Evidence Based Treatment of Vestibular Migraine 2020

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This simple summary with supporting links is intended to make proven treatment options available to clinicians who treat Vestibular Migraine. Most vestibular migraine treatment mirrors treatment of chronic migraine headache. Listed here are the agents with usefulness in Vestibular Migraine documented in published studies. Some useful medications are listed that are helpful and proven in migraine headache treatment but await published studies regarding effectiveness for vertigo prevention in VM.

Diet/Caffeine Cessation

16% response at 6 weeks

Mikulec AA, et al., Am J Otolaryngol. 2011 Jun.

Abortive Medications

1. Almotriptan (Axert)12.5mg 18pts, 55% complete, 28% had 50% reduction
   Cassano D, Pizza V, Busillo V. P074. Almotriptan in the acute treatment of vestibular migraine: a retrospective study. J Headache Pain. 2015;16(Suppl 1):A114.
2. Sumatriptan (Imitrex) 53pts Efficacy for HA4, for vertigo 3(1-4)
   Maione A. Migraine-related vertigo: diagnostic criteria and prophylactic treatment. Laryngoscope. 2006;116(10):1782–6.
3. Prednisone 50mg/d- no studies
4. Promethazine 25mg- no studies

Abortive Neuromodulation Treatments(devices)

Cefaly device- 19/19 patients reported improvement in vertigo severity with 20m eTNS. 61% improvement in vertigo/ 77%improvement in headache.

Beh SC External trigeminal nerve stimulation: Potential rescue treatment for acute vestibular migraine. J Neurol Sci. 2019 Oct 25;408

Non-invasive vagus nerve stimulation- 18 pts. 47% reduction in vertigo severity/ 63% reduction in headache

Shin C. Beh, Deborah I. Friedman Acute vestibular migraine treatment with noninvasive vagus nerve stimulation Neurology Oct 2019, 93 (18) e1715-e1719

Preventive Medications

1. Amitriptyline 25-50mg daily, Significant improvement in 77% taking 25 mg daily, 100% taking 50 mg daily
   Salmito MC, et al. Prophylactic treatment of vestibular migraine. Braz J Otorhinolaryngol. 2017;83(4):404-10.
2. Nortriptyline 25-75mg daily: 46% response
   Mikulec AA, et al., Am J Otolaryngol. 2011 Jun.

3. Propranolol 40 mg daily titrating up to a maximum of 160 mg,-vertigo decreased 12.6/mo to 1.9
-severity 7.3 decreased to 2.1

Salviz, M et al, Propranolol and Venlafaxine for Vestibular Migraine Prophylaxis: A Randomized Controlled Trial, Laryngoscope 2016 Jan;126(1):169-74.

Propranolol (average dose 80 mg), 73% improvement

Van Ombergen A, et al. Vestibular migraine in an otolaryngology clinic: prevalence, associated symptoms, and prophylactic medication effectiveness. Otol Neurotol. 2015;36(1):133–8.

Propranolol 38 pts. 40-60mgbid. DHI before and after treatment were 50.21±22.39 (range: 8-92) and 9.31±9.86 (range: 0-58)

Çelik O et al. The Effectiveness of Medical Prophylactic Treatment on Vestibular migraine and Its Effect on the Quality Of Life. J Int Adv Otol. 2019 Jul 26. doi: 10.5152/iao.2019.6522.

Metoprolol 95mg/d 130 pts Randomized Placebo Controlled Study- No benefit over placebo

Bayer O Results and lessons learnt from a randomized controlled trial: prophylactic treatment of vestibular migraine with metoprolol (PROVEMIG). Trials. 2019 Dec 30;20(1):813. doi: 10.1186/s13063-019-3903-5.

4. Topiramate 25 or 50 mg twice daily, vertigo attacks decreased from 5.5 to 1/mo, severity dec by 75% headache decreased from 4 to 1/mo, severity decreased by 50%

Gode S, et al. Clinical assessment of topiramate therapy in patients with migrainous vertigo. Headache. 2010;50(1):77–84.

Topiramate 25-50mg BID 25% response

Mikulec AA, et al., Am J Otolaryngol. 2011 Jun.

Topiramate 50mg BID- improved tinnitus, mild HL in 10/10 VM pts

Carmona S, Settecase N. Use of topiramate (topamax) in a subgroup of migraine-vertigo patients with auditory symptoms. Ann N Y Acad Sci. 2005;1039:517–20.

5. Venlafaxine 37.5 mg daily titrated up to a maximum of 150 mg
-vertigo decreased 12.2 to 2.6/mo, severity decreased 7.9 to 1.8

Salviz, M et al, Propranolol and Venlafaxine for Vestibular Migraine Prophylaxis: A Randomized Controlled Trial, Laryngoscope 2016 Jan;126(1):169-74.

6. Acetazolamide 250mg BID, vertigo decreased 3.9 to 1.4/mo, headache decreased 4.31 to 2.85.

Celebisoy N, et al. Acetazolamide in vestibular migraine prophylaxis: a retrospective study. Eur Arch Otorhinolaryngol. 2016;273(10):2947–51.

7. Lamotrigine 100 mg daily, (Na+ blocker, mood stabilizer)vertigo decreased 18.1 to 5.4/mo.
26% complete response

Bisdorff AR. Treatment of migraine related vertigo with lamotrigine an observational study. Bull Soc Sci Med Grand Duche Luxemb. 2004;2:103–8.

8. Cinnarizine (not available in USA)(Ca++ channel blocker) 37.5 mg for 3 days then increased to 75 mg
HA frequency decreased 3.9 to 0.75/mo, duration dec 24 to 3 h, intensity dec 8 to 1/10
Vertigo decreased from 3.8 to 0.4/mo

Taghdiri F, et al. Cinnarizine for the prophylaxis of migraine associated vertigo: a retrospective study. Spring. 2014;3:231.

Cinnarizine effective and tolerated in adolescents-20 subjects 15-19. VAS dizziness improved from 7.2-2.6 and headache frequency dropped from 20d/mo to 5.75.

Choi Yun-Ju; Lee Seung-Han Effect of Cinnarizine For the Prophylaxis of Vestibular Migraine In Adolescents (abstract)

9.Flunarizine (not available in USA)(Ca++ channel blocker) 10 mg + betahistine 16 mg tid, 64% decreased vertigo, 61% decreased vertigo severity

No change in headache

Lepcha A, et al. Flunarizine in the prophylaxis of migrainous vertigo: a randomized controlled trial. Eur Arch Otorhinolaryngol. 2014;271(11):2931–6.

Flunarizine 10 mg, 68% reported improvement in vestibular symptoms

Van Ombergen A, et al. Vestibular migraine in an otolaryngology clinic: prevalence, associated symptoms, and prophylactic medication effectiveness. Otol Neurotol. 2015;36(1):133–8.

Flunarizine 10 mg, 9/10 sig improvement

Salmito MC, et al. Prophylactic treatment of vestibular migraine. Braz J Otorhinolaryngol. 2017;83(4):404-10.

10. Diltiazem(Ca++ channel blocker) 120mg daily- no studies
11. Verapamil – modest reductions in HA and vertigo frequency and severity in 11 of 17 pts with MV and MD on very low dose verapamil(40mg bid)

Kaya I, Can verapamil be effective in controlling vertigo and headache attacks in vestibular migraine accompanied with Meniere's disease? A preliminary study.J Neurol. 2019 Sep;266(Suppl 1):62-64. doi: 10.1007/s00415-019-09309-w. Epub 2019 Apr 15.

Vestibular Rehabilitation

Mixed results in 6 studies: tendency to improvement. None with controls. Many patients had other diagnoses, Many patients cannot tolerate PT- "Dose" of therapy is important. May help if concurrent BPPV, unilateral weakness.

Alghadir A, Anwer S. The Effects of Vestibular Rehabilitation in the Management of a Vestibular Migraine: A Review. Frontiers in Neurology. 2018;9:article 440

Rationale for use of agents for treatment of VM and needed areas of study

There are still no placebo controlled studies in this area.

GABA enhancers γ-Aminobutyric acid (GABA) is considered to be the major inhibitory neurotransmitter in the brain. Loss of GABA inhibition has been clearly implicated in epileptogenesis but may also play a role in VM as GABAergic projections from the cerebellum to the vestibular nuclei inhibit activity.

-Benzodiazepines are GABA modulators, act centrally to suppress vestibular responses. Gain is decreased and time constant increased.

- Gabapentin, cyclic analogue of GABA, enhances GABA synthesis and decreases neuronal calcium influx via a specific subunit of voltage-dependent calcium channels.
- Topiramate acts, via an action on a novel site of the $GABA_A$ receptor. It is also a sodium channel blocker.
- Tiagabine elevates synaptic GABA levels by inhibiting the GABA uptake transporter, GAT1, and preventing the uptake of GABA into neurons and glia. NO data in VM
- 4-Aminopyridine. Aminopyridines augment GABA release by cerebellar Purkinje cells by a primary action on potassium channels. Useful for many cerebellar disorders and well tolerated. NO data in VM.
- Acetazolamide, augments GABAergic neuronal activity, may change the excitability of neurons by a pH shift towards acidification.

- Valproic acid, increases brain GABA levels and may suppress migraine-related events in the cortex, perivascular parasympathetics or trigeminal nucleus caudalis.

CGRP ligand/receptor binders Calcitonin gene-related peptide (CGRP) receptor blockers. CGRP plays an important role in cerebral autoregulation. In migraine CGRP activates vanilloid receptors and is responsible for vasoactive inflammatory neuropeptide release from unmyelinated c-fibers. Migraine-related sensitization of the trigeminal nuclei affects the sensitivity of structures that receive trigeminal nuclear projections. Blocking CGRP may decrease activity of projections to the vestibular nuclei and prevent vestibular sensitization in migraine patients. 2 classes:

Monoclonal antibodies Do not enter cells or cross BBB
- erenumab NO data
- fremanezumab NO data
- galcanezumab NO data

Small molecules May enter cells and cross BBB

Release for clinical use expected 2020-21

Beta-Blockers While beta blockers block sympathetic/adrenergic-induced vasoconstriction their beneficial effects in migraine headache prophylaxis are unclear. Studies show stabilization of the CNS with restoration of habituation to light stimuli at the occipital cortex. Exact mechanisms and sites of activity are unknown. They can be quick acting in migraine as evidenced by reports of timolol eye drop effectively aborting migraine headache. Long used in migraine headache prophylaxis, and used to treat VM there is one RCT documenting efficacy in VM.

Calcium Channel Blockers Voltage-dependent Ca2+ channels are integral membrane proteins that permit extracellular Ca2+ to enter cells down their electrical and concentration gradients and have a universal role in stimulus-response coupling in excitable cells. Calcium channel blockers reduce channel opening in response to membrane depolarization in neurons thereby stabilizing neural tissues and can also decrease vasoconstriction by decreasing calcium influx into muscle cells. There is ample evidence supporting the use of Ca2+ blocking agents in migraine headache prophylaxis.

Anticonvulsants The mechanisms of these drugs in migraine are not well understood. It is thought that anticonvulsants act on voltage- and receptor-gated sodium ion channels promoting stabilization of neuronal membranes and preventing repetitive firing. They are thereby able to block excitation leading to cortical spreading depression that may be a central precipitator in migraine. These agents have variable GABA enhancing effects as well.

Tricyclic Antidepressants Long used in migraine headache these have many potentially beneficial effects. They are medium potency sodium and calcium channel blockers so stabilize membranes and can prevent cortical depression, are anticholinergic so suppress vestibular function and dysautonomia associated with increased parasympathetic outflow common in migraine, and are serotonin and norepinephrine reuptake inhibitors. Varying populations of serotonin receptors are found in the trigeminal nucleus, vestibular nuclei, inner ear and in serotonergic pathways from the dorsal raphe nucleus to the vestibular nuclei.