which are active in the inner ear, trigeminal ganglion and brainstem vestibular and trigeminal nuclei and solitary nucleus as well as shared central neuronal circuits for vestibular and nociceptive information processing [43].

5.5 Migraine and Orthostatic Intolerance and Syncope

Transient loss of consciousness has since long been known as a prominent symptom in basilar migraine as described by Bickerstaff [44]. However, orthostatic hypotension and syncope also frequently occur in other subtypes of migraine. Orthostatic symptoms were more common in patients with migraine than in controls (68 % vs. 8 %) [45]. Among 451 females aged 15–44 years, fainting spells were more frequently reported by women with migrainous headaches (11 %) than by those without migraine (2 %) [46]. In the population-based CAMERA study, migraineurs showed an elevated lifetime prevalence of syncope (43 % vs. 31 %), recurrent syncope (13 % vs. 5 %) and orthostatic intolerance (32 % vs. 12 %) compared to non-migraineurs [24]. Syncope during migraine attacks has been reported to occur in 5 [41] to 10 % [47] of migraineurs. In a series of 248 patients with frequent syncope, a high rate of migraine headaches preceding or following syncopal episodes was reported (30 %), leading to the hypothesis of 'syncopal migraine', i.e. recurrent syncopes caused by a primary migrainous mechanism [48].

Case studies on autonomic function in migraine patients have yielded conflicting results, reporting both hypo- and hyperfunction of the sympathetic and parasympathetic systems [24]. However, the CAMERA study, despite the finding of an increased prevalence of syncope and orthostatic hypotension among migraine sufferers, did not reveal clear interictal signs of autonomic nervous system failure in migraineurs [24].

5.6 Migraine and Cerebellar Function

Cerebellar dysfunction causes imbalance, which patients may experience as dizziness. In recent years, several neuronal disorders presenting with a variable phenotype of episodic vertigo, *cerebellar ataxia* and different subtypes of migraine have been identified to be caused by defect ion channels that are expressed in the cerebellum and other brain structures. Patients with *familial hemiplegic migraine* (FHM), a rare subtype of migraine, may develop progressive cerebellar ataxia and nystagmus [49]. Mutations in the CACNA1A gene coding for the 1A subunit of a neuronal Ca2+ channel, which is heavily expressed in the cerebellum, have been identified not only in FHM but also in episodic ataxia type 2 (EA-2) [50] and spinocerebellar ataxia type 6. Episodic ataxia (EA-2) is characterized by short attacks of cerebellar ataxia or vertigo and interictal nystagmus. Approximately half of the patients with EA-2 also have migraine [34]. Both FHM and EA-2 may be associated with typical symptoms of basilar migraine [34, 51]. Subtle interictal signs of vestibulocerebellar dysfunction have also been found in 83 % patients with migraine and were more pronounced in patients with migraine with aura [52]. Similarly, up to two thirds of patients with VM show interictal central vestibular and ocular motor deficits indicating mild cerebellar and brainstem dysfunction which tend to somewhat progress with time [16, 27, 53]. However, the search for genetic mutations of ion channels involved in other subtypes of migraine and progressive cerebellar ataxia has been negative in VM so far [54, 55].

5.7 Association of Migraine and Dizziness with Psychiatric Disorders

Migraine, dizziness and psychiatric disorders are interrelated in a complex way. Migraine has been identified as a risk factor for several psychiatric disorders [25, 26]. Migraineurs carry a three- to fourfold risk to suffer from major depression [26] and panic disorders [25] compared to non-migraineurs. Conversely, a previous history of major depression or panic disorder is associated with an increased likelihood to develop migraine [25, 26], the bidirectional associations being strongest in migraine with aura [25, 26].

Dizziness is the second most common symptom of panic attacks after palpitations and can be a prominent symptom of major depression and somatoform disorders as well. Patients with panic and anxiety show an increased rate of vestibular test abnormalities [56]. Conversely, patients with vestibular disorders carry an elevated risk to develop secondary *anxiety* and depressive disorders [57, 58]. Patients with VM show the highest rate of concurrent anxiety and depressive disorders (up to 70 %) compared to other vestibular disorders [57, 58]. Of note, while a previous history of psychiatric illness increases the risk of emotional distress and anxiety in response to vestibular disorders, the extent of vestibular abnormalities seems to have no impact on the development of secondary psychiatric disorders in these patients [57]. Psychiatric comorbidity is associated with sustained dizziness symptoms in VM [57]. Because of the frequent association of dizziness, migraine and anxiety, a new syndrome named migraine-anxiety-related dizziness (MARD) has been proposed, and hypotheses on neuroanatomical links connecting the vestibular system to neuronal pathways involved in emotional processing have been formulated [59].

Thus, in patients with migraine and vertigo/dizziness symptoms, the clinician has to determine if vertiginous symptoms are caused by VM or if they are due to a primary or coexistent psychiatric disorder. Since psychiatric comorbidity increases the risk for development of chronic dizziness symptoms in VM, early recognition and treatment of underlying psychiatric disorders is essential.

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