J Neurol (2009) 256:711–716
DOI 10.1007/s00415-009-5050-5

REVIEW

Vestibular migraine: a critical review of treatment trials

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Received: 19 June 2008 / Revised: 26 December 2008 / Accepted: 13 January 2009 / Published online: 1 March 2009

Abstract Vestibular migraine (VM), also known as migraine-associated vertigo, is a common cause of dizziness in adults. We performed a comprehensive literature search regarding treatment for VM or migraine-associated vertigo during the period of 1990–2008 and used, individually or in combination, the search terms VM, migraine-associated vertigo, migraine-associated dizziness, migrainous vertigo, migraine and vertigo, migraine and disequilibrium, and headache and vertigo. We found nine publications that address treatment strategies for VM. One small randomized clinical trial found some benefit from the use of zolmitriptan for abortive treatment of VM. The other eight observational studies showed marginal improvement with migraine prophylactic medications such as nortriptyline, verapamil, or metoprolol. Until more specific treatment options become available, patients with VM need to be managed with similar prophylactic and abortive strategies as those used for migraine in adults.

Keywords Vestibular migraine · Migraine-associated vertigo · Migraine · Vertigo · Dizziness · Headache

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Introduction

Vertigo, dizziness, and migraine are quite common in the general population, and in some patients, they may be inter-related [6, 7, 10, 13, 15]. The prevalence of migraine, according to the criteria of the International Headache Society (IHS) [1], is at least three times higher in those with vertigo [7, 15]. Patients with various forms of disequilibrium and some manifestations of migraine may have a condition known as vestibular migraine (VM), also known as migraine-associated vertigo or migrainous vertigo [7].

Savundra et al. [17] retrospectively analyzed 363 patients who presented to a neurotology clinic with vertigo and found 116 patients (32%) with migraines. Of those, 85% had no other explanation for their vertigo in contrast to only 51% of nonmigraineurs with idiopathic vertigo, suggesting that in a large proportion of patients with vertigo, VM is under-diagnosed. This underdiagnosis may be due to several factors, including the wide variability in presentation of patients with VM, lack of a widely accepted pathophysiologic model linking migraine and vertigo, and significant overlap with depression or anxiety. In some patients, the history of vertigo may be seen as a nonspecific manifestation of panic attacks.

Given the high prevalence of VM, we performed a review of the literature to determine the optimal prophylactic and abortive treatment options for this condition.

Methods

A literature search was performed via PubMed, Ovid, and MD Consult using the following search terms: VM (209 papers), migraine-associated vertigo (82), migraine-

associated dizziness (7), migrainous vertigo (49), migraine and vertigo (281), migraine and disequilibrium (31), headache and vertigo (1,215). The search was performed exclusively for articles in English for the period of 1990–2008. After reviewing the abstracts, we focused on nine articles that addressed specific therapeutic interventions and their outcomes for VM.

Results

Only one small randomized, double-blinded, placebo-controlled study addressed treatment of VM (Table 1). Neuhauser et al. [14] found improvement of vertigo symptoms at 2 h in eight patients treated with zolmitriptan, as compared to the response in nine patients treated with placebo. The inclusion criteria were episodic vestibular symptoms of at least moderate severity, current or previous history of migraine according to IHS criteria [1], migrainous symptoms during at least two of the vertiginous attacks, and no other identifiable cause of vertigo. These researchers found that 38% of patients treated with zolmitriptan had a positive response (CI 9–76%) compared to 22% of patients taking placebo (CI 3–60%). Results were deemed inconclusive due to the limited power of the study.

Baloh et al. [2] studied the effectiveness of acetazolamide in a family with familial migraine, vertigo, and essential tremor. All five patients who were treated showed marked decrease in the frequency of headaches, vertigo spells, and the severity of essential tremor.

Bikhazi et al. [3] performed a survey of 111 patients who had previously presented to a headache clinic with history of symptoms of dizziness or vertigo; they found that medications that targeted the treatment of headache were also effective in treating the vertigo associated with the migraine. Responses were graded from 1 to 4, with 4 being the most effective treatment, and were based on patients' recall of the effectiveness of the therapeutic intervention. Sumatriptan received a median efficacy score of 4 for abortive treatment of migraine and 3 for symptomatic relief of vertigo. The abortive drugs (NSAIDS, opiates) received a score of 3 for migraine and 2 for vertigo, and the commonly used prophylactic treatments (beta blockers, calcium-channel blockers, tricyclic antidepressants, methylsergide, valproic acid, cyproheptadine) received a median efficacy score of 2 for treating migraine overall, and 1 for treatment of vertigo. The temporal relationship of the dizziness to the migraine did not influence therapeutic efficacy.

In another study, Johnson evaluated the effects of a number of different medications for symptomatic relief in a retrospective review of 89 patients diagnosed with migraine-related dizziness or vertigo [9]. Seventy-nine patients were treated pharmacologically, some receiving a single medication and others receiving a combination of up to six medications, depending on their individual requirements. Medications used included benzodiazepines, tricyclic antidepressants, beta blockers, and calcium-channel blockers. With this approach, substantial response (defined as improvement of symptoms such that they would no longer interfere with daily activities) was seen in 92% of patients with episodic vertigo, 89% of patients with positional vertigo, 86% of patients with nonvertiginous dizziness, 85% of patients with aural fullness, 63% of patients with ear pain, and in 89% of patients with phonophobia. They concluded that management of this population must take a multifaceted approach that includes dietary changes, stress management, sleep improvement, physical therapy, and pharmacologic therapy.

Several other retrospective observational studies provide limited data and varying responses to treatment. Reploeg and Goebel [16] identified 81 patients by chart review with migraine-associated vertigo or disequilibrium and instituted sequential therapy first with dietary manipulation alone, then diet with nortriptyline, and then diet with atenolol or calcium-channel blockers. Responses were graded as complete resolution, well-controlled (>75% reduction in frequency of symptoms), poorly controlled (<75% reduction in frequency of symptoms), or no response. Of the 13 patients treated with diet alone, 100% experienced significant relief—either complete resolution or good control of symptoms. Of the 31 patients treated with diet plus nortriptyline, 78% had significant relief. Finally, of the 37 treated with diet plus either atenolol or a calcium-channel blocker, 57% had significant relief. Overall, 58 of the 81 patients (72%) experienced resolution or >75% reduction in the frequency of their attacks of vertigo and disequilibrium.

In another small case-report study, 16 patients who presented with chronic vertigo and a history of headaches (38% presented with a history that was strongly suggestive of migraine) were treated with a variety of different medications: pizotifen, dothiepin, propranolol, and verapamil. All patients, regardless of the type of intervention, reported either complete resolution or marked improvement in both headache severity and vertigo [19].

Bisdorff [4] conducted a retrospective observational study of 19 patients who suffered from migraine and migraine-related vertigo and were treated prophylactically with lamotrigine (LTG). Patients were interviewed regarding the frequency and duration of headache and vertigo attacks during the 2 months before and after 3–4 months of LTG administration. Patients took 25 mg of LTG every morning for 2 weeks, then 50 mg for 2 weeks, to reach a target dose of 100 mg after 4 weeks. With LTG

Table 1 Summary of studies addressing treatment strategies for vestibular migraine

References	Type Number of cases/control	Criteria for diagnosis	Type of intervention	Period of intervention	Outcome
Neuhauser et al. [14]	RCT 8/9	• Episodic vertigo • History of migraine • One or more migrainous symptoms during vertiginous attacks • No other identifiable causes of vertigo	Zolmitriptan, 2.5 mg	NS	Improvement in vertigo in 38% compared to 22% of control (CI 3%–60%)
Baloh et al. [2]	OP 5/NS	• Migraine headaches • Visual aura • Recurrent spontaneous vertigo	Acetazolamide, 250–750 mg	3–30 months	Marked decrease in vertigo and headache in all patients
Bikhazi et al. [3]	OR 111	• Dizziness (vertiginous versus nonvertiginous) • Temporal relationship between migraine and dizziness	Sumatriptan (DNS) Abortive drugs (ergots, NSAIDS, opiates, sumatriptan) Prophylactic drugs (beta blockers, calcium-channel blockers, TCA, methylsergide, valproic acid, cyproheptadine)	NS	Sumatriptan TES[a] • 4 (migraine) • 3 (vertigo) Abortive drugs TES • 3 (migraine) • 2 (vertigo) Prophylactic drugs TES • 2 (migraine) • 1 (vertigo)
Johnson [9]	OR 89/none	• True vertigo or nonvertiginous dizziness • Headache with or without association to dizziness • Subjective or objective hearing loss • Aural fullness, ear pain	Dietary modification, BDZ (clonazepam, alprazolam, lorazepam, or prazepam), amitryptyline, propranolol, calcium-channel blocker (verapamil, diltiazem), SSRI (sertraline, fluoxetine, paroxetine)	NS	Complete or substantial control of vestibular symptoms was achieved in 68 (92%) of 74 patients with episodic vertigo; in 56 (89%) of 63 patients with positional vertigo; and 56 (86%) of 65 patients with nonvertiginous dizziness. Aural fullness was completely resolved or substantially improved in 34 (85%) of 40 patients; ear pain in 10 (63%) of 16 patients; and phonophobia in 17 (89%) of 19 patients.
Reploeg and Goebel [16]	OR 81/none	• Vertigo • Disequilibrium • Migraine with aura • Migraine history	Stepwise treatment with: 1. Dietary manipulation 2. Diet and TCA (nortriptyline 10–25 mg; titrate to 50 mg) 3. Diet and "other" [atenolol (DNS) or calcium-channel blocker (DNS)]	54.5 weeks	1. Diet alone—13 patients treated, and improvement of symptoms seen in 100% 2. Diet + TCA—31 patients treated, and significant improvement seen in 78% 3. Diet + other—37 patients treated, and significant improvement in 57%

Table 1 continued

References	Type Number of cases/control	Criteria for diagnosis	Type of intervention	Period of intervention	Outcome
Waterston [19]	OR 16/none	• Vertigo (positional or spontaneous) • Motion sickness/intolerance • History of headache	Pizotifen, 0.5 mg daily Dothiepin, 25 mg daily Propranolol, 40 mg twice daily Verapamil, 40 mg twice daily	NS	Complete or almost complete resolution of symptoms seen in all 16 patients irrespective of the drug used
Bisdorff [4]	OR 19	Migraine Migraine-related vertigo	Lamotrigine, after titration of 4 weeks, 100 mg/day	3–4 months	50% reduction in headache frequency in 9 (47%); ≤50% reduction in 2; 7 unchanged, 1 became worse. >50 reduction in vertigo frequency in 18 of 19; 1 unchanged. Complete relief of headache symptoms in 10.5% and of vertigo symptoms in 26.3%.
Maione [11]	OP 53/none	• At least five attacks of vertigo or dizziness • History of migraine • Family history of migraine and/or strong motion intolerance	Varying doses of propranolol, metoprolol, clonazepam, flunarizine, or amitriptyline	6 months (subset was followed out to a maximum of 42 months)	69.3% reported satisfactory control of symptoms (sum of complete resolutions and substantial controls), and 81.8% had at least a 50% reduction of the vertiginous episodes frequency.
Carmona and Settecase [5]	OP 10	VM with auditory symptoms	Topiramate twice daily, 100 mg/day	6–16 months	All patients, including one who discontinued treatment after 9 months, without symptoms.

RCT randomized clinical trial, *NS* not specified, *CI* confidence interval, *OP* observational prospective trial, *OR* observational retrospective trial; *DNS* dose not specified, *NSAIDS* nonsteroidal anti-inflammatory agents, *TCA* tricyclic antidepressants, *BDZ* benzodiazepines, *SSRI* selective serotonin reuptake inhibitors

[a] Therapeutic efficacy score range: 1–4 (1 = least effective, 4 = most effective) in treatment of migraine or vertigo symptoms

treatment, nine patients reported reduction of 50% in attack frequency of headaches; two patients improved by ≤50%, seven were unchanged, and one became worse. Vertigo frequency was reduced by >50% in 18 of 19 patients and remained unchanged in one. Complete relief of symptoms for vertigo was reported by 26.3% of patients and for headache by 10.5%.

Maione [11] evaluated the efficacy of migraine pharmacologic prophylaxis in a group of patients considered to be affected by migraine-related vertigo. In this prospective observational study, 33 of the 36 patients who completed the trial had reported recurrent vertiginous spells before the trial. At evaluation after 6 months of treatment with propranolol, metoprolol, clonazepam, flunarizine, or amitriptyline, satisfactory control of symptoms (sum of complete resolutions and substantial controls) was reported by 19 of the 33 (69.3%), >50% reduction was reported by eight (24.2%), <50% reduction was reported by five (15.2%), and one patient (3%) reported no reduction.

In a prospective observational study of 10 patients with VM with auditory symptoms, Carmona and Settecase [5] treated with topiramate twice daily (average dose, 100 mg/day) for 6–16 months. All patients, including one who discontinued treatment after 9 months, remained without symptoms.

Most of the studies summarized above analyzed data concerning prophylactic treatment [2, 4, 5, 11, 16, 19]. One focused on acute treatment of vertigo attacks [14], and two focused on both acute and prophylactic treatment [3, 9].

Discussion

From our analysis of existing literature, we have found a lack of commonly used criteria for diagnosis of VM and, as a result, a lack of solid data to support the optimum pharmacologic agent for treatment of this common cause of dizziness in adults. To date, several observational analyses and only one randomized, double-blinded, placebo-controlled study have been conducted to address its treatment. Findings from these studies suggest that certain therapeutic interventions, such as abortive treatment with triptans, may be of significant benefit, but the limited power of the studies, the lack of placebo-controlled groups in retrospective analyses, and the inconsistency of criteria used for diagnosis of VM, severely hinder the establishment of treatment guidelines. For example, even in the large study by Bikhazi et al., less than half had true VM (58 of 111 patients completed the questionnaire; of those, only 53 fulfilled the inclusion criteria. Of those, 75%, 40, reported nonvertiginous dizziness as imbalance or lightheadedness).

Neuhauser et al. [12] proposed an operational diagnostic criterion for migrainous vertigo with separate categories of definite and probable migrainous vertigo that attempt to address the issue of sensitivity and specificity. A "definite" diagnosis of VM requires recurrent spontaneous vestibular symptoms, the occurrence of at least one migrainous headache during at least two vertiginous episodes. A "probable" diagnosis requires a less direct link between migraine symptoms and vertigo attacks. It is critically important to follow these criteria for making a diagnosis of VM, to separate them from other similar conditions such as Meniere disease and vestibular paroxysmia [8].

Based on our review of the literature and the fact that topiramate has been an effective medication for treatment of migraine with aura [18], we suggest a clinical trial with the following parameters: include patients with definite VM diagnosis based on Neuhauser criteria, include patients who have dizziness symptoms at least 3–4 times per month, administer either placebo or increasing doses of topiramate for 6 months, monitor patients monthly and closely document their adherence to therapy.

Until better medications become available, the principles of migraine treatment hold true for the management of patients with VM. Lifestyle modifications such as a balanced diet, regular exercise, and good sleeping habits play a vital role in the management of this patient population. It is also important to identify and eliminate any possible triggers. Patients should monitor their attacks by keeping a diary of events. Treatment response should be evaluated after 3 months, with >50% reduction in attack frequency being a realistic goal. Selected patients may benefit from vestibular rehabilitation [20].

Acknowledgement We thank Dr. David Newman-Toker for his thorough and extensive review of the manuscript. His thoughtful comments are greatly appreciated.

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