The Journal of Laryngology & Otology

cambridge.org/jlo

A systematic review and meta-analysis of prophylactic medication of vestibular migraine

C Yiannakis, L Hamilton, M Slim and G Kontorinis

Department of Otolaryngology, Queen Elizabeth University Hospital, Glasgow, Scotland, UK

Abstract

Objective. Vestibular migraine is in the process of recognition as an individual clinical entity. At present, no guidelines exist for its management. This study aimed to conduct a systematic review and meta-analysis to determine the effectiveness of available prophylactic medication.
Method. A literature search was performed using PubMed, Ovid and Embase databases. Qualitative and quantitative analysis were performed as well as risk of bias analysis. Meta-analysis for the mean differences for pre- and post-treatment impact based on Dizziness Handicap Inventory and Vertigo Symptom Scale were performed. Proportionate transformation meta-analysis for the successful event rate based on complete symptoms control was explored.
Results. Thirteen publications were identified: 3 were randomised, controlled trials and 10 were non-randomised, controlled trials. Propranolol and venlafaxine improved the Vertigo Symptom Scale score by −13.31 points and −4.16 points, respectively, and the Dizziness Handicap Inventory score by −32.24 and −21.24, respectively. Only propranolol achieved statistically significant impact with 60 per cent of patients achieving complete symptom control.
Conclusion. Propranolol should be offered as the first-line treatment for vestibular migraine followed by venlafaxine. Amitriptyline, flunarizine and cinnarizine showed a trend for symptom improvement, but this was not statistically significant.

Review Article

Dr C Yiannakis takes responsibility for the integrity of the content of the paper

Cite this article: Yiannakis C, Hamilton L, Slim M, Kontorinis G. A systematic review and meta-analysis of prophylactic medication of vestibular migraine. *J Laryngol Otol* 2023;**137**: 953–961. https://doi.org/10.1017/S0022215122001979

Accepted: 2 August 2022
First published online: 6 October 2022

Keywords:
Migraine; vertigo; propranolol; venlafaxine hydrochloride; dizziness; therapeutics

Corresponding author:
Dr C Yiannakis;
E-mail: c.yiannakis@nhs.net

Introduction

Dizziness and migraine are both common in the general population. However, there is increasing evidence that they can be inter-related.[1–4] Vestibular migraine, as an individual clinical entity, is gradually being recognised as a cause of episodic vertigo, affecting approximately 2.7 per cent of adults with a lifetime prevalence of 0.98 per cent.[3,5]

However, this is felt to be an underestimate because it is likely that vestibular migraine is under-diagnosed.[6,7] This is in part because of the broad variability in presentation alongside the absence of a widely accepted pathophysiological model that links migraine with vertigo. The overlap of vestibular migraine, anxiety and depression should also be considered.

Vestibular migraine typically presents with episodes of acute imbalance or vertigo that can last for minutes to days. Although it is sometimes associated with a migrainous headache (pulsatile, but not always unilateral), it is more frequently associated with aura type symptoms, such as photophobia or phonophobia. Vestibular migraine can present at any age, with a reported male-to-female ratio of 1.5:5.[8]

The pathophysiology of vestibular migraine is poorly understood and predominantly based on the knowledge of migraine. This shared aetiology is based on the response of vestibular migraine to classical migraine therapy.[9] Neurotransmitters thought to be involved in migraine, such as noradrenaline, serotonin and dopamine, may also be involved in vestibular migraine. This, in turn, impacts the treatment options.[8,10,11] A further theory regarding its pathophysiology is the possibility of reciprocal connections between structures that modulate trigeminal nociceptive inputs and the brainstem vestibular nuclei.[6] In particular, the trigeminal-cervical complex can provide sufficient explanation for the wide variety of pain distribution in migraine as well as the involvement of other cranial nerves and nuclei.[12,13] The proximity and connections of the trigeminal nerve to certain structures and cranial nerves provides sufficient explanation of symptoms related to temporary dysfunction of such nerves.[12,13]

Diagnosis relies on the clinical history and the exclusion of other causes of dizziness, such as Ménière's disease or benign paroxysmal positional vertigo, because outside of an acute attack, neuro-otological examination is either inconclusive or normal.[14,15] At present, the definition of vestibular migraine is based on the diagnostic criteria outlined by the Bárány Society and the International Headache Society.[16]

Given the association with migrainous headaches and the lack of an alternative pathophysiological mechanism, prophylactic treatment of vestibular migraine is based on that offered for classical migraine.[17–19] Empirically, this includes calcium channel blockers, β-blockers, anti-depressants and anti-epileptics. Lifestyle changes, such as sleep hygiene and dietary modifications (avoiding red wine, chocolate, coffee and glutamate), have also been shown to reduce the intensity and frequency of attacks.[20]

At present, no guidelines exist for the management of vestibular migraine, with treatment largely being based on an individual clinician's personal preferences and familiarity with various drugs. To date, most evidence regarding the prophylactic management of vestibular migraine is based on retrospective or observational studies, frequently lacking a control arm. Given the increasing prevalence of vestibular migraine, its debilitating impact on people's quality of life and the lack of strong evidence for a treatment regimen, we conducted a systematic review and meta-analysis to determine the effectiveness of current available prophylactic medication used in vestibular migraine.

Materials and methods

Protocol and registration

Prospero registration was completed (registration number: CRD42020207295). We performed our review according to the Preferred Reporting Items for Systematic Review and Meta-Analyses ('PRISMA') checklist.[21]

Literature search

A literature search was performed using PubMed, Ovid and Embase databases. The following medical subject headings search terms were included: vestibular migraine, migraine-associated vertigo, migraine and vertigo, migraine-associated dizziness, head and vertigo, and migraine and disequilibrium. This study aimed to review what the prophylactic treatment options are for vestibular migraine as well as review the available evidence. Because of the emerging nature of the diagnosis, the search was limited to publications in the last 20 years and those written in English and German. Case reports, abstracts and conference proceedings were excluded.

All publications were assessed by two authors independently (CY and LH) using the following eligibility criteria: (1) studies assessing only the management of vestibular migraine, with those including other causes of vertigo excluded and; (2) management to include at least one pharmacological treatment.

We excluded studies with: (1) patients under the age of 16 years; (2) purely conservative management without any medication, and; (3) a focus solely on epidemiology or pathogenesis or descriptive studies.

In case of discrepancies, a decision was made following discussion with the senior author (GK) to reach consensus.

Documented factors

In addition to basic demographic data, the following information was also collected: study design (type, randomisation, and whether it was prospective or retrospective); whether study power was recorded; treatment and, if used, control arms; outcome (both how this was defined and measured and the result); and side effects.

Risk of bias assessment

The Risk of Bias 2 tool was used for randomised, controlled trial (RCT) studies.[22] Meanwhile, non-RCTs were evaluated using the Risk of Bias in Non-Randomised Studies of Interventions tool.[23] Assessments were performed by the third author independently (MS), and these were then subsequently validated by two other authors (CY and LH).

Data extraction and statistical analysis

Meta-analysis was performed using the R-language when equal to or more than two studies addressed the outcome measures with the same prophylactic medication.[24,25] Trials reporting outcomes based on validated patient-reported outcome measures for vestibular migraine, such as the Dizziness Handicap Inventory and Vertigo Symptom Scale were extracted independently by one of the authors (MS) to enable prophylactic treatment effect size exploration based on the pre- and post-treatment mean differences. Proportionate meta-analysis with the Freeman–Tukey double arcsine transformation for prophylactic treatment successful event rate was also performed on studies reporting outcomes for complete control of vestibular migraine symptoms only. Mean differences for frequency of headache and vertigo were also explored. The random effect model was selected because of the variation in prophylactic treatment available for vestibular migraine.[24] The Egger's test and meta-regression were not performed because there were less than 10 studies identified.[24]

Results

Out of an initial 56 publications, a total of 13 publications were identified (Fig. 1) meeting the inclusion criteria.

Basic demographic data

The median number of patients included in each study was 39 (range: 12–100).[20,26–37] The gender ratio of 1 male to 2.8 females (152 males and 428 females) was in keeping with the reported female preponderance, although this ratio was slightly lower than reported elsewhere.[20,26–37]

Study design

Of the 13 publications reviewed, only three were RCTs,[27,35,36] and the remaining 10 studies were non-RCTs.[20,26,28–34,37] The majority (61.5 per cent) were retrospective studies,[20,28–32,34,37] with only 5 studies (38.5 per cent) being prospective.[26,27,33,35,36] The following drugs were evaluated within the RCTs: propranolol, venlafaxine, valproic acid and flunarizine. The following drugs were evaluated in the non-RCTs: acetazolamide, venlafaxine, cinnarizine, amitriptyline, valproate, lomerizine, propranolol, metoprolol, topiramate, lamotrigine, flunarizine, butterbur root extract and nortriptyline. Power calculations were only performed in 3 (23.1 per cent) studies.[30,35,36]

The minimum follow-up time was three months (seven studies),[20,27,29,31,32,35,36] with one study following patients up for six months[33] and only two studies for longer than six months.[30,37] Three studies did not specify a follow-up period.[26,28,34]

Risk of bias assessment

Three studies were RCTs (Fig. 2),[27,35,36] and 10 studies were non-RCTs (Fig. 3).[20,26,28–34,37] One study had a low degree of bias,[36] 2 studies had a moderate degree of bias[30,32] and 10 studies were judged to have a high degree of bias.[20,26–29,31,33–35,37]

Patient-reported outcomes of prophylactic treatment

Propranolol

Two recent studies (Fig. 4) evaluated the prophylactic impact of propranolol on vestibular migraine and reported their outcomes based on the Vertigo Symptom Scale.[30,36] Here,

https://doi.org/10.1017/S0022215122001979 Published online by Cambridge University Press

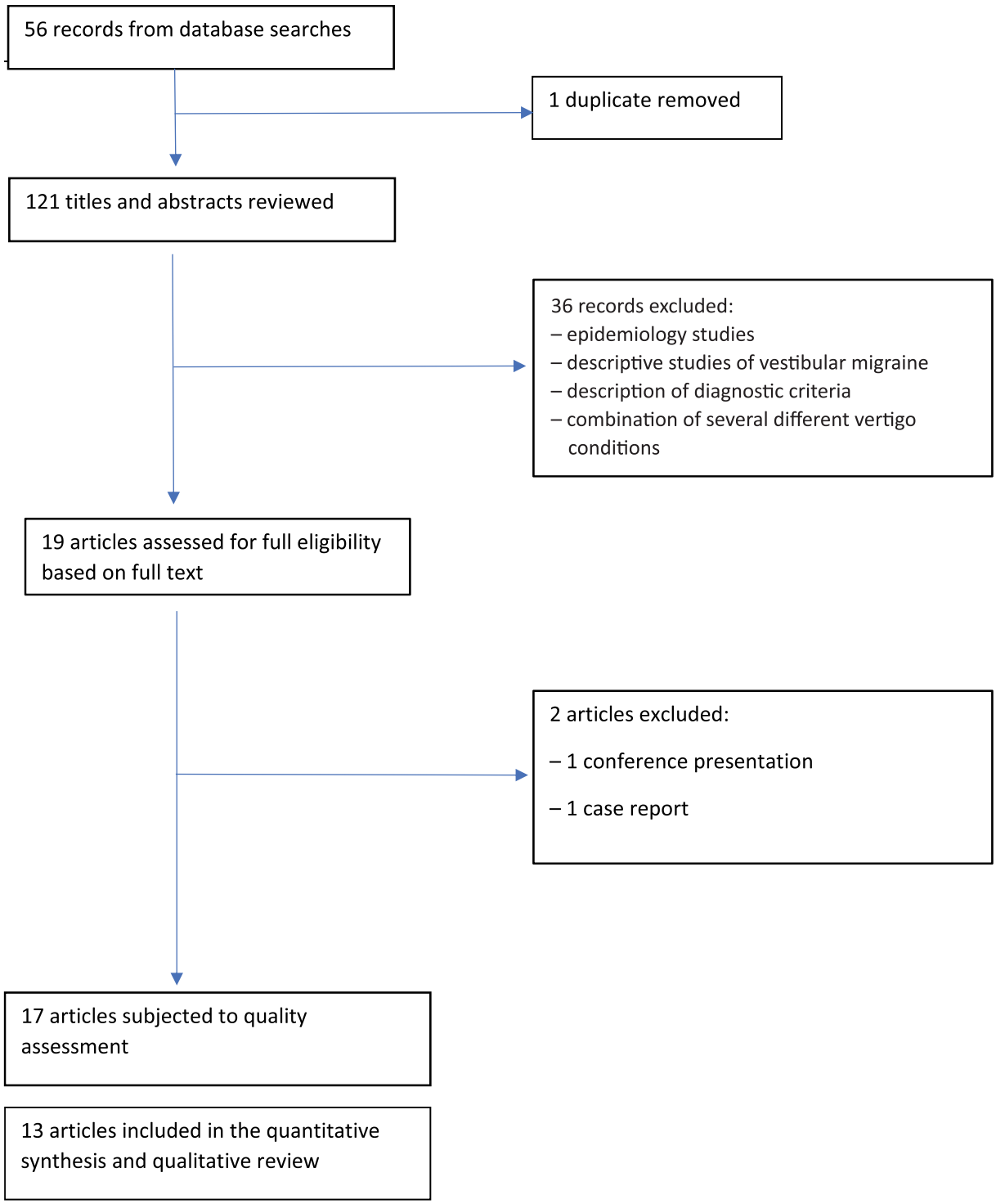

Figure 1. Preferred Reporting Items for Systematic Review and Meta-Analyses ('PRISMA') flow diagram. Moher D *et al.*[21]

propranolol improved the Vertigo Symptom Scale score by −13.31 points (95 per cent confidence interval (CI) = −29.41 to 2.79) following treatment ($p < 0.01$). However, the included studies were highly heterogeneous (I^2: 99 per cent). Dizziness Handicap Inventory was also reported in these studies (Fig. 5).[30,36] Beneficial impact by −32.24 points (95 per cent CI = −48.29 to −16.19) was noted ($p < 0.01$). Again, heterogeneity was high (I^2: 94 per cent).

Venlafaxine

Two studies (Fig. 4) evaluated the impact of venlafaxine using the Vertigo Symptom Scale, showing improvement by −4.16 points (95 per cent CI = −8.01 to −0.32; $p < 0.01$; I^2: 99 per cent).[35,36] Beneficial impact was also noted for Dizziness Handicap Inventory (Fig. 5) by −21.24 points (95 per cent CI = −41.36 to −1.12; $p < 0.01$; I^2: 95 per cent).

Prophylactic treatment successful event rate outcomes

Eleven studies (Fig. 6) reported appropriate outcome measures to enable meta-analysis for the proportional successful event rate on achieving complete vestibular migraine symptoms control. These were based on four types of prophylactic treatment: propranolol,[30,31,34,36] venlafaxine,[31,36] amitriptyline[26,31] and flunarizine.[27,31,34] On average, any of these prophylactic treatments will achieve successful complete control of their

https://doi.org/10.1017/S0022215122001979 Published online by Cambridge University Press

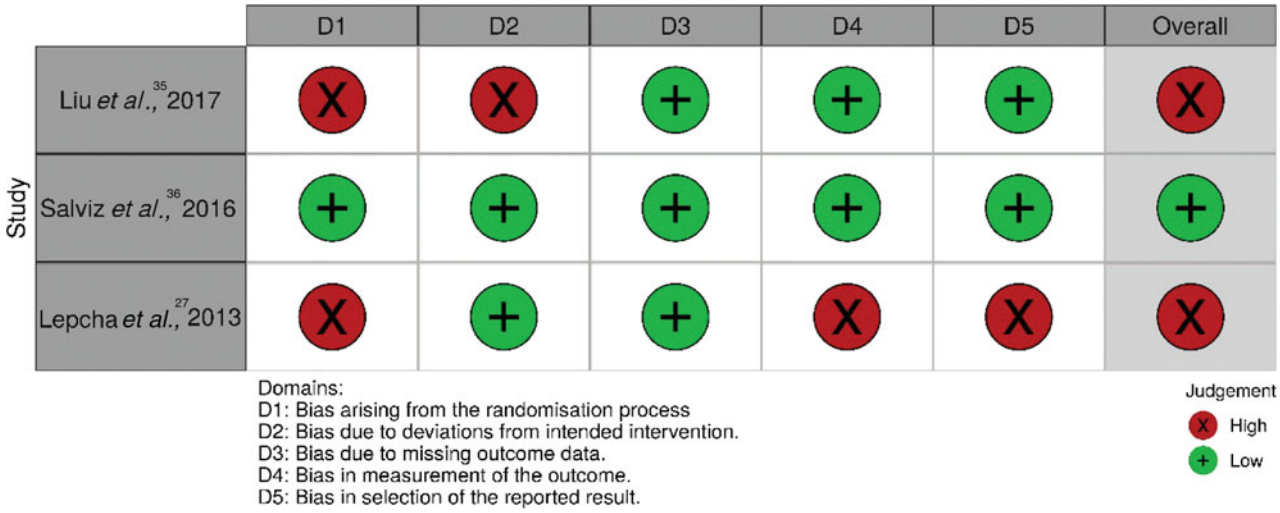

Figure 2. Risk of Bias 2 tool domains diagram.

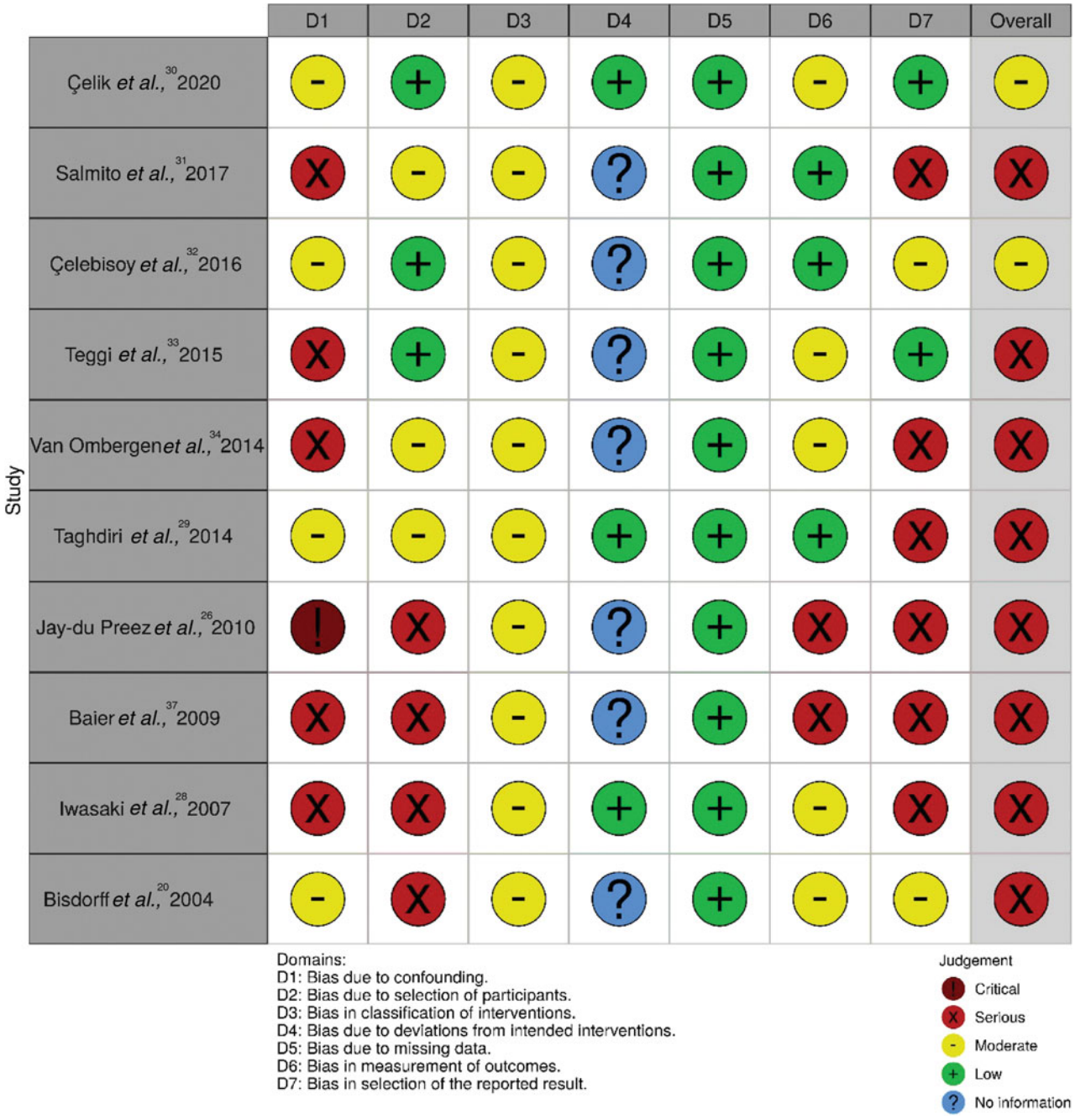

Figure 3. Risk of Bias in Non-Randomised Studies of Interventions domains diagram.

https://doi.org/10.1017/S0022215122001979 Published online by Cambridge University Press

Figure 4. Forest plot showing the meta-analysis for VSS (Vertigo Symptom Scale) mean differences. SD = standard deviation; IV = inverse variance; CI = confidence interval; NA = not available

vestibular migraine by 72 per cent (95 per cent CI = 0.56 to 0.85; $p < 0.01$; I^2: 74 per cent). Overall, a statistically significant impact can be appreciated from the propranolol group only, with a beneficial trend from the venlafaxine, amitriptyline and flunarizine groups.

Propranolol

Four studies evaluated the outcome with propranolol, with 60 per cent of patients (95 per cent CI = 0.37 to 0.82; $p < 0.01$; I^2: 80 per cent) achieving complete vestibular migraine symptoms control, although there was considerable heterogeneity.[30,31,34,36]

Venlafaxine

Two studies evaluated the outcome with venlafaxine, with 48 per cent (95 per cent CI = 0.08 to 0.90; $p = 0.26$; I^2: 21 per cent) achieving vestibular migraine control.[31,36] However, these results did not reach statistically significant difference, with only one sample size contribution from Salmito *et al.* despite acceptable heterogeneity.[31,36]

Amitriptyline

Two studies evaluated the outcome with amitriptyline, with 87 per cent (95 per cent CI = 0.62 to 1.00; $p = 0.60$; I^2:0 per cent) achieving vestibular migraine control.[26,31] This analysis showed complete homogeneity of the data but did not reach a statistically significant difference and there was small sample size.[26,31]

Flunarizine

Three studies evaluated flunarizine in vestibular migraine prophylaxis.[27,31,34] Vestibular migraine control was achieved by 81 per cent of patients (95 per cent CI = 0.65 to 0.94; $p = 0.14$; I^2: 49 per cent).[27,31,34] Even though the sample size was bigger than the venlafaxine and amitriptyline groups, it failed to reach statistically significant difference despite having substantial heterogeneity.

Other prophylactic medication outcomes

Cinnarizine

Cinnarizine was explored by two studies.[29,33] Teggi *et al.* noticed improvement in the frequency of vertigo and headache following treatment, with 18 per cent and 68 per cent of patients reporting 50 per cent symptom improvement, respectively.[33] Decreases in the frequency of vertigo and headache were also seen by Taghdiri *et al.*[29] Subsequent explorative meta-analysis at the end of each study follow up (Fig. 7) showed a decrease in the frequency of vestibular migraine symptoms during the treatment (mean differences: −3.19; 95 per cent CI = −3.50 to −2.87; $p = 0.61$; I^2: 0 per cent) but this was not statistically significant for either headache (mean differences: −3.06; 95 per cent CI = −3.50 to −2.63; $p = 0.31$; I^2: 4 per cent) or vertigo (mean differences: −3.34; 95 per cent CI = −3.82 to −2.86; $p = 0.80$; $I^2 = 0$ per cent) despite homogeneity.

Valproate and valproic acid

Single agent usage of either valproate or valproic acid was explored by three studies only.[31,35,37] Liu *et al.* had the largest

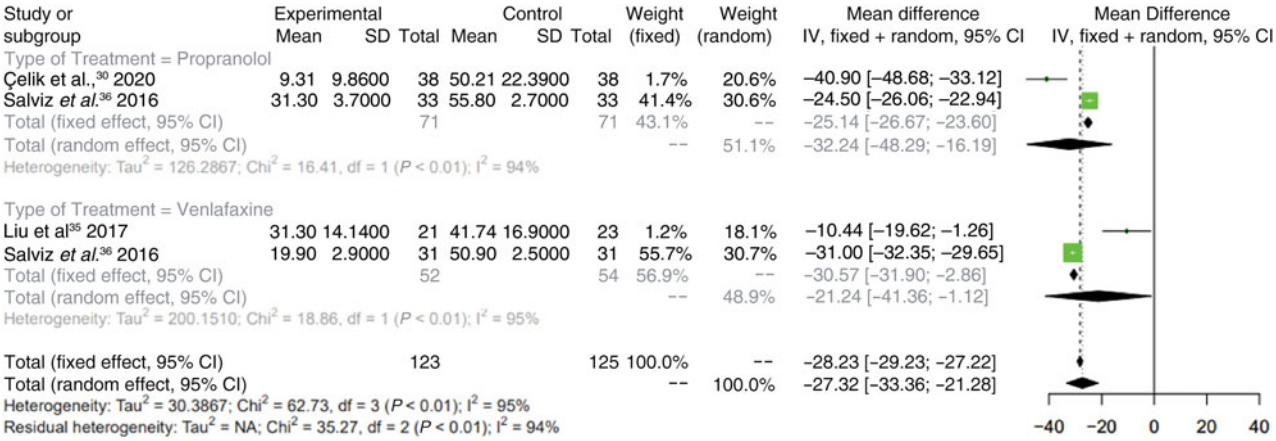

Figure 5. Forest plot showing the meta-analysis for DHI (Dizziness Handicap Inventory) mean differences. SD = standard deviation; IV = inverse variance; CI = confidence interval; NA = not available

https://doi.org/10.1017/S0022215122001979 Published online by Cambridge University Press

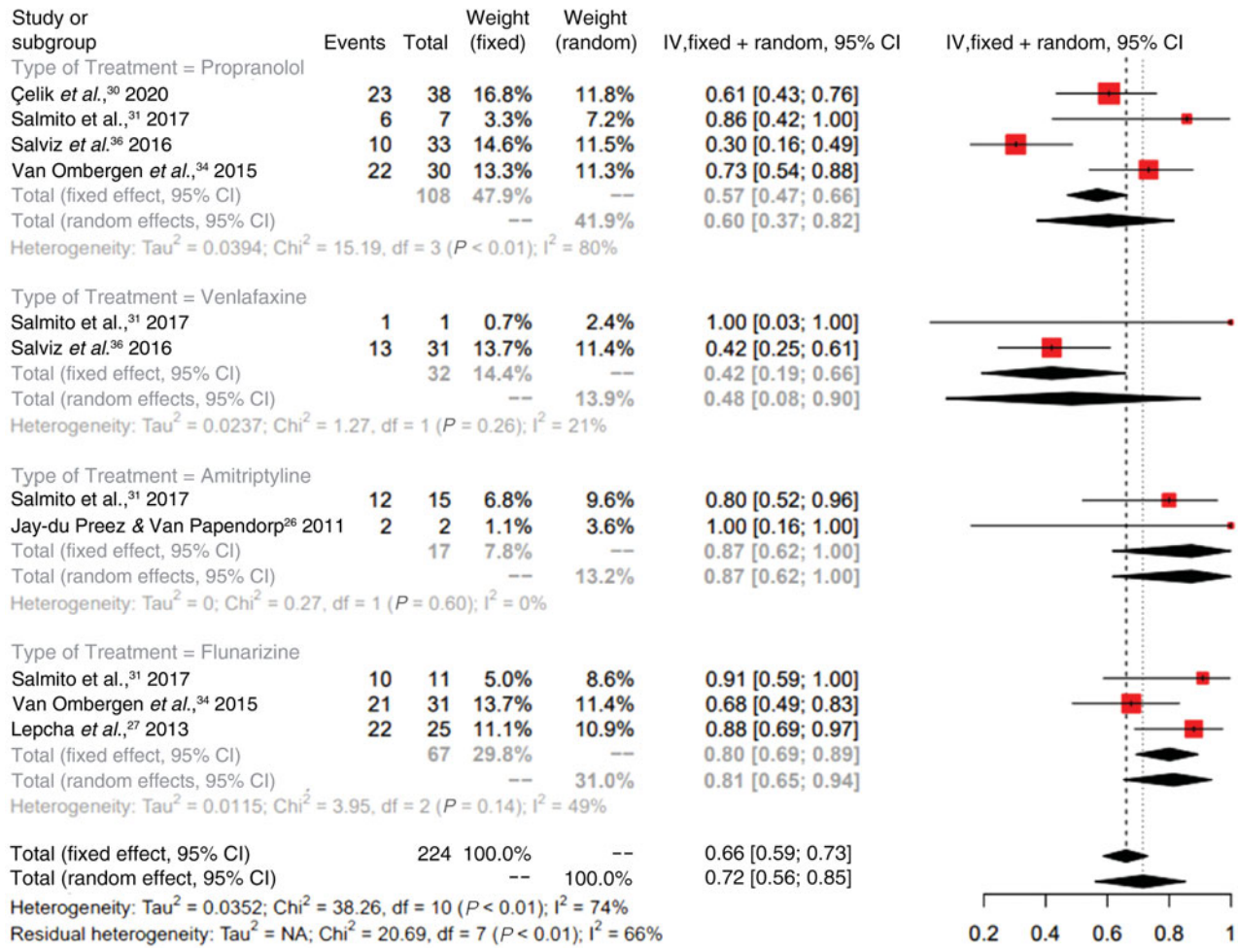

Figure 6. Forest plot showing the proportional meta-analysis of vestibular migraine with successful control. IV = inverse variance; CI = confidence interval; NA = not available

sample size ($n = 20$) and was the only study that explored Vertigo Symptom Scale (5.8 ± 1.82 *vs* 5.3 ± 1.08; $p = 0.27$) and Dizziness Handicap Inventory (46.80 ± 13.45 *vs* 38.7 ± 13.58; $p = 0.02$), which both showed a benefit of valproate or valproic acid.[35] All studies reported improvement in the frequency of attacks; however, the information disclosed was not sufficient to enable meta-analysis to be performed.[35,37]

Side effects

Side effects were not recorded in seven studies.[20,26,28,30,31,34,36] Of the six studies that recorded side effects, five discussed them in some detail, and these are summarised in Table 1.[27,29,32,33,35] Baier *et al.* only briefly mentioned side effects.[37]

Discussion

Main findings

The lack of understanding of vestibular migraine pathophysiology, coupled with the lack of specific findings on clinical examination, has led to considerable difficulties in both the diagnosis and management of this condition. However,

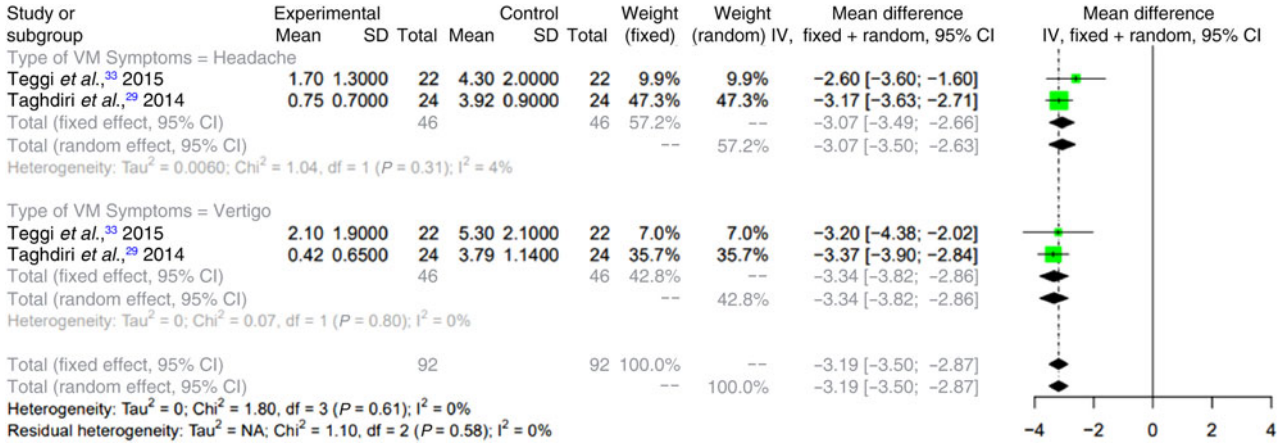

Figure 7. Forest plot showing the meta-analysis for the mean differences in headache and vertigo for vestibular migraine. SD = standard deviation; IV = inverse variance; CI = confidence interval; NA = not available

https://doi.org/10.1017/S0022215122001979 Published online by Cambridge University Press

Table 1. Reported medication side effects

Study	Medication	Side effects
Liu *et al.*,[35] 2017	Flunarizine	Somnolence; nausea
	Venlafaxine	Nausea; insomnia; palpitation; lethargy
	Valproic acid	Nausea; somnolence; indigestion
Çelebisoy *et al.*,[32] 2016	Acetazolamide	Paraesthesia; change in taste; fatigue; nausea
Teggi *et al.*,[33] 2015	Cinnarizine	Drowsiness with or without dry mouth; gastrointestinal irritation; weight gain
Taghdiri *et al.*,[29] 2014	Cinnarizine	Weight gain; blurred vision; somnolence
Lepcha *et al.*,[27] 2014	Flunarizine	Somnolence; weight gain; acne and weight gain

increasing awareness of the problem means that the need for effective management strategies is coming to the attention of clinicians. The restrictions associated with this poor understanding means that the principles of management have been 'borrowed' from that of classical migraine. Although there is some evidence that these treatments are effective, it does not negate the need for specific, evidence-based treatments targeted at vestibular migraine.

Based on our meta-analysis (Figs. 4, 5 and 6), we would recommend propranolol as the first-line prophylactic treatment because its impact on vestibular migraine symptoms control has been explored using both validated patient-reported outcome measures and subjective measures, which have showed statistically significant impact. However, both studies that assessed subjective measures (Table 2) used a different dosing regimen; thus, we are not able to conclude which one is the best, although the importance of titration is emphasised.[30,36]

Venlafaxine has shown some promising impact on vestibular migraine symptoms control based on patient-reported outcome measures (Figs. 4 and 5) without reaching the level of statistical significance in our meta-analysis. Subjective vestibular migraine symptoms control evaluation also did not show any substantial and meaningful improvement from either venlafaxine or amitriptyline (Fig. 6). Venlafaxine, with a better side effect profile when comparing it against amitriptyline, should be considered as the second-line prophylactic treatment for vestibular migraine (Table 2).[35,36,38]

What has become apparent from exploring the pathophysiology of vestibular migraine is the overlap with anxiety and depression.[39,40] Anxiety and depression should also be considered as potential confounding factors when deciding on appropriate treatment and assessing treatment response. Whether this represents a shared pathophysiological pathway, suggests a somatic element to vestibular migraine or a combination of both is unknown. The effect of diet and lifestyle needs to be considered as well as any co-existing anxiety or depression. This link can also be seen in the aetiology of classical migraine. Consequently, the importance of holistic management, including the potential for psychological interventions, should always be considered when assessing therapeutic options for vestibular migraine. However, assessing lifestyle changes was not the purpose of the present work. We believe that it would be valuable to assess not only the significance of lifestyle modifications on the control of vestibular migraine but also the role of vestibular rehabilitation.

A recent meta-analysis by Byun *et al.* was unable to determine a preferred treatment for vestibular migraines because of the lack of standardised reporting of outcomes as well as heterogenicity of the studies.[41] While the aim of their meta-analysis was the same as ours and we encountered similar limitations, there are several differences that may account for the different outcomes. First, they included non-pharmacological treatment in the form of vestibular rehabilitation, whereas we limited our analysis to purely pharmacological interventions. Second, the outcomes reported also differed. Instead of just Dizziness Handicap Inventory, we also included the Vertigo Symptom Scale. Our event rate of success was defined as the proportion of patients who have complete symptomatic control based on the selected studies rather than vertigo frequency, or more than 50 per cent reduction in subjective symptoms. This improved the number of studies eligible for the meta-analysis to 11 when compared with the 6 (vertigo frequency) and 7 (symptom improvement) studies used in Byun *et al.*[41] Lastly, our approach to data extraction and analysis may also have contributed to the different conclusions. We also chose to discuss the pros and cons of medications included in this analysis, making our review unique.

Pros and cons of medication

The evidence in this review points to propranolol being used as first-line therapy. The advantages of this medication include beneficial scores obtained from Dizziness Handicap Inventory and Vertigo Symptom Scale, with significant numbers of patients obtaining successful complete vestibular migraine symptoms control (Figs. 4, 5 and 6). As it is an established drug, its safety profile is well documented. However, it needs to be used with caution in patients with a history of cardiac pathology or on anti-hypertensive medication, or in those with asthma or another obstructive airway disease.

Table 2. Propranolol and venlafaxine vestibular migraine prophylactic regimen

Regimen	Study	Starting dose	Titration
Propranolol	Çelik *et al.*,[30] 2020	20 mg twice a day	Titration after 1 month: ≤60 kg, 40 mg twice a day; >60 kg, 60 mg twice a day
	Salviz *et al.*,[36] 2016	40 mg once a day	Titration after 1 week: 40 mg twice a day up to a maximum of 160 mg a day
Venlafaxine	Liu *et al.*,[35] 2017	25 mg at night	Titration after 6 days: 37.5 mg a day
	Salviz *et al.*,[36] 2016	37.5 mg at night	Titration after 2 weeks: 75 mg at night for 2 weeks up to a maximum of 150 mg a day

https://doi.org/10.1017/S0022215122001979 Published online by Cambridge University Press

Patients treated with venlafaxine also improved (Figs. 4, 5 and 6). However, given the small numbers of patients included in the studies, it was not possible to draw any statistically significant conclusions, and we therefore believe that it should be used as a second-line therapy. The fact that it can also be used to treat any anxiety or depression is advantageous. It should, however, be used with caution in patients with known epilepsy or bleeding disorders, and it is high risk for causing cardiac arrhythmias, heart disease and diabetes.

Amitriptyline is commonly used to treat neuropathic pain and migraine, both classical and vestibular. However, no statistically significant differences were seen (Fig. 6) despite the homogeneity of the studies. Unlike venlafaxine, it should not be used in patients with a history of significant mental health problems. It is also contraindicated in pregnancy and should be used with caution in patients with cardiac, liver or renal co-morbidities as well as those with diabetes and glaucoma. It has been shown to increase seizure activity in patients with epilepsy.

Flunarizine also failed to reach a statistical significance on successful vestibular migraine symptoms control rate despite a larger sample size than for venlafaxine and amitriptyline. Like amitriptyline, it is contraindicated in patients with depression. Because of the risk of extra-pyramidal side effects, it could be used with caution in older patients and with those known to have extra-pyramidal disorders, such as Parkinson's disease. Meanwhile, cinnarizine has been shown to be beneficial at decreasing the frequency of headache and vertigo in vestibular migraine based on individual studies,[29,33] but it failed to show significant impact on meta-analysis (Fig. 7).

Limitations

The heterogeneity of the studies demonstrated in this review, both in terms of study design, level of bias and also in terms of the therapeutic regimen means that it is difficult to reach a statistically sound conclusion. However, we felt that meta-analysis exploration of the current evidence was needed to pave the way for better future study design. Thus, caution should be applied when interpreting the meta-analysis here (Figs. 4, 5, 6, 7).

Further heterogeneity is introduced by the fact that a variety of outcome measures were used. This ranged from the use of validated questionnaires, such as Dizziness Handicap Inventory and Vertigo Symptom Scale, to patient-reported reduction in severity, duration and frequency of vertigo attacks. Several studies used a combination of outcome measures. One of the included studies did not even specify what outcome measure was used.[26] Although it is positive that there is now an accepted definition of vestibular migraine through both the International Headache Society and Bárány Society, there is still a large range of alternative terms used to describe vestibular migraine. This has the potential to create ambiguity in the literature and contribute to the difficulty in ascertaining the true effect of various treatments.

Vertigo Symptom Scale and Dizziness Handicap Inventory have been shown to give similarly sound scores when it comes to patient-reported outcome measures; thus, they have been used in the literature to assess how patients perceive their vertigo severity. If we accept that both scales assess the severity of symptoms equally well, then despite the heterogeneity in the dizziness severity assessment methods among studies, propranolol appears to be the best first-line prophylactic treatment (Figs. 4 and 5).

Another potential confounding factor is the use of lifestyle factors or changes as a potential management technique. Several of the studies included in this systematic review included lifestyle changes as an intervention.[33,37] However, these changes in lifestyle modifications are frequently poorly described and, unlike a pharmaceutical intervention, it is extremely difficult to regulate the degree of compliance and replicability in the other studies. In addition, what is meant by 'conservative management' is also poorly defined. This has an understandable knock-on effect to the overall results. What is more, it is almost impossible to standardise the lifestyle changes themselves. Collectively this means that careful thought and planning needs to occur for any study that includes lifestyle changes as a therapeutic option, and results should be interpreted with caution. If vestibular rehabilitation exercises are to be included in any treatment plan, this also needs to be clearly defined and documented as accurately as possible.

Although vestibular migraine may be frustratingly vague in its aetiology and presentation, we feel that it is important that future research continues to explore its management. Although it is positive that several therapeutic interventions show promise in managing vestibular migraines, there ultimately needs to be robust prospective RCTs assessing these options. These should assess the effect of non-pharmaceutical interventions, such as lifestyle, diet and vestibular rehabilitation, alongside the more traditional medical management used in classical migraine. We believe reaching a consensus on the best outcome measure for response to treatment would be fundamental to this.

Conclusion

Based on the available evidence so far, propranolol, if not contraindicated, should be offered as the first-line treatment followed by venlafaxine for the prophylactic treatment of vestibular migraine. Although amitriptyline, flunarizine and cinnarizine showed a trend for symptoms improvement, we were unable to identify any statistically significant differences. However, patient factors, such as co-morbidities and current medication, and a clinician's familiarity with the medication and the relevant side effects should always be taken into account.

Acknowledgements. The authors would like to thank the library services at Greater Glasgow and Clyde NHS Trust for their help with the literature search.

Competing interests. None declared.

References

1 Eggers SD. Migraine-related vertigo: diagnosis and treatment. *Curr Pain Headache Rep* 2007;**11**:217–26
2 Kroenke K, Price RK. Symptoms in the community. Prevalence, classification, and psychiatric comorbidity. *Arch Intern Med* 1993;**153**:2474–80
3 Neuhauser H, Leopold M, von Brevern M, Arnold G, Lempert T. The interrelations of migraine, vertigo, and migrainous vertigo. *Neurology* 2001;**56**:436–41
4 Neuhauser HK, von Brevern M, Radtke A, Lezius F, Feldmann M, Ziese T *et al.* Epidemiology of vestibular vertigo: a neurotologic survey of the general population. *Neurology* 2005;**65**:898–904
5 Neuhauser HK, Radtke A, von Brevern M, Feldmann M, Lezius F, Ziese T *et al.* Migrainous vertigo: prevalence and impact on quality of life. *Neurology* 2006;**67**:1028–33
6 Sohn JH. Recent advances in the understanding of vestibular migraine. *Behav Neurol* 2016:1801845

https://doi.org/10.1017/S0022215122001979 Published online by Cambridge University Press

7 Geser R, Straumann D. Referral and final diagnoses of patients assessed in an academic vertigo center. *Front Neurol* 2012;**3**:169
8 Cass SP, Furman JM, Ankerstjerne K, Balaban C, Yetiser S, Aydogan B. Migraine-related vestibulopathy. *Ann Otol Rhinol Laryngol* 1997;**106**:182–9
9 Baloh RW, Jen JC. Genetics of familial episodic vertigo and ataxia. *Ann N Y Acad Sci* 2002;**956**:338–45
10 Cutrer FM, Baloh RW. Migraine-associated dizziness. *Headache* 1992;**32**:300–4
11 Johnson GD. Medical management of migraine-related dizziness and vertigo. *Laryngoscope* 1998;**108**:1–28
12 Dodick DW. Migraine. *Lancet* 2018;**391**:1315–30
13 Kontorinis G, Tyagi A. Potential association between recurrent facial nerve palsy and migraines. *J Laryngol Otol* 2020;**134**:1–4
14 von Brevern M, Zeise D, Neuhauser H, Clarke AH, Lempert T. Acute migrainous vertigo: clinical and oculographic findings. *Brain* 2005;**128**:365–74
15 Teggi R, Colombo B, Bernasconi L, Bellini C, Comi G, Bussi M. Migrainous vertigo: results of caloric testing and stabilometric findings. *Headache* 2009;**49**:435–44
16 Lempert T, Olesen J, Furman J, Waterston J, Seemungal B, Carey J *et al.* Vestibular migraine: diagnostic criteria. *J Vestib Res* 2012;**22**:167–72
17 Lee SH, Jeong SH, Kim JS, Kim HJ, Choi KD, Choi JH *et al.* Effect of prophylactic medication on associated dizziness and motion sickness in migraine. *Otol Neurotol* 2018;**39**:e45–51
18 Linde M, Mulleners WM, Chronicle EP, McCrory DC. Gabapentin or pregabalin for the prophylaxis of episodic migraine in adults. *Cochrane Database Syst Rev* **2013**;(6):Cd010609
19 Maione A. Migraine-related vertigo: diagnostic criteria and prophylactic treatment. *Laryngoscope* 2006;**116**:1782–6
20 Bisdorff A. Management of vestibular migraine. *Ther Adv Neurol Disord* 2011;**4**:183–91
21 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;**6**:e1000097
22 Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I *et al.* RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:l4898
23 Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M *et al.* ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;**355**:i4919
24 Harrer M, Cuijpers P, Furukawa TA, *Ebert DD. Doing meta-analysis in R: a hands-on guide*. Erlangen: Protect Lab, 2019
25 Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Health* 2019;**22**:153–60
26 Jay-du Preez T, Van Papendorp D. Migraine-associated vertigo and dizziness as presenting complaint in a private general medical practice. *South African Family Practice* 2011;**53**:165–9
27 Lepcha A, Amalanathan S, Augustine AM, Tyagi AK, Balraj A. Flunarizine in the prophylaxis of migrainous vertigo: a randomized controlled trial. *Eur Arch Otorhinolaryngol* 2014;**271**:2931–6
28 Iwasaki S, Ushio M, Chihara Y, Ito K, Sugasawa K, Murofushi T. Migraine-associated vertigo: clinical characteristics of Japanese patients and effect of lomerizine, a calcium channel antagonist. *Acta Otolaryngol Suppl* 2007:45–9
29 Taghdiri F, Togha M, Razeghi Jahromi S, Refaeian F. Cinnarizine for the prophylaxis of migraine associated vertigo: a retrospective study. *Springerplus* 2014;**3**:231
30 Çelik O, Tanyeri Toker G, Eskiizmir G, İncesulu A, Şahin Süyür N. The effectiveness of medical prophylactic treatment on vestibular migraine and its effect on the quality of life. *J Int Adv Otol* 2020;**16**:28–33
31 Salmito MC, Duarte JA, Morganti LOG, Brandão PVC, Nakao BH, Villa TR *et al.* Prophylactic treatment of vestibular migraine. *Braz J Otorhinolaryngol* 2017;**83**:404–10
32 Çelebisoy N, Gökçay F, Karahan C, Bilgen C, Kirazlı T, Karapolat H *et al.* Acetazolamide in vestibular migraine prophylaxis: a retrospective study. *Eur Arch Otorhinolaryngol* 2016;**273**:2947–51
33 Teggi R, Colombo B, Gatti O, Comi G, Bussi M. Fixed combination of cinnarizine and dimenhydrinate in the prophylactic therapy of vestibular migraine: an observational study. *Neurol Sci* 2015;**36**:1869–73
34 Van Ombergen A, Van Rompaey V, Van de Heyning P, Wuyts F. Vestibular migraine in an otolaryngology clinic: prevalence, associated symptoms, and prophylactic medication effectiveness. *Otol Neurotol* 2015;**36**:133–8
35 Liu F, Ma T, Che X, Wang Q, Yu S. The efficacy of venlafaxine, flunarizine, and valproic acid in the prophylaxis of vestibular migraine. *Front Neurol* 2017;**8**:524
36 Salviz M, Yuce T, Acar H, Karatas A, Acikalin RM. Propranolol and venlafaxine for vestibular migraine prophylaxis: a randomized controlled trial. *Laryngoscope* 2016;**126**:169–74
37 Baier B, Winkenwerder E, Dieterich M. "Vestibular migraine": effects of prophylactic therapy with various drugs. A retrospective study. *J Neurol* 2009;**256**:436–42
38 Sauer H, Huppertz-Helmhold S, Dierkes W. Efficacy and safety of venlafaxine ER vs. amitriptyline ER in patients with major depression of moderate severity. *Pharmacopsychiatry* 2003;**36**:169–75
39 Yuan Q, Yu L, Shi D, Ke X, Zhang H. Anxiety and depression among patients with different types of vestibular peripheral vertigo. *Medicine* (*Baltimore*) 2015;**94**:e453
40 Formeister EJ, Rizk HG, Kohn MA, Sharon JD. The epidemiology of vestibular migraine: a population-based survey study. *Otol Neurotol* 2018;**39**:1037–44
41 Byun YJ, Levy DA, Nguyen SA, Brennan E, Rizk HG. Treatment of vestibular migraine: a systematic review and meta-analysis. *Laryngoscope* 2021;**131**:186–94

https://doi.org/10.1017/S0022215122001979 Published online by Cambridge University Press