

Allergy and Its Relation to Meniere's Disease

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KEYWORDS

• Meniere's disease • Vertigo • Tinnitus • Hearing loss

In 1861, Prosper Ménière first associated dizziness with the inner ear.¹ Later, the syndrome of fluctuating sensorineural hearing loss, episodic vertigo, and tinnitus was named after him. Subsequently, the pathogenesis of Meniere's disease (MD) was found to be a hydropic distension of the endolymphatic system. In its guidelines for MD diagnosis and evaluation of treatment, the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) describes MD as a "clinical disorder defined as the idiopathic syndrome of endolymphatic hydrops... For clinical purposes (treatment and reporting), the presence of endolymphatic hydrops can be inferred during life by the presence of the syndrome of endolymphatic hydrops. This syndrome is defined as the presence of... recurrent, spontaneous, episodic vertigo; hearing loss; aural fullness; and tinnitus."² AAO-HNS guidelines further define the vertigo episodes as a "spontaneous rotational vertigo lasting at least 20 minutes." **Box 1** lists the classification of MD based on the AAO-HNS criteria.

The initial vertigo attack—the feeling of intense motion when sitting or standing still—can cause the subject to fall to the ground and is accompanied by nausea and vomiting. An incidence of 15 per 100,000 and a prevalence of 218 per 100,000 have been reported for MD in the United States.⁴ Although idiopathic, MD has been ascribed to various causes, including trauma, viral infections, metabolic disorders, allergies, and autoimmune factors. The first author emphasizes that MD, at the time of writing, is idiopathic. She believes that there may be some genetic predisposition to the development of MD and/or endolymphatic hydrops, with the final "insult" resulting in disease development being inflammatory or a dysregulation of ion channels. She does not believe that MD, per se, is caused by allergies; rather, in some patients who probably have a genetic predisposition, an allergic reaction produced by a food and/or inhalant allergen may stimulate an inflammatory reaction resulting in the development of symptoms. In this article, the authors specifically look at the evidence, historical and

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Box 1**Classification of Meniere's Disease based on the AAO-HNS criteria****Certain Meniere's Disease**

- Definite MD plus histopathologic confirmation

Definite Meniere's Disease

- Two or more definite spontaneous episodes of rotational vertigo for 20 minutes or longer
- Audiometrically documented hearing loss (uni- or bilateral) on at least one occasion
- Tinnitus or aural fullness in the affected ear
- Other causes excluded, such as vestibular schwannoma

Probable Meniere's Disease

- One definite episode of rotational vertigo
- Audiometrically documented hearing loss (uni- or bilateral) on at least one occasion
- Tinnitus or aural fullness in the affected ear
- Other causes excluded

Possible Meniere's Disease

- Episodic vertigo of the Meniere's type without documented hearing loss, or
- Sensorineural hearing loss (uni- or bilateral, fluctuating or fixed, with dysequilibrium but without definite episodes of vertigo
- Other causes excluded³

current, linking some cases of MD to an underlying allergic state and do not address other potential stimuli, such as viral antigen or autoimmune reaction other than the Type I Gell and Coombs reaction characterized by allergy.

In this article, the authors review the immunology of the inner ear followed by literature from 2002 to 2009 on MD, allergy, and autoimmunity.

REVIEW OF IMMUNOLOGY

The inner ear has little exposure to pathogens and few resident cells that are associated with immunologic function. In the past, this led to assumptions that it was immunologically privileged, similar to the brain. More recent research indicates that the inner ear is actually more immunoresponsive than the brain.⁵ The labyrinth exhibits a blood-labyrinthine barrier analogous to the blood-brain barrier, which maintains the cochlea's unique ionic characteristics. There is no lymphatic drainage from the inner ear, and, although immunoglobulins are present in the perilymph, the amount is only one-thousandth of that in the serum.⁶

The inner ear demonstrates cellular and humoral immunity. Most leukocytes enter the cochlea via the spiral modiolar vein.⁷ The innate immunity of the cochlea has been suggested to allow an adaptive local response to antigen challenge.⁸ Hashimoto and colleagues⁸ have suggested that the inner ear may be primed by lipopolysaccharides or other viral or bacterial antigens, resulting in the upregulation of interleukin (IL)-1C in the spiral ligament fibrocytes permitting leukocytes to enter. Subsequently, in those having lymphocytes primed to react against inner-ear antigens, an initiated immune response may result in local inflammation. Altermatt and colleagues⁹ have suggested that the seat of immunoactivity in the inner ear seems to be the endolymphatic sac

(ES) and duct. Immunoglobulin (Ig) G, IgM, IgA, and secretory component are found in the ES, and numerous plasma cells and macrophages reside in the perisaccular connective tissue.

Additionally, the labyrinth exhibits active components of allergic reactivity. Mast cells have been identified in the perisaccular connective tissue. Following sensitization, IgE-mediated degranulation of mast cells has resulted in eosinophilic infiltration of the perisaccular connective tissue, and, clinically, the production of endolymphatic hydrops.¹⁰

The ES is capable of processing antigen and producing its own local antibody response.^{11,12} Surgical destruction of the ES results in decreased antigen and antibody responses.¹² The highly vascular subepithelial space of the ES contains numerous fenestrated blood vessels,¹³ with arterial branches of the posterior meningeal artery supplying the ES and duct.¹⁴ Although the labyrinth is protected by the blood-labyrinthine barrier, the posterior meningeal artery is fenestrated, offering a peripheral portal of circulation. Fenestrated vessels supplying organs involved in absorption (eg, kidney, choroid) are especially susceptible to damage by immune complex deposition.

Despite evidence of immune activity, only 30% of patients with MD show a true autoantibody response on Western blot assay to specific antiochlear antibody.¹⁵ Tests of abnormal cell-mediated immunity are either inconsistent or normal, even in patients with known causes of inner ear autoimmune dysfunction, including Cogan syndrome.¹⁵ Despite increased understanding of labyrinthine immunoreactivity, a reliable laboratory marker has not been developed to prove autoimmune or allergic causation in patients with suspected inflammatory hearing loss.

POSSIBLE MECHANISMS INVOLVING ALLERGY

The first published report that MD was believed to be provoked by an allergic reaction was in 1923.¹⁶ Inhalant and food allergies have been linked with MD symptoms.¹⁷ Many of MD's clinical characteristics suggest an underlying inflammatory, if not autoimmune, cause, such as its propensity to wax and wane with periods of remission. It is also bilateral in a significant number of cases.^{18,19}

There are different possible mechanisms by which an allergic reaction produces MD symptoms.²⁰ First, the ES itself could be a target organ of the allergic reaction. The sac's peripheral and fenestrated blood vessels could allow antigen entry, stimulating mast cell degranulation in the perisaccular connective tissue. The resulting inflammatory mediator release could affect the sac's filtering capability, resulting in a toxic accumulation of metabolic products and interfering with hair cell function. Also, the fenestrated blood vessels to the ES could be pharmacologically vulnerable to the effects of vasoactive mediators such as histamine, which are released in a distal allergic reaction. The unique blood supply of the interosseous ES would serve as a portal for these mediators to exert a direct pharmacologic effect. The potent vasodilating effects of histamine or other mediators could affect the resorptive capacity of the ES. Yan and colleagues²¹ have shown that Waldeyer ring in the nasopharynx is the anatomic site of T-cell homing to the ES. In systemically sensitized rodents, intranasal antigen stimulation with keyhole limpet hemocyanin in Waldeyer ring resulted in an antigen-specific reaction in the ES and perilymphatic vessels, suggesting that viral or allergic antigen could be processed in the nasopharynx with the resulting specific immune reaction occurring at the ES.

A second possible mechanism involves the production of a circulating immune complex, such as a food antigen, which is then deposited through the fenestrated

blood vessels of the ES, producing inflammation. An increased incidence of circulating immune complexes in the serum has been described in MD and allergic rhinitis.^{22,23} The inflammatory response resulting from the deposition of immune complexes along vascular basement membranes is the hallmark of an immune complex disease. Although the binding of the complexes to the cell membranes facilitates their phagocytosis, it also results in the release of tissue-damaging enzymes. This is believed to be the mechanism of unexplained sensorineural hearing loss in patients with Wegener granulomatosis, a prototype immune-complex-mediated disease. On examining the temporal bones of patients with Wegener granulomatosis and unexplained sensorineural hearing loss, the cochlea is found to be normal; the pathology occurs in the ES.²⁴

Alternatively, circulating immune complexes may be deposited in the stria, causing the normally intact blood-labyrinthine barrier to leak as a result of increased vascular permeability. In addition to disrupting normal ionic and fluid balance in the extracapillary spaces, this could facilitate the entry of autoantibodies into the inner ear.

A third possible mechanism is a viral antigen-allergic interaction. A predisposing viral upper respiratory infection in childhood (eg, mumps, herpes) antigenically stimulates Waldeyer ring, with subsequent T-cell homing to the ES,²¹ resulting in a chronic low-grade inflammation. This is not enough initially to result in hearing loss or vertigo, but it does produce mild impairment of ES absorption. Later in adult life, something in the system stimulates excess fluid production. Several investigators have assumed that viral infections play a direct or indirect role in the cause of MD. Viruses are also capable of exacerbating allergic symptoms by several mechanisms. Live and ultraviolet light-inactivated viruses have been shown to enhance histamine release, an effect believed to be mediated by interferon. Viruses can also damage epithelial surfaces, thereby enhancing antigen entry and increasing the responsiveness of target organs to histamine. It has long been noted that patients with poorly controlled allergy are more likely than nonallergic persons to develop upper and lower respiratory viral infections.

EPIDEMIOLOGY

In a survey the authors performed of 734 patients with MD, the prevalence of skin test-confirmed concurrent allergic disease was 41%.²⁵ Although the prevalence of allergic rhinitis is often quoted as 20% or more, the recent Allergies in America report, the largest survey to date regarding prevalence and disease burden of allergic rhinitis, found that physician-diagnosed allergic rhinitis in patients with rhinitic symptoms is 14%.²⁶ Hence, the prevalence of physician-diagnosed allergy in American patients diagnosed with MD is almost 3 times that of the general population.²⁵ In a more recent survey of patients with MD, the authors found that patients reported a 58% rate of allergy history, and again, a 41% rate of positive skin or in vitro test.¹⁹

In his original description, Prosper Ménière suggested an association between migraine and MD.¹ Many authors have subsequently noted paroxysmal headache independently occurring in many patients with MD.²⁷⁻²⁹ Radtke and colleagues³⁰ published a well-designed prospective trial based on strict diagnostic criteria, which established an increased lifetime prevalence of migraine in patients diagnosed with MD.

A recent study reported an increased incidence of self-reported migraine and allergic rhinitis in patients with MD, as compared with a control group of age- and sex-matched patients without MD attending an otolaryngology clinic.³¹ Sen and colleagues³¹ used a Web-based questionnaire to recruit 108 patients with MD and a control group of 100 patients attending the otolaryngology clinic for other problems. The migraine prevalence in MD sufferers was 39% compared with 18% in the

control group, whereas the prevalence of allergy in those with MD was 51.9% compared with 23% in the control group. In the MD group, a history of allergy was significantly more prevalent in patients with migraine (71%) than in those without migraine (39%). There was no such link between allergy and migraine in the control group, with the combination of allergy and migraine 9 times more prevalent in the MD group (adds ratio 9.23; 95% confidence interval 3.11–27.32).

The study by Sen and colleagues³¹ is interesting because it suggests that in that large subset of patients with MD who also have migraine, the vast majority report an additional diagnosis of allergy. One weakness of their Web-based questionnaire is that the allergy history is obtained by asking subjects whether they or their family members suffer from any allergy, without confirmatory skin or in vitro testing. However, all patients—control and MD groups—were asked the same question and gave such differing responses as to add credence to the supposition that there is a much higher incidence of allergy and migraine in patients with M.D.

More recently, Ibekwe and colleagues³² reported that 32% of patients presenting to a clinic in Nigeria and diagnosed by an otolaryngologist with MD also had associated features of migraine, compared with 5.3% of the overall population. Migraine without aura (“common migraine”) was the most common presentation, occurring in approximately 62.5% of patients. This study shows that a history of allergy is much more common in patients with MD and migraine than in those without migraine. The investigators suggest that the vasodilatory effects of allergy or possible extravasations of immune complexes may serve as a common pathway for migraine and MD. Although a weakness of this paper is the small number of patients reported, there is a striking similarity in the prevalence of migraine in this study and that reported by Sen.

Although the list of causes for migraine is extensive, it has long been noted that allergic reactions were a common trigger in many sufferers. There are striking similarities in symptom presentation and vascular changes between MD, allergy, and migraines. All 3 tend to recur cyclically, and sufferers are often able to note a cause and effect between a particular suspected “exposure” or event and the subsequent development of symptoms. All the entities also show similar vascular changes during the course of symptom production: vasoconstriction, vasodilatation, and plasma extravasations. There is an elevation in IgG-containing immune complexes in the meningeal vessels of patients with migraine and in the subepithelial layer of the ES in patients with MD.³² The elevated level of circulating immune complexes in MD has already been mentioned.²³

Ibekwe hypothesized that there may be a common defective ion channel in both disease states, with the predominant expression in the inner ear and brain, resulting in a local increase in extracellular potassium and the production of symptoms.

PATHOPHYSIOLOGY

Paparella and Djalilian³³ provide an excellent article for the practitioner of the temporal bone correlates of the clinical symptoms of MD. They review various theorized causes of MD symptoms including allergy. They conclude that the fundamental cause of MD is probably a multifactorial inheritance, suggesting that the most likely predisposing factors are hypoplasia of the mastoid air cell system, vestibular aqueduct, and ES and the other physical abnormalities that have been frequently reported in patients with MD.

The authors also believe that MD is probably multifactorial in cause. It is not their contention that MD is caused by allergy. However, if they accept that most patients with MD do have an anatomic abnormality including a smaller than average ES size,

factors that may affect either excessive endolymph production or reduction of endolymph absorption may promote MD symptoms. Inflammatory stimulation by an inhaled or ingested allergen in a genetically predisposed individual should be considered as one possible trigger.

IMMUNOPATHOLOGY

Savastano and colleagues³⁴ studied the validity of serologic nonspecific immune tests in determining a possible role of immunopathology in a series of 200 patients with MD compared with a control group of 50 healthy blood donors. All patients and controls had no known diagnosis of autoimmune disease or steroid treatment. Results indicated negative or insignificant levels of IgG, IgM, IgA, erythrocyte sedimentation rate, C-reactive protein, complement factors, and cryoglobulins in most patients. However, more than half had significant elevations in levels of circulating immune complexes. Rates of elevation of circulating immune complexes, lymphocyte subpopulations (especially IL-2 receptor), and autoantibodies were higher in the MD group than in controls.

Savastano and colleagues³⁴ also attempted to relate immunologic findings to disease severity, using the 1985 AAO-HNS Pearson and Brackmann classification of disability for reporting results in MD treatment (it is unclear why they did not use the currently accepted AAO-HNS functional disability scale from the 1995 guidelines). In the 1985 system, grade I exhibits mild or no disability, with intermittent or continuous dizziness precluding work in a hazardous environment; grade II, moderate disability with intermittent or continuous dizziness/unsteadiness requiring employment in a sedentary occupation; and grade III, severe disability/disabling symptoms precluding gainful employment. There was a significant relationship between disease severity and test abnormalities for circulating immune complexes, CD4, and CD4-to-CD8 ratio, with the highest rate of serologic abnormalities found in group III with disabling symptoms and the lowest rate, in group I. A trend was also found for differences in C-reactive protein, C3 complement, and early T-activation.

Elevated circulating immune complexes in patients with MD have been reported by Brookes²² and by Derebery and colleagues.²³ It would have been interesting for Savastano and colleagues³⁴ to have done a subanalysis of patients with bilateral MD (not identified in the text). Derebery and colleagues²³ have found a direct relationship between larger elevations in circulating immune complexes and disease bilaterality.

The study by Savastano and colleagues³⁴ adds credence to a possible underlying inflammatory cause in most patients with MD. The investigators suggest that monitoring serum levels of circulating immune complexes, CD4, and CD4-to-CD8 ratios may be useful as prognostic markers of disease progression. However, they did not elaborate on possible treatments, immune-suppressive or allergic, resulting from their conclusions.

Keles and colleagues³⁵ performed another study of MD immunopathology; they attempted to evaluate the possible role of allergy in producing MD symptoms by examining the cytokine profiles, allergic parameters, and lymphocyte subgroups of patients with MD versus controls.

Forty-six adult patients with classic MD were compared with an identical number of healthy volunteers in the same age group and socioeconomic class living in the same region of Turkey. These researchers performed an extensive immune profile, measuring monoclonal CD4, CD8, CD23 antibodies, interferon (IFN)-H, IL-4, total

serum IgE, and antigen-specific IgE pertaining to regionally important tree pollens, molds, and common foods in the local diet.

Significant differences were found between the patients with MD and the controls in CD4, CD4/CD8, CD23, IFN- γ , and IL-4 levels. Keles and colleagues³⁵ also found significant positive correlations between levels of CD23 and total serum IgE, CD8 and total serum IgE, CD4/CD8 and IgE, and CD23 and CD8, although correlation coefficients were not provided for the reader to determine strength of the relationships. Elevation of total serum IgE was found in 43.3% of the MD group compared with only 19.5% of the control group. Additionally, 67.3% of the patients with MD gave a positive history of allergy, whereas the same was found in only 34.7% of the control group. Significant elevations of antigen-specific IgE in the patients with MD were not present in the control group.

Keles and colleagues³⁵ suggest that future therapies could potentially be beneficial, such as suppressing production of IL-4 and IL-1 or stimulating a helper T1 (T_H1) cell predominance by the application of BCG vaccine. This study does not change the current treatment parameters for MD. However, it documents that unselected patients with MD have serologic findings that correlate strongly with atopy.

TREATMENT

The authors review several studies related to treatment of MD on immunologic aspects of the disease. Jeck-Thole and Wagner³⁶ published a review of safety data on betahistine, which is often sold under the trade name Serc (Solvay Pharmaceuticals, Marietta, GA, USA). Betahistine contains a structural analogue of histamine and is prescribed in the treatment of vestibular disorders such as MD for symptomatic treatment of vertigo. Betahistine is said to be the most commonly prescribed medication for MD. Although not currently available in the United States, it can be obtained by compounding pharmacies or through sources in Canada or Europe. The typical adult dose is 16 mg thrice daily. The reader occasionally may see a patient with MD using betahistine and reporting good clinical results.

In the United States, the most commonly prescribed medications for treating symptoms of MD are antihistamines (eg, meclizine, diphenhydramine, dimenhydrinate). Therefore, it might appear to be counterintuitive to prescribe a histamine analogue to treat these same symptoms. In tissue, histamine is primarily stored in mast cells and may be released by various drugs, venoms, or allergens, resulting in hypersensitivity reactions, gastric acid secretion, and increased capillary permeability. In association with the peripheral actions of histamine, its function as a central neurotransmitter was postulated. Subsequently, various receptor subtypes were described, including histamine H₁, H₂, H₃ and, eventually, H₄.^{37,38}

Betahistine acts as a neurotransmitter modulator of the complex histaminergic receptor system with no known affinity for any other receptors.³⁹ Betahistine is a weak partial H₁-receptor agonist with a distinctly lower affinity than histamine. It has almost no affinity for the H₂ receptor, having extremely weak effects on gastric secretion.⁴⁰ In contrast, betahistine shows a potent antagonistic effect on the H₃ receptor. The H₃ heteroreceptor, belonging to a class of presynaptic receptors, is involved in the synthesis and release of histamine and other neurotransmitters, including dopamine, γ -aminobutyric acid, acetylcholine, norepinephrine, and serotonin.⁴¹ Actions that are mediated by the H₁ receptor are blocked by negative H₃-receptor feedback. Betahistine has an antagonistic effect on the H₃ receptor followed by an increased histamine release. Betahistine's H₃-receptor antagonistic action is believed to be responsible for improvement in the inner ear microcirculation and

subsequent reduction of endolymphatic pressure.^{42,43} Betahistine has also been shown to inhibit the basal spike generation of the vestibular neurons in the lateral and medial vestibular nuclei, both crucial for controlling posture. A recent meta-analysis of treatment with betahistine in treating vertigo in non-MD patients has shown it to be efficacious.⁴⁴

In terms of side effects or drug interaction, betahistine is nonsedating and free from psychomotor impairment. Theoretically, because betahistine and histamine are similar, betahistine could interact with an antihistaminic agent, such as diphenhydramine or cetirizine, or even induce or support hypersensitivity reactions with regard to the H₁-agonistic quality. However, betahistine affinity at the receptor site has been shown to be significantly weaker than histamine affinity. Betahistine-induced histamine release from mast cells has also not been described.⁴⁵

INDICATIONS FOR TESTING

Classically, Powers described suggestive history including a seasonal relationship of symptoms (eg, hearing loss, vertigo attacks) and the presence of other symptoms suggesting allergy, such as rhinitis, as indicators.¹⁷ These are actually a useful guide. The first author feels that other details of history are useful guides, including bilateral symptoms, strong family history of allergy, a history of childhood allergy that one has outgrown, and obvious factors such as the production of MD symptoms within a short time after exposure to a food or inhaled antigen.

There are varying thoughts on the relative sensitivity versus specificity of various tests, including intradermal, intradermal titration, intradermal dilutional provocative food testing, and *in vitro*. Readers are encouraged to perform their own review of the subject. The authors would suggest that irrespective of testing type, the patient be tested with inhalant and food antigens, despite the acknowledged lesser sensitivity of food testing when compared with inhalant.

Their preferred method of testing is intradermal titration, or, less so, prick testing, with single dilution intradermal testing in the case of negative results with a prick test. They have observed that the reactivity of patients with suspected inhalant allergic triggers to their MD symptoms is often relatively low, typically in the range of 1/500 weight/volume of antigen.⁴⁶ Likewise, Topuz and colleagues⁴⁷ also noted that there was a large increase of abnormal electrocochleographic (ECOG) results from pre-prick testing to post-testing in patients with MD (29% of diseased ears vs 78% post-testing) and that the inner ear did not appear to require a strong antigen dose to be objectively stimulated. Similar ECOG changes have also been noted in patients with MD who have been tested with dietary antigen stimulation by provocative food testing, nasal provocation with inhalant antigens, and prick testing.⁴⁸ The purpose of testing for allergy is to establish objectively whether a patient is allergic to a particular allergen rather than to infer that the amount of antigen that produces a positive skin test directly relates to the type or severity of induced symptoms.

TREATMENT OUTCOME STUDIES

The authors used a questionnaire on symptoms to evaluate the effect of specific allergy immunotherapy and food elimination of suspected food allergens on patients with MD for whom allergy treatment had been recommended.²⁰ The 113 patients treated by desensitization and diet showed a significant improvement in allergy and MD symptoms after treatment. The patient ratings of frequency, severity, and interference with daily activities of their MD symptoms also seemed better after allergy treatment compared with ratings from the control group of 24 untreated patients. Results

indicated that patients with MD can show improvement in tinnitus and vertigo symptoms when receiving specific allergy therapy, suggesting that the inner ear may also be a direct or indirect target of an allergic reaction.

Because the study asked patients to retrospectively rate their pretreatment symptoms, a prospective study was undertaken in which 68 patients completed the questionnaire before and at an average of 23 months after treatment.⁴⁹ Severity of vertigo, tinnitus, and unsteadiness decreased significantly, as did frequency of vertigo, frequency and interference of unsteadiness, and ratings on the AAO-HNS disability scale. Quality of life improved significantly on 4 of 8 Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) scales. Initial SF-36 scores indicated that patients with MD and allergy have poorer scores than the general US adult population on several quality-of-life aspects. Paired comparisons between SF-36 scale scores at initial and follow-up intervals identified significant improvements in subtests that were less than normal initially. Statistical analyses strongly suggested that these improvements were independent of natural history and of other medical treatment for MD that the patients may have received during the immunotherapy period.

A weakness of these and other studies is that there are no control groups receiving saline injections or given diets eliminating foods that were negative on testing. The authors have observed that patients with MD are reluctant to commit to months or a year of possible placebo injections to prove that immunotherapy may help improve symptoms of vertigo, hearing loss, and/or tinnitus. Presently, they rely on using statistical control and research that demonstrates the ability of allergy immunotherapy to down-regulate T_H2 cell-driven inflammatory responses in patients with allergic rhinitis and asthma.⁵⁰ If MD is believed to be a chronic condition with an inflammatory component, it is logical that down-regulating the production and release of proinflammatory and vasoactive mediators promoting fluid extravasation and/or retention could help lessen symptoms. This is the rationale for using steroids and restricting dietary salt in patients with MD.

The classic first-generation antihistamines commonly used for their desired anticholinergic effects to lessen vertigo severity do not change the underlying pathology of hydropic distention of the endolymphatic space. Pharmacologically, these agents have limited effect and do not block the effects of other inflammatory mediators, such as leukotrienes, released with mast cell degranulation. In the authors' experience, nonsedating antihistamines have limited benefit in treating vertigo and/or dizziness. Effective immunotherapy with its induced immunologic changes can prevent mast cell degranulation. Additionally, an appropriate elimination diet for documented food allergies can prevent an immune-mediated reaction.

In the authors' clinical experience, the symptoms of MD are generally better controlled, with fewer vertigo attacks and more stable hearing, in those patients with allergy and MD whose underlying allergic disorder is down-regulated with immunotherapy and/or dietary avoidance of reactive food allergens. The ideal proof of the role of allergy in a large subset of patients who develop MD would be a double-blind, placebo-controlled trial of immunotherapy for the minimum of 2 years, as required by the AAO-HNS for evaluating the effects of surgical procedures for MD; however, realistically, recruiting patients for such a study would be a challenge because of the potentially disabling symptoms of MD.

SUMMARY

The prevalence of migraine and atopy is much higher in patients with MD than in the normal population. Unselected patients with MD have serologic findings that correlate

with underlying atopy and inflammation. Indications for allergy testing in a patient with MD should include a seasonal or food relationship to symptom production, a known history of allergy or clear allergic symptoms in a patient with MD, and a known past childhood history or a strong family history of allergy. Additional consideration should be given for testing in those patients with bilateral MD. Although there are no double-blind, placebo-controlled trials comparing outcomes of patients with MD treated with specific allergy immunotherapy, clinical case reports strongly suggest that such treatment lessens severity and frequency of vertigo and results in more stable hearing. Objective outcomes of successful medical and surgical treatment of MD symptoms have been established and published and may be used as a reference for assessing treatment response by specific allergy immunotherapy or dietary elimination of food allergy.

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