Migraine-associated vertigo and dizziness as presenting complaint in a private general medical practice

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Abstract

Background: Migraine-associated vertigo (MV) remains a developing entity because accepted diagnostic criteria are unavailable. Patients present with debilitating dizziness without experiencing headache, and are often misdiagnosed as anxious. The condition is manageable in primary care without the need for neurological referral. The aim of this study was to investigate the prevalence of MV and migraine-associated dizziness (MD) as presenting complaints.

Methods: Patients presented with dizziness probably or definitely associated with migraine history based on the criteria of the International Headache Society. Patients with other vestibulopathies and medical conditions were excluded. Patients were evaluated over a period of nine months. Seven hundred and seventeen patients were examined. The numbers of patients were recorded as a percentage of the population visiting a general practitioner. Response to migraine prophylactic medications was regarded as supporting evidence of the diagnosis. Response was regarded as a complete resolution of symptoms.

Results: Of the 717 patients seen, 12 were identified as having probable or definite MV. Five patients were treated with migraine prophylactic medications, namely amitriptyline 25 mg nocte and/or sodium valproate CR 300 mg bd, and all showed a response to the treatment.

Conclusions: We conclude that the prevalence of MV as presenting complaint may be as high as 1.67%. This figure does however not reflect the total patient population that suffers from the condition – this figure may be much higher. Of those patients treated for MV the response was 100%, further supporting the diagnosis. MV is a relevant complaint that is often misdiagnosed as psychogenic in origin.

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Introduction

Migraine-associated vertigo (MV) is a relatively common condition that is often misdiagnosed in general practice, despite the fact that the condition can be managed medically and without neurological referral.[1] Patients presenting with idiopathic dizziness are often misdiagnosed as suffering from anxiety, despite a history that may distinguish between psychogenic dizziness and migraine-associated dizziness (MD). Most studies on this condition have only been carried out during the past two decades,[2] commencing with Kayan and Hood's classic paper on the subject.[3] To date there are no known studies investigating the prevalence of this debilitating illness in general practice in South Africa. The prevalence of MV in the United States is approximately 3.0–3.5% of the population.[4]

Background

MV was originally diagnosed by Aretaeus of Cappadocia around 100 AD.[5] However, this condition remains a developing entity, because there are no accepted diagnostic criteria.[2] The International Headache Society (IHS)[6] does not provide criteria for its diagnosis (see Tables I and II). The only available criteria are those proposed by Neuhauser et al[7] which are modelled on the IHS classification of migraine (see Table III). The diagnosis in itself is based on history and not on special investigations. Special investigations do have a place where the index of suspicion for conditions such as multiple sclerosis is high.

Approximately 16% of adults are affected by migraine at some point in their lives, whereas the lifetime prevalence of dizziness is about 23%.[2,8] In a recent study the prevalence

Table I: International Headache Society diagnostic criteria for migraine without aura

A. At least 5 attacks fulfilling criteria B–D
B. Headache attacks lasting 4–72 hours
C. Headache has at least two of the following characteristics: 1. Unilateral location 2. Pulsating quality 3. Moderate or severe pain intensity 4. Aggravation by or causing avoidance of routine physical activity (walking or climbing stairs)
D. During headache at least one of the following: 1. Nausea and or vomiting 2. Photophobia and/or phonophobia
E. Not attributed to another disorder

Source:
International Headache Society Classification Subcommittee. International classification of headache disorders. 2nd edn. Cephalalgia 2004:24 (Suppl 1):1–160. http://ihs-classification.org

Table II: International Headache Society diagnostic criteria for typical aura with migraine headache

A. At least two attacks fulfilling criteria B–D
B. Aura consisting of at least one of the following but no motor weakness: 1. Fully reversible visual symptoms including positive features (e.g. flickering lights, spots or lines) and/or negative features (i.e. loss of vision) 2. Fully reversible sensory symptoms including positive features (i.e. pins and needles) and/or negative features (i.e. numbness) 3. Fully reversible dysphasic speech disturbance
C. At least two of the following: 1. Homonymous visual symptoms and/or unilateral sensory symptoms 2. At least one aura symptom develops gradually over more than or equal to 5 minutes and/or different aura symptoms occur in succession over more than or equal to 5 minutes 3. Each symptom lasts more than or equal to 5 minutes but less than or equal to 60 minutes
D. Headache fulfilling criteria B–D for migraine without aura begins during the aura or follows the aura within 60 minutes
E. Not attributed to another disorder

Source:
International Headache Society Classification Subcommittee. International classification of headache disorders. 2nd edn. Cephalalgia 2004:24 (Suppl 1):1–160. http://ihs-classification.org

Table III: The diagnostic criteria of Neuhauser et al for definite and probable migrainous vertigo

Diagnostic criteria for definite migrainous vertigo:
A. Episodic vestibular symptoms of at least moderate severity
B. Current or previous history of migraine according to the 2004 criteria of the IHS
C. One of the following migrane symptoms during two or more attacks of vertigo: migrainous headache, photophobia, phonophobia, visual or other auras
D. Other causes ruled out by appropriate investigations
Comment: Vestibular symptoms are rotational vertigo or another illusory self or object motion. They may be spontaneous or positional. Vestibular symptoms are moderate if they interfere with but do not prohibit daily activities and severe if patients cannot continue daily activities.
Probable migrainous vertigo:
A. Episodic vestibular symptoms of at least moderate severity
B. One of the following: 1. Current or previous history of migraine according to the 2004 criteria of the IHS 2. Migrane symptoms during vestibular symptoms 3. Migraine precipitants of vertigo in more than 50% of attacks: food triggers, sleep irregularities, hormonal change 4. Response to migraine medications in more than 50% of attacks
C. Other causes ruled out by appropriate investigations

Source:
Lempert T, Neuhauser H. Migrainous vertigo. Neurologic Clinics 23(2005):715–30.

of migraine, according to IHS criteria, was found to be 1.6 times higher in 200 patients in a dizziness clinic than in 200 age- and sex-matched controls in an orthopaedic clinic (38% vs 24%, P 0.01).[7] It has also been found that episodic vertigo occurs in 25–35% of all migraine patients.[4]

Patients may present with dizziness or true vertigo in the absence of headache, or the dizziness may precede the migraine, occur with a headache, or follow after it.[4] In some cases migraine attacks may have ceased in the patient's younger years, whilst MV only manifests itself much later, predominantly when patients are in their thirties.[1] Where dizziness or vertigo exist in the absence of headache, careful history taking may reveal a history of migraine, or concurrent symptoms such as photophobia and phonophobia, or auras. Interestingly, the dizziness may be triggered by dietary triggers, sleep disorders or lack of sleep, and hormonal changes such as premenstrual tension.[2] Auras may present in the absence of headache and may include simple numbness of extremities, pins and needles, visual auras such as flashing lights, and even speech disturbances (see Table II).

The occurrence, with seemingly idiopathic dizziness with aura symptoms, may then lead to a diagnosis of psychogenic dizziness or anxiety if the physician neglects to ask the patient about headache or migraine symptoms. Once again, these symptoms may be obscure, because vertigo can be triggered by certain foods, or there can be an abnormal sensation in one or more limbs accompanying the major symptom, namely dizziness.[6]

A recent study identified a progesterone receptor variant as being significantly associated with MV, while no synergistic effect between the oestrogen receptor variant and MV was found.[9] It is an interesting fact that most studies on MV show a clear female predominance that also correlates with the predominance of migraine in the female population.[1,9,10] There are studies linking an increased risk of stroke in females in their thirties that suffer from migraine with aura and use the oral contraceptive pill (OCP).[11] For this reason use of the OCP is contraindicated in women suffering from migraine with aura. The aura phenomenon may well

be linked to vasospasm and risk may be compounded where other stroke factors exist. Furthermore, episodes of transient hearing loss with or without associated vertigo have been reported in young women with migraine around the time of their menstrual period.[12]

Symptoms

Patients with MV often present with symptoms of chronic dizziness that may last for days or months, or just a couple of seconds. There is a bimodal distribution for the duration of symptoms, with most patients experiencing symptoms lasting minutes to hours, or all day and longer.[1,13] Dizziness or vertigo may be so debilitating as to severely restrict daily activities. Other symptoms may be a migraine headache preceding, during or after the vertigo, or it may be absent. Photophobia, phonophobia and visual auras may accompany the attack or may be absent. Vertigo may be spontaneous or positional. Migraine precipitants may be present in more than 50% of attacks of dizziness. Precipitants can include food triggers like red wine, chocolate or cheese, sleep irregularities or lack of sleep, as well as hormonal changes such as premenstrual tension and oestrogen fluctuation or withdrawal.[2,7] (See Table III).

Aura symptoms may include a subjective feeling of numbness in one or both limbs, ataxia or feeling off balance, dysphasia or dysarthria, a feeling of fullness or pressure in the ears, visual auras such as flashing lights or blindness, pins and needles in the face or limbs, photophobia, hyperaccusis, or even a sense of anxiety prior to the aura. Osmophobia or a hypersensitivity to smells is virtually diagnostic of migraine (see Table II).

MD and MV may also occur with history of migraine alone, making the diagnosis more difficult. In these cases a response to migraine medications may warrant a diagnosis of probable MV.[2,7]

Patients also eventually experience anxiety as a result of symptoms, and it may be misinterpreted as a cause of the symptoms. Furthermore, and to complicate matters, studies have proven a link between migraine and an increased risk of panic disorders and depression.[2] Diagnostic fallacy often prevails when the physician fails to elicit a history of accompanying headaches or migraine precipitants.

Methods

A study was conducted to determine the prevalence of patients that presented with possible or definite MD and vertigo in a general medical practice. The study was conducted in a private medical practice in Pretoria. The duration of the study was from 12 January 2009 to 12 September 2009. Patients were diagnosed as having migraine according to the IHS criteria of 2004,[6] and furthermore, definite or probable MV according to the diagnostic criteria of Lempert and Neuhauser[2] and Neuhauser et al[7] (see Table III). Patients with likely vestibular pathology or Ménière's disease were excluded and patients with a medical condition or drug usage that could cause the symptoms were excluded. Patients were excluded if there was a strong suspicion of psychogenic dizziness or where the likelihood of an anxiety-related disorder was high.

No audiometric testing was carried out because this is not routinely done in general practice, but an otological (ear, nose and throat) examination and general medical examination (including measurement of blood pressure) were performed on each patient. The clinical presentation of MD is variable and the association with migraine may be subtle. Key to the diagnosis is the repeated concurrence of migraine symptoms and vertigo, migraine precipitants, and a response to antimigraine drugs and prophylactic medications.[2] If there were other symptoms that could have indicated possible multiple sclerosis, patients were not included in the study unless they first had a magnetic resonance brain scan to rule out pathology attributable to multiple sclerosis.

Results

A total number of 866 patient visits were recorded. As some of these visits included patients that were seen more than once, a total number of 717 different patients were seen. Of these, 18 visits were related to dizziness that was diagnosed as being migraine associated. A total number of 12 patients out of 717 persons in the general examined population were diagnosed as having probable or definite MV as presenting complaint. Of these 12 patients, nine were female. Ages of the affected patients ranged from 14 to 50 years. The average age of presentation was 34.0 years, which correlates well with Reploeg and Goebel's reported average age of 36.6 years at presentation.[1]

All of the patients in the affected group fulfilled the criteria for definite or probable MV. Nine of the patients fulfilled the criteria for definite MV and three of the patients (2 females and 1 male) fulfilled the diagnostic criteria for probable MV (see Table IV). Seven patients experienced occasional pins and needles or numbness in the face or limbs, four patients experienced photophobia and three patients experience hyperaccusis. Three patients had occasional visual auras, one patient experienced occasional pressure in the ears, and one patient reported occasional speech disturbance (see Table V).

Of the 12 patients diagnosed, five patients desired and needed medical treatment. Amitriptyline and sodium

Table IV: Results of this study

Gender	Male	Female
Number of patients diagnosed	3	9
Definite MV	2	7
Probable MV	1	2
Response to sodium valproate and amitriptyline combination (3 patients treated), 100% response	1	2
Response to amitriptyline alone (2 patients treated), 100% response	None treated	2

Table V: Symptoms experienced by patients

Symptoms	Number of patients
Pins and needles, or numbness in limbs or face	7
Photophobia	4
Hyperaccusis	3
Ataxia	3
Visual auras	3
Pressure in ears	2
Speech disturbances	1
Tremor	1

Note that all 12 patients had a history of present or past migraine.

valproate are both used as migraine prophylactic drugs. Three patients used amitriptyline 25 mg nocte with sodium valproate controlled release formula 300 mg 12 hourly, in combination, and two patients used amitriptyline 25 mg nocte alone. All five of the treated patients had complete resolution of all symptoms within one month. (Note that the dosage of amitriptyline used was too low to have a real mood altering effect. Dosages of 75 mg and even 150 mg are used when the drug is used as an antidepressant.) Eight of the female patients used the OCP and the other female was on hormone replacement therapy (HRT).

Discussion and pathophysiology

There are several theories for the pathophysiology of MV, despite the fact that it is poorly understood. There are theories that involve both central as well as peripheral defects.

One of the most popular theories is that proposed by Cutrer and Baloh:[13] episodes of dizziness in duration similar to that of aura (less than 60 minutes) that are time-locked with the headache are related to a spreading wave of cortical depression, the same as other aura phenomena. This theory proposes that a stimulus results in a transient wave that suppresses central neuronal activity. This stimulus spreads in all directions from its origin. Concomitantly there can be increases in intracellular potassium (K^+) and decreases in extracellular calcium (Ca^{2+}). These increases may lead to reduced cerebral blood flow in the areas where there is depression of cortex function. This theory is supported by studies in which sudden hearing loss is linked to migraine and attributed to vasospasm of the internal auditory artery.[12] Some authors propose that peripheral cochleovestibular dysfunction in migraine sufferers may similarly be due to vasospasm of the internal auditory artery, with possible ischaemia.[4,17] This proposal may be more plausible in relation to patients who experience short attacks of MV.[2] The attacks of MV may, however, last for days or weeks in the majority of patients.[1] A further problem is that most patients with MV have dizziness that shows no specific relation to the headache.[2,4] Benson et al[4] noted that changes in sensorineural hearing are rarely a significant feature of MV, but they rather help to differentiate it from other causes of vertigo, especially Ménière's disease.

Reploeg and Goebel[1] argue against the vasospasm theory, and state that functional imaging studies have proved that cortical oligaemia rather than ischaemia occurs after a wave of spreading cortical depression. They suggest that migraine is primarily a neurogenic rather than a vasogenic disorder.

This proposal led to the development of a further theory by Cutrer and Baloh,[13] which suggests that if the dizziness is unrelated to headache, it may be caused by the release of neuropeptides (substance P, neurokinin A, and others). These peptides may have an excitatory effect on the baseline firing rate of the sensory epithelium of the inner ear and possibly also on the vestibular nuclei in the pons of the brainstem. Prolonged symptoms may be caused by neuropeptides diffusing into the extracellular fluid. There may also be progression of persistent spontaneous vertigo, followed by benign positional vertigo and then motion sensitivity.

Furthermore, Lee et al[9] report a positive association of a progesterone receptor with migraine-associated vertigo. Eight of the female patients used the OCP and the remaining female was on HRT. This may correlate with the theory of an associated progesterone receptor variant in MV. It may however lead to an increase in the number of females presenting with the diagnosis. (Note that the cessation of hormone usage forms part of the treatment of MV.[11])

Another theory involves serotonin as an important substrate in migraine development. Serotonin may have a direct effect on the firing rate of vestibular nucleus neurons.[4] This may lead to theoretical complications when the incorrect diagnosis of panic disorder or anxiety disorder is made, and a selective serotonin reuptake inhibitor is prescribed. Note that patients with MV may respond to benzodiazepines because it is a vestibular suppressant.[1]

Over the past decade, genetic defects in ion channels, specifically voltage-gated calcium channels, have been investigated. This is because an abnormal voltage-gated calcium channel gene was identified in familial hemiplegic migraine and episodic ataxia type 2.[1,2] To date, however, no calcium channel defect has been identified in the case of MV. Acetazolamide has however been found to be effective in the treatment of MV, and this may be due to its effects on calcium channels.[4]

Several neurotransmitters that are involved in the pathogenesis of migraine (calcitonin gene-related peptide, serotonin, noradrenaline and dopamine) also modulate vestibular neurons and may contribute to the pathogenesis.[2]

The author wishes to propose that both migraine and MV may be associated with a dopamine hypersensitivity, because the dopamine-blocking effects of tricyclic antidepressants and even antiepileptic medications, as well as cetirizine and prochlorperazine (used to treat nausea related to migraine), may be responsible, in their efficacy in treating both migraine in a prophylactic sense, as well as preventing or treating MV. Withdrawal of dopamine-blocking agents such as sulpiride may lead to dopamine hypersensitivity with associated dizziness and vertigo as well as nausea. Medications that increase the levels of dopamine in the brain may similarly lead to dizziness. It was found that orthostatic symptoms were more frequent in patients who had migraine than in controls (68% vs 8%). Orthostatic hypotension can by induced by small doses of dopamine agonists, such as bromocriptine, and counteracted by dopamine antagonists in migraineurs but not in controls, suggesting hypersensitivity to dopaminergic stimulation as an underlying cause of MV.[2,14]

Conclusions

We are of the opinion that the prevalence of probable or definite MV as presenting complaint in the general population may be as high as 1.67%. This figure does however not reflect the total patient population that suffers from the condition or has suffered from it – this figure may be much higher. This may correlate with the 3–3.5% prevalence of MV in the USA in the general population.[4] Other studies have found the lifetime prevalence of the condition to be 0.98% (95% confidence interval 0.7–1.37%).[15]

Of those patients treated with migraine prophylactic medications, the response was 100%, further supporting the diagnosis. We conclude by stating that MD and MV are relevant complaints that are often misdiagnosed and mismanaged as psychogenic dizziness or anxiety. MD can be effectively managed with migraine prophylactic drugs without the necessity of neurological referral.

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