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Contemporary Review

Medical Management Of Ménière's Disease

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Objectives: Ménière's disease (MD) is poorly understood with respect to its etiology, pathophysiology, clinical course, and treatment. Furthermore, in the absence of controlled clinical studies, empiric treatments have been used with varying degrees of success. In this paper, the authors review the current medical management of MD.

Study Design: Literature review.

Results: Because of a dearth of well-controlled studies, the medical management of MD remains empirical and is largely restricted to lifestyle changes, pharmacotherapy, and office-based procedures. The development of transtympanic therapies represents a true therapeutic advance that has largely supplanted surgical intervention. A treatment algorithm for acute and chronic medical management is reviewed.

Conclusions: Despite absence of a complete understanding of MD, medical management or its natural history leads to control of vertigo in the majority of patients. Basic research is needed to understand its pathophysiology so that directed therapies can be developed and can be tested in well-controlled clinical trials.

Key Words: Ménière's disease, endolymphatic hydrops, salt restriction, intratympanic gentamicin.

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INTRODUCTION

When Prospere Ménière presented his landmark paper to the French Imperial Academy of Medicine in January 1861, the suggestion that hearing and balance were both controlled by labyrinthine organs was considered extremely controversial and therefore poorly received. It would take 40 years before Hallpike and Portman histologically confirmed endolymphatic dilation in patients with episodic vertigo, fluctuating hearing, and low-pitched tinnitus. Yet, even today, nearly 150 years since Ménière first described the now eponymous disorder, Ménière's disease (MD) continues to be incompletely understood, and the true etiology and pathophysiology of this entity remain elusive.

The presentation of MD is highly variable and its clinical course characterized by acute exacerbation and spontaneous remission. The diagnosis is based on clinical presentation because there is no definitive objective test available. To define the certainty of diagnosis of MD, the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) promulgated diagnostic and reporting guidelines, published in 1972, 1985, and 1995, but these remain poorly or incorrectly used (Tables I to IV).[1] Although nearly 80% of the 128 papers on MD published from 1988 to 1999 used the AAO-HNS Committee on Hearing and Equilibrium (CHE) criteria, only 50% did so correctly.[2] The pathophysiology of MD is presumed to be aberrant fluid homeostasis leading to endolymphatic hydrops, but this may be too simplistic. The capricious nature of the disease has made it difficult to prospectively determine the efficacy of therapeutic intervention, and thus the treatment of MD is primarily empiric. Absence of robust prospective, randomized, placebo-controlled studies has led to a variety of medical and surgical therapeutic interventions of uncertain value.[3,4]

Given the therapeutic void, the aims of management of MD are limited to 1) reducing the number and severity of acute attacks of vertigo; 2) aborting or ameliorating hearing loss (HL) and tinnitus associated with such attacks; 3) alleviating any chronic symptoms (e.g., tinnitus and imbalance); and 4) preventing progression of the disease, in particular, the loss of hearing and balance that characterizes the disorder.[5] We use the term "management" in lieu of "treatment" because currently there is no known treatment option that adequately addresses all four of the above criteria. MD should be considered a chronic condition for which interventions do not eliminate the underlying cause of disease. Moreover, no medical treatments appear to result in long-term preservation of hearing.[6] Nonetheless, despite the relative paucity of evidence-based research, current medical regimens can control disease (as defined by vertiginous attacks) in approximately 80% of patients. Following is an update and discussion of the medical modalities currently used in the management of MD (Table V).

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TABLE I.
Diagnostic Scale of Ménière's Disease of American Academy of Otolaryngology–Head and Neck Surgery Committee on Hearing and Equilibrium.*

Certain Ménière's disease
Definitive Ménière's disease, plus histopathologic confirmation
Definitive Ménière's disease
Two or more episodes of vertigo of at least 20 minutes
Audiometrically documented hearing loss on at least one occasion
Tinnitus and aural fullness
Probable Ménière's disease
One definite episode of vertigo
Audiometrically documented hearing loss on at least one occasion
Tinnitus and aural fullness
Possible Ménière's disease
Episodic vertigo without documented hearing loss
Sensorineural hearing loss, fluctuating or fixed, with disequilibrium, but without definitive episodes

*In all cases, other causes must be excluded.

ACUTE MANAGEMENT

In the acute setting, vestibular suppressants and antiemetic medication have been used to control acute spells of vertigo. They can be divided into different classes, including benzodiazepines, antihistamines, anticholinergics, and antidopaminergics.

Benzodiazepines act on the cerebellar GABA-ergic system that inhibits vestibular nuclei response. In the United States, benzodiazepines are favored for their vestibular suppression as well as anxiolytic properties. However, because benzodiazepines may impair vestibular compensation, their use beyond acute vertiginous episodes should be limited. Antihistamines, potent antivertiginous, and antiemetic medication, including meclizine and dimenhydrinate, have demonstrated efficacy in MD when compared with placebo.[7–9] However, care must be taken in patients with glaucoma or prostate disease because antihistamines can have excessive anticholinergic effects. Scopolamine is a naturally occurring belladonna alkaloid with anticholinergic properties commonly used to prevent nausea and vomiting associated with motion sickness.

The antidopaminergic metoclopramide can be administered orally, parenterally, or rectally and therefore offers a convenient alternative in the acute setting. Care must be taken at higher or prolonged doses to avoid extrapyramidal and endocrine dysfunction. Promethazine (Phenergan, Wyeth, Madison, NJ), a phenothiazine derivative with antihistamine, anticholinergic, and antidopaminergic activity, has antiemetic and anxiolytic properties. This coupled with versatility of administration and extremely low rate of extrapyramidal reaction makes it an effective treatment in acute MD. Similarly, prochlorperazine

TABLE II.
American Academy of Otolaryngology–Head and Neck Surgery Committee on Hearing and Equilibrium Criteria for Reporting Hearing in Méniè.re's Disease.

Stage	Four-Tone Average (dB)
1	≤25
2	26–40
3	41–70
4	>70

Staging is based on four-tone average (arithmetic mean rounded to nearest whole number) of pure-tone thresholds at 0.5, 1, 2, and 3 kHz of worst audiogram during interval 6 months before treatment. This is same audiogram that is used as baseline evaluation to determine hearing outcome from treatment. Staging should be applied only to cases of definite or certain Ménière's disease.

TABLE III.
American Academy of Otolaryngology–Head and Neck Surgery Committee on Hearing and Equilibrium Criteria for Reporting Function in Ménière's Disease: Functional Level Scale.

Regarding my current state of *overall* function, *not just during attacks* (check the ONE that best applies):

1.	My dizziness has no effect on my activities at all.
2.	When I am dizzy I have to stop what I am doing for a while, but it soon passes and I can resume activities. I continue to work, drive, and engage in any activity I choose without restriction. I have not changed any plans or activities to accommodate my dizziness.
3.	When I am dizzy I have to stop what I am doing for a while, but it does pass and I can resume activities. I continue to work, drive, and engage in most activities I choose, but I have had to change some plans and make some allowance for my dizziness.
4.	I am able to work, drive, travel, take care of a family, or engage in most activities, but I must exert a great deal of effort to do so. I must constantly make adjustments in my activities and budget my energies. I am barely making it.
5.	I am unable to work, drive, or take care of a family. I am unable to do most of the active things that I used to. Even essential activities must be limited. I am disabled.
6.	I have been disabled for 1 year or longer and/or I receive compensation (money) because of my dizziness or balance problem.

TABLE IV.
American Academy of Otolaryngology–Head and Neck Surgery Committee on Hearing and Equilibrium Summary of Reporting Guidelines in Ménière's Disease.

Numerical Value	Class
0 (complete control of definitive spells)	A
1 to 40	B
41 to 80	C
81 to 120	D
>120	E
Secondary treatment initiated because of disability from vertigo	F

Numerical value = (X/Y) × 100, rounded to nearest whole number, where *X* is average number of definitive spells per month for 6 months 18 to 24 months after therapy and *Y* is average number of definitive spells per month for 6 months before therapy.

TABLE V.
Medical Management of Ménière's Disease.

Acute management
Vestibular suppressants
Anti-emetics
Rehydration
Electrolyte adjustment
Chronic management
Lifestyle adjustment
Trigger avoidance
Salt restriction
Pharmacology
Diuretics
Vasodilators
Corticosteroids
Aminoglycoside ablation
Complementary and alternative medicine
Devices
Meniett
P-100
Rehabilitation therapy
Vestibular
Tinnitus
Hearing

(Compazine, GlaxoSmithKline Pharmaceuticals, Philadelphia, PA), also a phenothiazine derivative, may be used acutely for treatment of severe nausea and vomiting. The availability of promethazine and prochlorperazine in a suppository form make them specially useful for an acute attack of vertigo associated with vomiting where it may be difficult for the patient to take medication orally.

In lending some credence to the immunogenic theory of MD, some authors promote the use of oral or intratympanic steroids to lessen the severity of attacks and possibly even promote earlier recovery of hearing.[3] Severe episodes can be treated with burst courses of oral steroids tapered over 5 to 14 days.

The administration of all these and other medications, alone or in combination, have all been described and tried in the management of acute MD, although, to date, little to no strong evidence exists for any of these practices. In addition to medication, it is important to remember the role of rest and hydration (especially with vomiting) as a therapeutic adjuvant in the acute setting.

CHRONIC MANAGEMENT

Lifestyle Adjustment

Avoidance of triggers. Some patients with MD note acute exacerbations of their condition with certain triggers. Offending agents include high salt intake, caffeine, alcohol, nicotine, stress, fatigue, monosodium glutamate, and allergy. Avoidance of these triggers can play a crucial role in the prevention of Ménière's attacks. A normal hormonal milieu has also been implicated in MD; an association between MD and menstruation has been suggested, although the clinical relevance of such a correlation remains to be elucidated.[10]

Emotional stress has been associated with increased frequency and severity of attacks.[11] Animal studies have demonstrated histologic evidence of endolymphatic hydrops in guinea pigs exposed to stress.[12] However, recent findings of elevated levels of cortisol in patients with longer histories of MD as compared with those with shorter histories suggests that stress is likely the result of, and not the cause of, MD.[13] The true relationship between stress, vertigo, and MD remains to be elucidated.

Nonetheless, structured psychological support has been recommended in the management of MD.[6,14] Elwood et al.[15] showed that behavioral therapy aimed at reducing the anxiety associated with anticipating attacks of MD in public helped patients to recapture their social lives and cope with stress. However, simple patient education by the otolaryngologist may be the most important part of conservative management and should include detailed explanation of the disease to the patient. The non–life-threatening nature should be emphasized, and, if necessary, repeated, and discussions regarding the various expectations in natural history or therapy had with the patient. According to Kinney et al.,[6] encouragement by family support systems, social support systems, and MD support groups may significantly relieve some emotional stresses caused by MD.

Thus, identification and avoidance of environmental or psychological triggers can play an important role in the management of MD. Unfortunately, for the majority of patients, no such specific trigger can be identified, and further intervention is usually necessary.

Salt restriction. Anecdotally, some patients have described acute symptoms after high salt exposure, and treatment protocols based on sodium restriction have been a foundation of the management of MD since the 1930s.[16] Recent evidence has suggested that the effects of sodium on endolymphatic hydrops are far more complex than mere fluctuations in endolymphatic levels.[17] Experimental data from both animals and humans have shown that a low-sodium diet results in nearly no change in plasma sodium levels. In addition, endolymphatic levels of sodium are essentially normal in histologically proven hydrops.[17] Although endolymphatic hydrops is seen in all patients diagnosed with MD, the reverse is not true; all patients with endolymphatic hydrops do not necessarily demonstrate symptoms of MD.[18] These findings by Merchant et al.[18] question the established dictum that hydrops is the physiologic endpoint of MD symptoms. Rather, the authors suggest that endolymphatic hydrops is a manifestation of some yet to be determined disorder of labyrinthine homeostasis.

Plasma osmolality, rather than absolute sodium levels, have led some researchers to shift focus from salt/sodium toward the transport and regulation of water itself.[19] Recent evidence suggests a possible role of arginine vasopressin, aquaporins, and antidiuretic hormone (ADH) in the development of MD.[20–26] Applying these findings, Naganuma et al.[27] found that increased water intake lowers ADH levels and more effectively improves and prevents HL compared with conventional therapy. Although

study size was limited, the simplicity and cost-effectiveness of such a treatment warrants further investigation.

Despite the incomplete understanding of its role in developing hydrops, sodium restriction continues to be widely supported in both the literature and clinical practice. Claes and Van de Heyning[28] have suggested that all patients should observe a low-salt diet with an intake of no more than 1 g of NaCl-enhanced salt per day, although no evidence for the benefit of this regimen was reviewed. To date, not one published study supports the efficacy of sodium restriction alone in the management of MD. Various regimens have been proposed, most restricting daily dietary sodium intake to less than 2,000 mg.

Patients are advised to eliminate the use of salt at the table and limit its use in cooking and baking. Herbs and spices can be used for taste enhancement. Patients must be counseled to carefully inspect product "nutritional information" labels not only for sodium content but also for serving size. Many high-sodium products show low listings based on a small serving size. Input of a nutritionist should be suggested in diet modification. See Table VI for a listing of common foods with very high sodium content per serving.

Pharmacologic Therapy

For some patients with MD, avoidance of certain triggers and dietary modification will result in adequate control of the disease. However, a significant proportion will require additional therapeutic intervention. Of note, the use of these therapies is not supported by prospective, randomized, placebo-controlled studies.

TABLE VI.
Sodium Concentrations in Common Food.

- Bacon, Canadian, 2,500
- Beef hamburger, 47
- Bouillon cubes, 24,000
- Cereals, commercial, 700 to 1,100
- Cereal, wheat flakes, 1,000
- Cheese, processed, 1,189
- Cheese, parmesan, 1,862
- Doughnuts, 500
- Mustard, prepared yellow, 1,252
- Olives, green, 2,400
- Peanut butter, 607
- Pickles, relish, sweet, 712
- Potato chips, up to 1,000
- Pretzels, 1,680
- Salad dressing, 700 to 1,300
- Tomato ketchup, 1,042
- Tuna in oil, 800

All values are given in milligrams of sodium for a 100 g (3.5 oz) food portion. For a detailed list, see Dr. Salt's Webpage: http://oto.wustl.edu/men/sodium.htm. Salt AN, sodium contents of common foods, http://oto.wustl.edu/men/sodium.htm

TABLE VII.
Classes of Diuretics Used in Management of Ménière's Disease.

Thiazide diuretics (e.g. hydrochlorothiazide)
Inhibit Na+/Cl- renal reabsorption
Potassium-sparing diuretics (e.g. spironolactone)
Inhibit renal Na+/K+ exchange
Loop diuretics (e.g., furosemide)
Inhibit renal cotransportation
Carbonic anhydrase inhibitors (e.g., acetazolamide)
Inhibit H+ secretion and promote Na+, K+ excretion

Diuretics

Diuretics are frequently used along with or as alternative to dietary salt restriction to reduce total body salt and consequently total body fluid. By decreasing the overall volume status of a patient, diuretics are believed to decrease the endolymphatic pressure and volume, or hydrops, of the inner ear.[29] Other proposed mechanisms include the reduction in endolymph production at the stria vascularis.

There are four main classes of diuretics that have been studied in the management of MD (Table VII): 1) thiazide diuretics (e.g., hydrochlorothiazide) inhibit Na^+/Cl^- renal reabsorption;[30–32] 2) potassium-sparing diuretics (e.g., spironolactone) inhibit renal Na^+/K^+ exchange;[33] 3) loop diuretics (e.g., furosemide) inhibit renal cotransportation;[34] and 4) carbonic anhydrase inhibitors (e.g., acetazolamide) inhibit H^+ secretion and promote Na^+ and K^+ excretion.[35] Each of the above classes of diuretics are assumed to affect fluid balance within the inner ear, although they are not without side effects. These include metabolic acidosis with hypokalemia and hypochloremia (thiazides), and hyperglycemia and diabetes mellitus exacerbation, hyperuricemia, renal and hepatic insufficiency, metabolic acidosis with low plasma bicarbonate, nephrocalcinosis, hyperhidrosis, distal paraesthesia, and gastrointestinal disturbance (carbonic anhydrase inhibitors).

Although the use of diuretics is commonplace, strong evidence to support their use is limited. A recent meta-analysis of diuretics in MD found "no trials of high enough quality" to meet the standard set for review.[5] Many clinicians refer to the early studies of Klockhoff and Lindblom,[30] which showed significant improvement in vertigo, HL, and overall quality of life when hydrochlorothiazide was compared with placebo. However, Ruckenstein et al.'s[36] re-evaluation of Klockhoff and Linblom's data found no statistical difference in measures of hearing, tinnitus, vertigo, or general condition between diuretic and placebo groups. The only published RTC on the subject showed that after 17 weeks of Dyazide (triamterene and hydrochlorothiazide) treatment, patients had significantly improved vestibular symptoms but no change in HL or tinnitus.[32] Storper et al.[37] showed that 2 mg of the anticholinergic glycopyrrolate twice daily results in significant benefit for MD patients already on salt restriction and diuretic.

Some clinicians have promoted the simultaneous use of diuretics together with salt restriction. Santos et al.,[38]

in a retrospective study, evaluated 54 patients treated with diuretics and a low-salt diet. After 24 months of therapy, vertigo control was complete or substantial in 79% of the patients, limited or insignificant in 19%, and worse in 2%. Hearing improved in 35% of the patients, was unchanged in 29%, was worse in 22%, and could not be classified in 14%. Hearing was also evaluated by comparison of individual thresholds before medical therapy and at 22 and 74 months after the start of medical therapy. They found a stabilization of low- and mid-threshold frequencies, with an average rate of HL approximating 0 dB/year with 74 months of follow-up. The results of this study suggest that diuretics and a low-salt diet may decrease the natural progression of sensorineural HL in patients with MD. With stabilization of the disease (marked by a symptom-free period of 6–12 mo), patients can be slowly weaned off their particular regimen. If necessary, therapy can be restarted.

Aminoglycoside Ablation

The aminoglycosides are toxic to the inner ear; streptomycin and gentamicin are selectively vestibulotoxic and destroy the endolymph-producing dark in the ampullary crista.[39] These properties of aminoglycosides have been harnessed to treat vertigo associated with MD. In 1948, Fowler[40] used systemic streptomycin in the treatment of MD. In 1956, Schuknecht[41] described middle ear perfusion with an aminoglycoside antibiotic for the treatment of MD. Over the past decade, intratympanic gentamicin (ITG) has become a common weapon in the arsenal, addressing the approximately 10% of patients with MD refractive to maximal medical treatment.

ITG is a means to perform chemical labyrinthectomy, which essentially exploits the vestibulotoxic properties of gentamicin. It can be delivered to the middle ear via myringotomy, tympanostomy tube, microwick, or microcatheter. The exact method of introduction to the inner ear may be through the round window membrane itself, the annular ligament, or vascular channels.[42] Once in the inner ear, the mechanism of vestibulotoxicity remains incompletely understood. Only one published report of histopathologic examination of the vestibular end organs in a patient with MD exists, which showed severe atrophy of the neuroepithelium of the semicircular canal cristae ampullares with undifferentiated cells, fibrosis, and edema of the stroma.[43]

The large number of published reports on the efficacy of ITG has led to near abandonment of surgical intervention.[44] However, a note of caution was raised by Cohen-Kerem et al.[45] in their meta-analysis of published studies using ITG as a sole treatment modality and using AAO-HNS reporting guidelines for MD: not a single acceptable double-blind or blinded, prospective control trial was identified. Variations in concentration, dose, frequency, and duration all limit standardization and comparison of results. Therefore, little consensus exists for the optimal protocols for delivery, even in the rare occurrence when outcomes measures are standardized. Hopefully, ongoing clinical trials will address this shortcoming.[46]

In patients with unilateral MD, the authors prefer to use the low-dose method described by Harner et al.[47] The procedure is office-based using either lidocaine injection or topical phenol for tympanic membrane anesthesia. Unbuffered gentamicin sulfate at a concentration of 40 mg/mL is drawn into a 1 mL tuberculin syringe. A 3.5 inch, 25-gauge needle is attached, and approximately 0.5 to 0.75 mL are injected into the middle ear space. A second needle hole is necessary to release middle ear air to allow for adequate injection. Patients are then left supine for 30 minutes and instructed to keep water out of their ear for 2 weeks. Patients return in 1 month when an audiogram is obtained. Such intervention resulted in a 76% improvement in vertigo and no change in hearing at 4 years postinjection. Approximately 15% to 20% of patients require a second ITG injection, usually at a 1 month interval; a third injection is rarely required. This low-dose method is rarely associated with HL.

Although easy to use, ITG should be used with caution. Given that 20% of patients develop bilateral disease, the risk of bilateral labyrinthine hypofunction during a patient's lifetime is high. The resultant disequilibrium and oscillopsia can be incapacitating and irreversible.[48] Vestibular evoked myogenic potential testing may be useful in identifying patients with unilateral symptoms who actually have subclinical contralateral (bilateral) disease. In patients with bilateral MD, we favor the use of intratympanic steroids or nonablative surgery (e.g., endolymphatic sac decompression).

Steroids

Immunologic dysfunction is considered an important etiologic factor in MD. Recent research suggesting an immune etiology of MD includes the presence of anti- endolymphatic sac autoantibodies in the serum of MD patients,[49] the presence of MD-like symptoms in other autoimmune disease (e.g., Cogan's periarteritis nodosa), raised immunoglobulin (Ig)M complexes and C1q component of complement,[50] IgG deposits in the endolymphatic sacs of patients undergoing shunt surgery,[51] the presence of lymphatics and immunocompetent cells close the endolymphatic space, responsiveness to IgE therapy,[52] and elevated antibodies directed against type II collagen in Ménière's patients compared with normal controls.[53] Brookes[54] showed circulating immune complexes in 54% of patients with MD. Tomoda et al.[55] reported that up to 6% of all patients with MD may have an autoimmune etiology.

Steroid responsiveness in MD patients with increased rate of expression of certain human leukocyte antigens further supports an immune mechanism. In addition, 20% of patients with MD have inhalant or food allergies, and treating these allergies with immunotherapy and diet modification improved allergic and Ménière's symptoms when compared with controls.[56] Immunosuppressive therapy such as low-dose methotrexate or etanercept (recombinant tumor necrosis factor-alpha) also show early promise, but definitive studies are needed.[57,58] The authors do not support the use of immunosuppressive therapy in uncomplicated MD but believe they should be considered in cases indicative of autoimmune disease, especially when an only-hearing ear is effected.

The concept of MD as an inflammatory or immune-mediated disease has led to the use of corticosteroids in

the management of its symptoms. In addition to immune and inflammatory regulation, corticosteroids are known to affect carbohydrate, electrolyte, protein, and lipid metabolism, making exact physiologic effects impossible to gauge. Furthermore, the discovery of glucocorticoid receptors in the inner ear suggests that steroids may also affect fluid homeostasis.[59] Nonetheless, the use of steroids in MD is largely empiric, based on successes of this technique in patients with sudden sensorineural HL, autoimmune HL, and tinnitus.

More recently, despite the absence of strong evidence, intratympanic steroids have gained in popularity both in the treatment of sudden sensorineural HL and MD. Similar to ITG, the advantages are numerous, including ease of administration, avoidance of surgery, contraindications to systemic therapy (e.g., patients with hypertension and diabetes), intolerance of systemic therapy (insomnia, gastrointestinal disturbances, etc.), salvage therapy when systemic treatment fails, and selection of the active ear for treatment.[60] Concentrations of steroids in the inner ear after intratympanic administration far exceed those seen in systemic administrations.[61,62] Complications include pain, short-lasting vertigo, otitis media, tympanic membrane perforation, vertigo (temporary or permanent), and HL. Optimal drug doses, schedule, duration, and means of delivery to the inner ear have yet to be standardized, and reporting of complications has been inconsistent.

The relatively few prospective studies that have been conducted suggest that although vertigo symptoms may improve, hearing and tinnitus do not significantly change.[63–65] Silverstein et al.[66] reported a 72% rate of substantial or complete vertigo control at 18 months, although this is not significantly different from ITG or endolymphatic sac decompression.[67] Lack of effect on hearing is in contrast with the anecdotal evidence that intratympanic steroids are effective in reversing HL in sudden sensorineural HL suggest different pathophysiologies for these two disorders. In MD patients in whom hearing improvement/preservation is not of primary concern or in those who have failed other medical therapies, intratympanic steroid injection may provide substantial benefit prior to more aggressive surgical options. Clearly, more prospective and controlled studies are needed to fully understand and use this treatment option.

Vasodilators

Microcirculation changes leading to ischemia of the stria vascularis has been thought to contribute to MD. Vasodilators have been used by some to relieve ischemia, with improved cochlear microcirculation leading to reduced endolymphatic pressure or possible inhibition of vestibular nuclei activity.[68,69] However, their efficacy in the treatment of MD is questionable.

Agents causing capillary dilation such as niacin, papaverine, nylidrin, isosorbide dinitrate, histamine (subcutaneous or sublingual), and betahistine (oral) have been used in the management of MD. Betahistine, used commonly in Europe, also inhibits the vestibular nuclei, independent of blood flow.[70] Nonetheless, not one RCT of histamine was found, and only a few RCTs of betahistine have been published. Salami et al.[71] reported a statistically significant benefit from betahistine over placebo in reduction of intensity and frequency of vertigo attacks. Fraysse et al.[72] likewise reported reduction in vertigo frequency, severity, and duration of vertigo after 60 days of betahistine treatment compared with flunazarine, a cerebrally active calcium antagonist. However, other studies have shown no significant improvement in vertigo over the long-term (>3 mo) setting.[73,74] No significant improvement, either short or long term, were seen in hearing, tinnitus, or aural fullness.[75] Most likely, any beneficial effects of vasodilators result from nonspecific central nervous system suppression rather than a direct effect on cochlear blood flow.

Complementary and Alternative Medicines

Patients with suboptimal improvement, as well as patients who have responded to allopathic treatment, are increasingly turning to complementary and alternative medicines (CAM) as both adjunct and alternative to traditional management. Anecdotal evidence abounds attesting to benefits of gingko biloba, niacin, bioflavonoids, lipoflavonoids, ginger root, and a host of other herbal supplements. Acupuncture, acupressure, and Tai Chi have long been used in the management of vertigo, nausea, and dysequilibrium.[76,77] Likewise, reports from chiropractic and osteopathic fields suggest common pathophysiology between MD and Parkinson's disease, trigeminal neuralgia, Bell's palsy, temporomandibular joint disease, and cervical spine disease.[78,79] Although no evidence exists on the efficacy of these modalities or for the existence of these associations, the otolaryngologist must be aware that many patients with MD have investigated or are using these options. More than a decade ago, in 1997, Eisenberg et al.[80] showed that 42% of patients have used or are using CAM, and 75% of them do not tell their physician. It is therefore imperative that the clinician asks his or her patients regarding the use of CAM and attempts to integrate viable CAM strategies with proven therapeutic options to create a treatment plan that is effective, safe, and meaningful to the patient.

Devices

A common complaint of patients with MD is that symptoms can wax and wane depending on ambient pressure changes. Densert et al.,[81] early investigators of this phenomenon, postulated that inducement of positive pressure changes to the inner ear could lead to increased exchange of inner ear fluids via the different communication routes. In 1986, Densert et al.[82] created a placebo-controlled, randomized clinical study of 39 definitive MD patients in whom they showed electrocochleographic parameters were improved by the application of positive pressure pulses of low amplitude in the middle ear. These and similar findings laid the foundation for the development of a portable low-intensity alternating pressure generator worn in the external auditory canal. The first such device was designed in Sweden and, since 2000, is now marketed in the United States as the Meniett device (Medtronic Xomed, Jacksonville, FL). Initial results of three randomized, controlled, double-blind trials demonstrated safety and efficacy in the short term.[83–85] Treated patients reported significant reduction in vertigo frequency

and severity. However, until recently, lack of evidence of long-term effectiveness had led to reluctance by clinicians to accept the Meniett as an established treatment option. In 2006, Gates et al.[86] reported their results of a long-term follow-up clinical trial of the Meniett device for patients with classic, unilateral MD unresponsive to traditional medical treatment. For the long-term, the authors found a gradual improvement in vertigo for most but not all participants. Sixty-seven percent (39/58) of patients achieved control of AAO-HNS Foundation class A (remission) or class B (greatly improved). Patients who went into remission were 80% likely to remain in remission for the long term, with nearly half of them achieving remission within the first year of use. Clearly, the Meniett offers an attractive option to patients with MD who have failed medical treatment, although there are a few shortcomings. The device requires the insertion of a long-term tympanostomy tube, which is itself rife with attendant complications, including middle and external ear infections. Moreover, use of the device without a patent tube can actually exacerbate symptoms because of middle ear pressure mechanics. No objective measurement of hearing has been performed, and subjective reports by patients suggest that hearing invariably does not improve in either the short or long term with the use of the Meniett device. The device is also expensive and rarely covered by insurers. In 2005, a manually operated device, the P-100 (Enttex, Hannover, Germany) debuted as a less-expensive alternative to the Meniett. However, little has been written about its efficacy.[87]

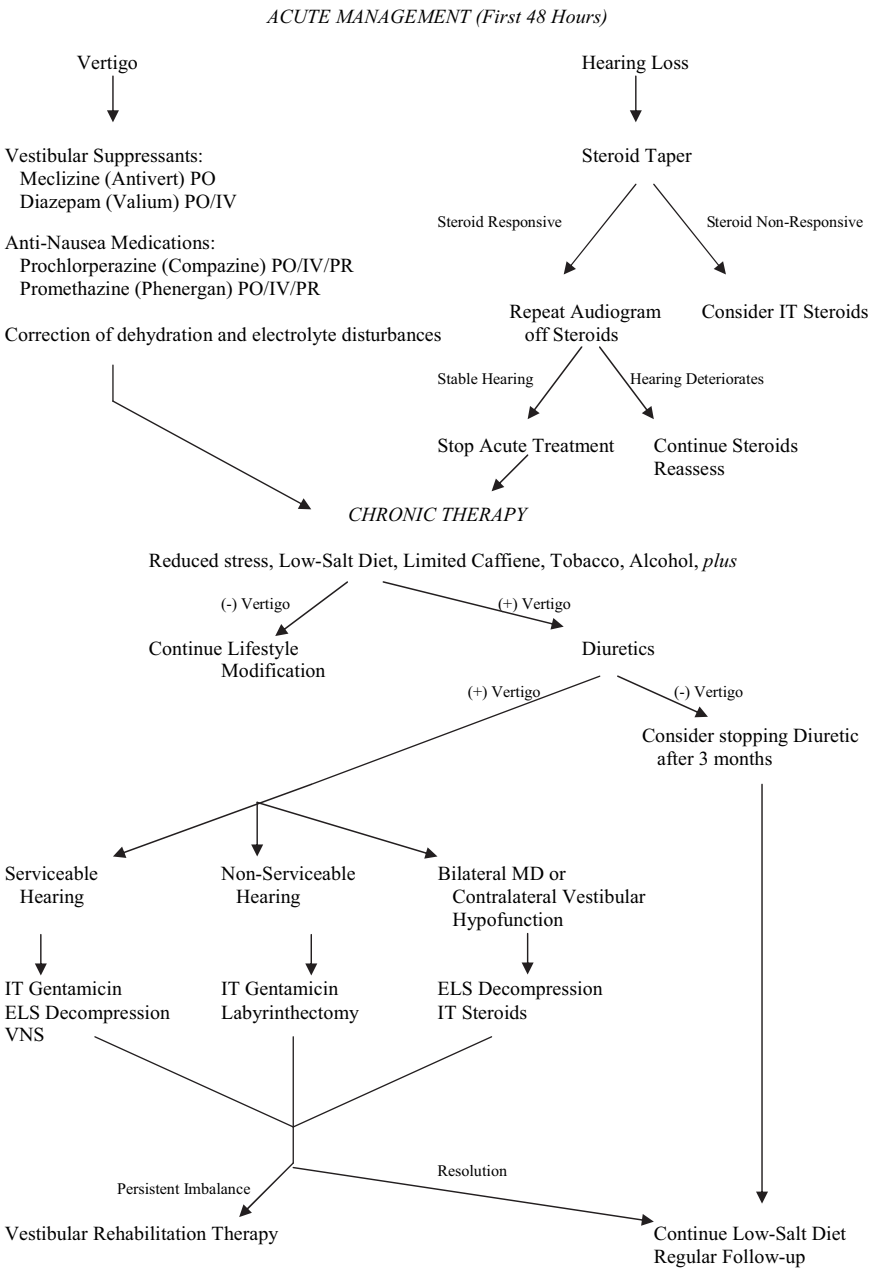

Fig. 1. Medical management algorithm for acute and chronic Ménière's disease.

Rehabilitation Therapy

There has been increasing interest in the use of vestibular rehabilitation in the management of vestibular dysfunction. The therapy, an exercise-based group of activities aimed at maximizing central nervous system compensation, has been used since first described by Cooksey[88] in 1946. By relying on plasticity, formation of internal models, learning of limits, and sensory weighting, patients can "recalibrate" their balance mechanisms. Traditionally, vestibular rehabilitation had not been frequently used in the acute management of MD owing to the intermittent nature of the disease. The patients originally referred for vestibular rehabilitation therapy were those who by medical or surgical ablation were cured of their vertiginous attacks but were left with persistent dysequilibrium. Yet, many patients with MD suffer from imbalance and disequilibrium between acute vertiginous spells and therefore could benefit from vestibular rehabilitation.[89] Furthermore, for those patients with MD who have exhausted the medical (or surgical) armamentarium or for those wishing to avoid it, vestibular rehabilitation provides an attractive option.[90]

Although the management of vertigo is successful in many cases, tinnitus still represents a significant challenge for the patient and practitioner alike. Feenstra[91] concluded that greater than 95% of tinnitus in MD patients can be successfully managed with simple directive counseling. Although many other modalities have been proposed, none can be recommended because of lack of compelling medical evidence.[92]

Hearing aids are an important part of rehabilitation and should be considered for any patient with severe impairment and good compliance. However, given the fluctuating nature of HL in MD, compliance may be limited before hearing deterioration has stabilized. Hearing aids may also prove beneficial when severe tinnitus is present.[93]

THE FUTURE

Research in MD has focused on what Semaan et al.[94] described as five principal areas: genetics and autoimmunity, intralabyrinthine fluid dynamics, cellular and molecular alterations, electrophysiologic tests in diagnosis, and creating ideal animal models. With recent advances in molecular biology and molecular genetics, great strides have been made in understanding MD, although no one single theory of pathogenesis has yet to become universally accepted. This inability to provide a unifying explanation for the clinical picture of MD prevents any significant translational application for more targeted and effective treatments. Lack of a unifying or single etiology likely reflects the clinically and genetically heterogeneous nature of MD and thus the lack of efficacy of any single treatment. Perhaps the most important result of ongoing research will be the earlier identification of patients with MD so that possible preventative measures can be taken. The reader is referred to Semaan et al.'s excellent review of ongoing basic science work in MD.

SURGERY FOR MD

Although the focus of this paper is the medical management of MD, no discussion can be complete without a few brief words on surgical intervention. When considering surgical intervention for MD, one must realize that the goal is primarily a quality of life issue because none of the surgical options (endolymphatic sac surgery, vestibular nerve section, cochleosacculotomy, transcanal or transmastoid labyrinthectomy) result in significantly changed long-term hearing outcome. Simply put, surgery does not address the underlying disease process, and therefore a "cure" is not possible. Using questionnaires, Söderman et al.[95] found no difference in overall quality between patients treated conservatively, surgically, or with ITG. Nonetheless, surgical intervention can play a valuable role in the management of patients with MD who fail to adequately respond to initial measures. Proper analysis would require an equally long discussion and is beyond the scope of this review. The reader is strongly encouraged to review recent literature regarding surgical options and outcomes for the management of MD.

CONCLUSION

In the absence of relevant clinical studies, the medical management of MD remains empirical, with the use of lifestyle changes, pharmacotherapy, and office-based procedures. The development of transtympanic therapies represents a true advance in therapeutics that has largely supplanted surgical intervention. Only with increasing understanding through continued high-quality basic, translational, and clinical research can we shift our management paradigm from that of control to that of cure. Until then, we offer our treatment algorithm as a guideline for the management of this challenging yet rewarding patient population (Fig. 1).

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