Chapter 14
Medical Management of Meniere's Disease

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Introduction

Meniere's disease refers to the clinical syndrome of fluctuating sensorineural hearing loss, tinnitus, aural pressure, and episodic vertigo [1]. While the principle underlying pathological finding in Meniere's disease is endolymphatic hydrops, the cause of endolymphatic hydrops and the mechanisms of hearing loss and episodes of vertigo remain unknown. The acute vertiginous attack characteristic of Meniere's disease is severe and incapacitating, lasting 20 min to several hours. Because no permanent changes initially occur in the function of the vestibular neuroepithelium and vestibular nerve, in-between the acute episodes of vertigo, most people feel their balance is normal. Recurrent episodes of vertigo occur with highly variable frequency. There may be days, weeks, or years between attacks. Overtime there is a tendency for the sensorineural hearing loss to become fixed and no longer fluctuate back to normal. Tinnitus and aural fullness often become permanent and vestibular hypofunction ensues.

Meniere's disease most often presents as a unilateral disorder, but the contralateral ear can also become involved (bilateral Meniere's disease). The exact incidence of bilateral Meniere's disease is unknown, but a reasonable estimate is that about 20% of patients with unilateral Meniere's disease will eventually have bilateral involvement within 5 years [2].

As the exact cause of Meniere's disease has yet to be elucidated, there are no definitive curative therapies available. Medical treatment is available however and is aimed at (1) treating endolymphatic hydrops and managing possible Meniere's disease cofactors, (2) reducing symptoms associated with acute vertigo, and (3) in cases of persistent disabling vertigo, reducing vestibular function in the affected ear (vestibular function ablation).

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Treating Endolymphatic Hydrops and Managing Meniere's Disease Cofactors

It is widely accepted that a structural inner ear abnormality, endolymphatic hydrops (excess endolymph within the scala media), is a necessary but not sufficient condition leading to the symptoms of Meniere's disease. Since it has been shown that endolymphatic hydrops can exist without ever producing symptoms of Meniere's disease, it is believed that endolymphatic hydrops alone is not sufficient to cause Meniere's disease. There must be an additional factor(s) combining with endolymphatic hydrops to give rise to the symptomatic disease [3]. Therefore, medical treatment can be directed at both the formation of endolymphatic hydrops itself and possible cofactors that "activate" the disease.

Commonly accepted treatments for endolymphatic hydrops include a low-salt diet and diuretic therapy (discussed further below). Potential Meniere's disease cofactors include chronic cerebrovascular disease, episodes of reduced blood flow, and/or activation of the inflammatory processes within the inner ear. Possible contributors to these cofactors include migraine, sleep apnea, hypertension, atherosclerosis, autoimmune disease, immunologic dysfunction, and food and environmental intolerances and allergy. A primary goal of medical treatment should be identifying and treating these underlying conditions. This requires a team approach that includes primary care providers and medical specialists who can help to ensure optimal assessment and management of cardiovascular risk factors and any immunologic abnormalities.

Lifestyle Changes

Some triggers of Meniere's attacks include caffeine, chocolate, stress, visual stimuli, and dropping barometric pressure. Trigger avoidance is recommended through dietary modifications with strong recommendation for low-salt (daily sodium less than 1500 mg) diet, limiting stimulants including caffeine, and regular sleep cycle with adequate sleep [4]. Food intolerances should be considered, and a trial of elimination diets can be beneficial. Food and environmental allergies can be investigated and treated.

Diuretic Therapy

It is well accepted that excess endolymph within the scala media plays a major role in the development in Meniere's disease. Consequently, initial treatment is aimed at reducing excess fluid by means of a diuretic and a low-sodium diet. Medical therapy directed at the underlying endolymphatic hydrops carries the potential advantage of

affecting the level of sensorineural hearing, tinnitus, fullness, as well as recurrent vertigo. Furstenberg (1934) popularized the notion that endolymphatic hydrops could be modified by controlling sodium and water metabolism and recommended inducing a general dehydration of the extracellular fluid space using a regimen of a low-salt diet and diuretic [5]. In 1941, Furstenberg and colleagues reported on the results of 35 patients with Meniere's disease treated with a low-salt diet and diuretic [6]. Satisfactory control of vertigo was reported in 83% of patients, while hearing loss stabilized in 65% but worsened in 26%. In a subsequent report of 125 patients treated with the Furstenberg regimen, good to excellent relief of vertigo was reported in 86% of severe, 94% of moderate, and 100% of mild cases of Meniere's disease. Hearing loss in these patients appeared to stabilize within the first 5 years of disease in the moderate to severe range of pure tone and speech audiometry [7].

Klockhoff and Lindblom (1967) also studied the effect of diuretic therapy in patients with Meniere's disease [8]. In the first 20 patients studied, patients with advanced disease (non-fluctuating sensorineural hearing loss) demonstrated no distinct improvement. But in all patients with fluctuating hearing loss, variable improvement of symptoms was noted. To answer the question whether the use of a diuretic truly had a positive effect or whether the improvements simply reflected the spontaneous course of the disease, Klockhoff and Lindblom selected an additional 30 patients with Meniere's disease and fluctuating hearing loss and studied them in a double-blind fashion using a diuretic and placebo. A significant positive effect during diuretic treatment was noted for hearing loss and vertigo, and no effect was found during use of a placebo. From this study, Klockhoff and Lindblom concluded that diuretics have a positive effect on vertigo and hearing loss but that the effect was partial, in that worsening of symptoms can still occur during treatment and longer follow-up of the study group suggested that hearing loss progressed in many patients while the severity of vertigo subsided.

In a study of 192 patients with Meniere's disease, Corvera and Corvera (I989) substantiated the clinical experience of Klockhoff and Lindblom [9]. They found that while diuretics are useful in managing vertigo and fluctuating hearing loss in the early stages of Meniere's disease, they have no effect on preventing the long-term deterioration of hearing.

A recent meta-analysis published in 2016 concluded that multiple low-level evidence studies support potential benefit of diuretic therapy in the medical management of Meniere's disease [10]. Improvement in frequency of vertigo was most often reported, but improvement in hearing outcomes was less often reported. Overall, however, there are insufficient high-quality studies to clearly support the efficacy of diuretics in Meniere's disease [11]. It is our view that until a definitive study can be performed, diuretic therapy provides, at a minimum, a safe and inexpensive opportunity for patients to exert control over the disease, thereby enhancing non-specific treatment effects.

The thiazide diuretic hydrochlorothiazide combined with the potassium-sparing diuretic triamterene is the most widely used diuretic in Meniere's disease given low cost and relatively low side effect profile. It should be avoided in patients on lithium therapy or those with sulfonamide allergies. It should be avoided or used cautiously

in patients with hypotension, renal disease, diabetes mellitus, and gout. Standard dosing is 25 mg–37.5 mg. For acute flare-ups, the dose can be doubled temporarily until symptoms are under control.

Other commonly used alternatives to triamterene-hydrochlorothiazide include acetazolamide and spironolactone. We often use acetazolamide for patients with Meniere's disease who have underlying migraines and in patients with bilateral Meniere's disease. The rationale behind this is that acetazolamide is not only a diuretic, but it also causes cerebral vasodilation and carbonic anhydrase inhibition. Both of these mechanisms are thought to play an important role in migraine prophylaxis. It should also be avoided in patients with sulfonamide allergies. Typical side effects include paresthesia and increased risk for kidney stones. Spironolactone can be safely used in patients with a sulfonamide allergy. Loop diuretics such as furosemide can also be used but require close monitoring of serum sodium and potassium levels from the start of therapy and renal function if used long term.

Betahistine

Betahistine is a vasodilator, a mild H1 histamine agonist, and a potent H3 histamine antagonist. The mechanism of action in Meniere's disease is unknown, but theories include reducing the endolymphatic pressure through improved circulation in the stria vascularis or inhibiting activity in the vestibular nuclei. It has been found to be a safe drug with a very low side effect profile. Betahistine was FDA approved for Meniere's disease in the US market for a short period of time in the 1970s, but approval was then rescinded due to lack of evidence supporting its efficacy. However, based on clinical experience and several observational studies, it is still widely used elsewhere in the world.

A Cochrane review of betahistine in Meniere's disease by James first published in 2001 and updated in 2011 included seven trials involving 243 patients [12]. Most trials suggested a reduction of vertigo with betahistine, and some suggested a reduction in tinnitus, and none showed an effect on hearing. However, this Cochrane review concluded that these trials were of low quality, and bias in the methods could have affected the results. In 2016, a carefully designed and executed trial of the medical treatment of Meniere's disease with betahistine (BEMED) was published [13]. This was a prospective, multicenter, double-blind, randomized, placebo-controlled trial to assess the long-term effects of betahistine dihydrochloride in two different doses and a placebo. The BEMED trial found a significant decline of vertigo attack rates in all three treatment arms over time and no difference in the number of vertigo attacks after 9 months of treatment with betahistine at a daily dose of 48 mg or 144 mg, compared with a placebo.

Despite the uncertainty over efficacy, betahistine appears to remain frequently prescribed for Meniere's disease in Europe. In the USA, betahistine is not approved by the Food and Drug Administration but can be obtained through US compounding pharmacies with a prescription.

Episodic Treatment of Acute Symptoms

The severity of acute vertigo and vegetative symptoms (nausea, vomiting, etc.) associated with attacks of Meniere's disease can be blunted using vestibular suppressant and/or antiemetic medications. Effective vestibular suppressants include anticholinergics (i.e., scopolamine), antihistamines (i.e., meclizine), phenothiazine (i.e., promethazine), benzodiazepines (i.e., diazepam), and Zofran.

Thus, patients should be provided medications to be used to abort or lessen the severity of symptoms associated with episodes of acute vertigo in the form of fast-acting vestibular suppressants and an antiemetic medication. These medications not only reduce the intensity of the vertigo and reduce symptoms of nausea and vomiting, but they give patients a form of control over their disease that is known to improve their well-being.

Vestibular suppressants include antihistamine and benzodiazepine medications. Given the sudden onset of vertigo with duration up to 24 h, medications with short onset and short half-life should be used. Commonly used antihistamine agents include meclizine and dimenhydrinate due to their ability to cross the blood-brain barrier and likely due to their anticholinergic properties. The exact mechanism of vestibular suppression is unknown. The primary adverse effect is sedation which can lead to falls and memory dysfunction. Use cautiously in elderly patients and in patients on concomitant sedating medications. Other side effects include dry mouth, dry eyes, blurry vision, constipation, and difficulty with urination due to anticholinergic properties. Commonly used benzodiazepines include diazepam, lorazepam, and clonazepam due to short onset of action. They cause central nervous system inhibition via GABA modulation. In addition to sedative effects, additional risks of benzodiazepines include tolerance and dependence. They should be avoided or used cautiously in patients with a history of drug or alcohol addiction.

Antihistamine	Dose	Onset of action (min)	Peak (h)	Half-life (h)
Meclizine	25–50 mg every 4–6 h	60	Unknown	4–6
Dimenhydrinate	50 mg every 4–6 h	15–60	1–2	Unknown
Benzodiazepines				
Lorazepam	0.5–1 mg BID	15–60	1–6	10–20
Clonazepam	0.5 mg BID	20–60	1–2	20–50
Diazepam	2–4 mg BID	30–60	1–2	20–50

It is important to emphasize that vestibular suppressants should only be used to decrease the intensity of acute vertigo or nystagmus. They are not to be used for general imbalance or disequilibrium that can be associated with advanced Meniere's disease in older people, as suppressing the vestibular system will only magnify these symptoms. The chronic use of vestibular suppressants is not appropriate since these medications do not affect the formation of endolymphatic hydrops or reduce the frequency of vertiginous episodes in Meniere's disease. Furthermore, vestibular

suppressants delay the adaptive mechanisms that function to reduce any residual vestibular imbalance following an acute episode of vertigo.

Nausea and vomiting are often associated with acute Meniere's attacks and can lead to dehydration and weakness. Antiemetics should be prescribed for the patient to have on hand in addition to vestibular suppressants. Common medications are rapidly dissolving ondansetron and rectal promethazine to mitigate the chance of vomiting the medication. Standard dose for rapidly dissolving ondansetron is 4 mg every 8 h. Onset of action is within minutes and is typically well tolerated. There is a concern for prolonged QT syndrome and serotonin syndrome with high doses. The standard dose for a promethazine suppository is 12.5–25 mg every 6 h, and side effects include sedation and anticholinergic effects.

Oral Corticosteroids

The mechanism of action of steroids on the inner ear is not well understood, but these medications decrease damage from an inflammatory response, regardless of the etiology. Oral corticosteroids are often used for symptom exacerbations though this is done based primarily on expert option because evidence of benefit is limited. Short-term treatment protocols vary using either oral Decadron, methylprednisolone, or prednisone for several days up to 2 weeks. Longer-term treatment protocols are sometimes used when immune-related inner ear disease is suspected. Use of oral steroids is based on expert opinion as no clinical trials have been performed.

Migraine

Migraine has been suggested as an associated factor in Meniere's disease since Prosper Meniere first described the condition in 1861. The pathophysiology of the relationship between the two has yet to be established; however, several studies have shown the higher incidence of migraine in patients with Meniere's disease compared to the normal population [14, 15]. We see this frequently at our institution and initiate migraine treatment early on.

The first line of treatment is conservative with avoidance of common migraine triggers, dietary changes, and dietary supplementation. These measures should be trialed for at least 4–6 weeks. Common triggers include hormonal changes, sleep deprivation, stress, visual motion, and barometric pressure changes. Common dietary triggers include monosodium glutamate (MSG), tyramine, and phenylethylamine. Supplements recommended by the American Academy of Neurology and the American Headache Society are magnesium (600 mg daily), riboflavin (400 mg daily), and feverfew (50–300 mg twice daily) with level B evidence and coenzyme Q10 (100 mg three times daily) with level C evidence [16].

When conservative measures fail to reduce vertigo spells in patients with migraine and Meniere's disease, migraine prophylaxis should be considered. Common prophylactic medications include amitriptyline, verapamil, propranolol, and topiramate. We often see that patients with migraine experience medication side effects with higher intensity and frequency than in patients without migraine. For this reason, we will often start migraine prophylaxis at sub-therapeutic levels and gradually increase the medication based on the patient's tolerability. Patients should remain on each medication at optimal dose for at least 4–6 weeks before the trial is complete to accurately assess response. If no benefit is noted, medication should be gradually weaned off. For partial response, increased dosing or addition of another migraine prevention medication should be considered. If patients fail to show a response with a trial of each of these medications, we recommend a neurology referral.

Allergy Treatment

Allergy has been associated with symptoms of Meniere's disease beginning with the observations of Duke in 1923 [17]. Throughout the intervening decades, several observers noted in case reports the role that both inhalant and food allergy can play in patients with hearing loss, tinnitus, aural fullness, and dizziness. The observed role of allergy in Meniere's disease has been strikingly demonstrated by Viscomi who demonstrated significant changes in ECOG SP/AP ratios in five patients given a food provocation allergen challenge [18]. The ECOG changes also correlated with skin wheal reaction and subjective symptoms.

Several outcome studies of allergy treatment of Meniere's disease are also available. Outcome studies by their nature are uncontrolled, non-placebo studies but can provide insight in the question at hand. In the 1970s, both Powers and Shaver reported that 32% of their patients with Meniere's disease responded to allergy treatment for vertigo or fluctuating hearing loss due to Meniere's disease [19, 20]. In 2000, Derebery reported favorable outcomes of allergy treatment with 82% feeling better subjectively, 48% with vertigo absent or substantially improved, and 61% with hearing stable or improved [21].

The prevalence of allergy in Meniere's disease may be greater than in comparison controls. Derebery reported that the prevalence of airborne and food allergy in patients with Meniere's disease (42% reported known airborne allergy and 27% reported known food allergy) was greater than control patients [22]. Keles measured cytokine profiles, allergic parameters, and lymphocyte subgroups in Meniere's disease patients and a matched control group of healthy volunteers ($N = 92$) [23]. They found a history of allergy in 31/46 (67%) of Meniere patients and 16/46 (35%) in the control group. Elevated total IgE levels were found in 41% of Meniere patients and in 20% of the control group.

In summary, there is a long history of a suspected connection between Meniere's disease and allergy. Most evidence of a connection are clinical observations and uncon-

trolled case series, and scientifically robust evidence is not available. Basic science information regarding immunology of the inner ear is supportive, but pathophysiology remains unknown. Nevertheless, allergy evaluation and treatment should be considered whenever there is a suspected relationship between ingestion of a particular food and seasonal variation of symptoms in a patient with a known history of allergy.

Vestibular Physical Therapy

Vestibular physical therapy is a specialized exercise-based intervention for management of dizziness and imbalance. In patients with peripheral vestibular disorders such as Meniere's, vestibular physical therapy seeks to adapt to vestibular insult via vestibular ocular reflex (VOR) adaptation, habituation, and substitution. VOR adaptation exercise produces retinal slip through eye/head exercises which involve moving the head while focusing on a stationary target. Habituation exercises focus on exposure by and desensitization to provoking stimuli. Substitution involves other eye movements (saccade modification or enhancing smooth pursuit) to effectively cancel the vestibular deficit and prevent the patient from perceiving smeared retinal images during head movements. Vestibular exercises have demonstrated efficacy in fall reduction, improved balance, decreased dizziness, and improved quality of life in patients with unilateral peripheral vestibular dysfunction [24]. However, this trend does not persist when isolated to Meniere's disease which can be attributed to the fluctuating nature of the disease in its early stages [25]. Guidelines for use of vestibular physical therapy in patients with peripheral hypofunction (typically patients with advanced Meniere's disease) are available [26].

Hearing Loss and Tinnitus Management

As Meniere's disease progresses, functional hearing including pure tone thresholds and word recognition decline. End-stage Meniere's disease is associated with a flat, severe sensorineural hearing loss around 60–70 dB with fair to poor word recognition. Hearing aids can be difficult to fit a fluctuating loss, though patients who have preserved word recognition can adjust the hearing aid as needed. For a flat loss at end-stage Meniere's disease, a Contralateral Routing of Signals (CROS) aid may provide the best benefit as poor word recognition typically prevents any benefit from a traditional hearing aid.

In addition to hearing loss, many patients experience tinnitus. Given the heterogeneous nature, varying emotional response, and the uncertainty of the neural basis for tinnitus, patient-specific treatment remains challenging; however, the goal of therapy is to reduce the tinnitus sound and emotional distress associated with it. Sound therapy options include hearing amplification, tinnitus maskers, and white noise generators. Other treatments include counseling, cognitive behavioral therapy, and mindfulness-based stress reduction [27].

References

1. Lopez-Escamez JA, Carey J, Chung WH, Goebel JA, Magnusson M, Mandalà M, Newman-Toker DE, Strupp M, Suzuki M, Trabalzini F, Bisdorff A. Diagnostic criteria for Menière's disease. J Vestib Res. 2015;25(1):1–7.
2. Palaskas C, Dobie R, Snyder J. Progression of hearing loss in bilateral Meniere's disease. Laryngoscope. 1988;98:287–90.
3. Foster CA, Breeze RE. Endolymphatic hydrops in Ménière's disease: cause, consequence, or epiphenomenon? Otol Neurotol. 2013;34(7):1210–4.
4. Nevoux J, Franco-Vidal V, Bouccara D, Parietti-Winkler C, Uziel A, Chays A, Dubernard X, Couloigner V, Darrouzet V, Mom T, Groupe de Travail de la SFORL. Diagnostic and therapeutic strategy in Menière's disease. Guidelines of the French Otorhinolaryngology-Head and Neck Surgery Society (SFORL). Eur Ann Otorhinolaryngol Head Neck Dis. 2017;134(6):441–4.
5. Furstenberg A, Lashmet F, Lathrop F. Meniere's symptom complex: medical treatment. Ann Otol Rhinol Laryngol. 1934;43:1035–46.
6. Fustenberg A, Richardson G, Lathrop F. Meniere's disease. Arch Otolaryngol Head Neck Surg. 1941;34:1083–92.
7. Boles R, Rice D, Hybels R, Work W. Conservative management of Meniere's disease: Furstenberg regimen revisited. Ann Otol Rhinol Laryngol. 1975;84:513–7.
8. Klockhoff I, Lindblom U. Meniere's disease and hydrochlorothiazide- a critical analysis of symptoms and therapeutic effects. Acta Otolaryngol. 1967;63:347–65.
9. Corvera J, Corvera G. Long-term effect of acetazolamide and chlorthalidone on the hearing loss of Meniere's disease. Am J Otol. 1989;10:142–5.
10. Crowson MG, Patki A, Tucci DL. A systematic review of diuretics in the medical management of Meniere's disease. Otolaryngol Head Neck Surg. 2016;154(5):824–34.
11. Thirlwall AS, Kundu S. Diuretics for Ménière's disease or syndrome. Cochrane Database Syst Rev. 2006;3:CD003599.
12. James A, Burton MJ. Betahistine for Ménière's disease or syndrome. Cochrane Database Syst Rev. 2001;1:CD001873.
13. Adrion C, Fischer CS, Wagner J, Gürkov R, Mansmann U, Strupp M, BEMED Study Group. Efficacy and safety of betahistine treatment in patients with Meniere's disease: primary results of a long term, multicentre, double blind, randomised, placebo controlled, dose defining trial (BEMED trial). BMJ. 2016;21:352.
14. Neff BA, Staab JP, Eggers SD, Carlson ML, Schmitt WR, Van Abel KM, Worthington DK, Beatty CW, Driscoll CL, Shepard NT. Auditory and vestibular symptoms and chronic subjective dizziness in patients with Ménière's disease, vestibular migraine, and Ménière's disease with concomitant vestibular migraine. Otol Neurotol. 2012;33(7):1235–44.
15. Radtke A, Lempert T, Gresty MA, Brookes GB, Bronstein AM, Neuhauser H. Migraine and Ménière's disease: is there a link? Neurology. 2002;59(11):1700–4.
16. Loder E, Burch R, Rizzoli P. The 2012 AHS/AAN guidelines for prevention of episodic migraine: a summary and comparison with other recent clinical practice guidelines. Headache. 2012;52(6):930–45.
17. Duke WW. Meniere's syndrome caused by allergy. JAMA. 1923;81(26):2179–81.
18. Viscomi GJ, Bojrab DI. Use of electrocochleography to monitor antigenic challenge in Meniere's disease. Otolaryngol Head Neck Surg. 1992;107(6):733–7.
19. Powers WH. Allergic factors in Meniere's disease. Trans Am Acad Opthalmol Otolaryngol. 1973;77:22–9.
20. Shaver EF Jr. Allergic management of Meniere's disease. Arch Otolaryngol. 1975;101(2):96–9.
21. Derebery MJ. Allergic management of Meniere's disease: an outcome study. Otolaryngol Head Neck Surg. 2000;122(2):174–82.
22. Dereberry MJ, Berliner KI. Prevalence of allergy in Meniere's disease. Otolaryngol Head Neck Surg. 2000;123:69–75.
23. Keles E, Godekmerdan A, Kalidag T, Kaygusuz I, Yalcin S, Cengiz AH, Aral M. Meniere's disease and allergy: allergens and cytokines. J Laryngol Otol. 2004;118(9):688–93.

24. Hillier SL, McDonnell M. Vestibular rehabilitation for unilateral peripheral vestibular dysfunction. Cochrane Database Syst Rev. 2011;2:CD005397.
25. van Esch BF, van der Scheer-Horst ES, van der Zaag-Loonen HJ, Bruintjes TD, van Benthem PP. The effect of vestibular rehabilitation in patients with Ménière's disease. Otolaryngol Head Neck Surg. 2017 Mar;156(3):426–34.
26. Hall CD, Herdman SJ, Whitney SL, Cass SP, Clendaniel RA, Fife T, Furman JM, Goebel J, Shepard NA, Woodhouse S. Vestibular rehabilitation for peripheral vestibular hypofunction: clinical practice guidelines. J Neurol Phys Ther. 2016;40:124.
27. Arif M, Sadlier M, Rajenderkumar D, James J, Tahir T. A randomised controlled study of mindfulness meditation versus relaxation therapy in the management of tinnitus. J Laryngol Otol. 2017;131(6):501–7.