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Ménière's Disease Review 2005

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Abstract

Ménière's disease (MD) is a complex, multifactorial disorder of the inner ear that is the most common cause of the syndrome of episodic vertigo combined with fluctuating hearing loss. In spite of a century of investigation, the etiology and pathophysiology of MD remain controversial and incompletely understood. Among the factors that have contributed to these controversies are the absence of (1) a validated clinical test, (2) an appropriate animal model, and (3) a specific treatment. Nonetheless, physicians are able to assist MD patients with a variety of tailored, symptom-specific medications and therapies. Given that the vertigo induced by MD, in general, is self-limited, the long-term outlook for balance function is good. The same cannot be said for the hearing dysfunction of MD.

Key Words: Ménière's disease, hydrops, otoacoustic emissions, vertigo, vestibular, therapy, treatment

Abbreviations: MD = Ménière's disease

Sumario

La enfermedad de Ménière (MD) es un trastorno complejo y multifactorial del oído interno, que resulta en la causa más común del síndrome de vértigo episódico combinado con hipoacusia fluctuante. A pesar de un siglo de investigaciones, la etiología y la fisiopatología de la MD continúa siendo controversial e incompletamente entendida. Entre los factores que han contribuido a esta controversia encontramos la ausencia de (1) una prueba clínica validada, (2) un modelo animal apropiado, y (3) un tratamiento específico. Sin embargo, los médicos pueden ayudar a los pacientes con MD usando una variedad de medicamentos y terapias para atacar síntomas específicos. Dado que en general el vértigo de la MD es autolimitado, el resultado a largo plazo para la función del balance es bueno. No se puede decir lo mismo para la disfunción auditiva de la MD.

Palabras Clave: Enfermedad de Ménière, hydrops, emisiones otoacústicas, vértigo, vestibular, terapia, tratamiento

Abreviaturas: MD = enfermedad de Ménière

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Prospere Ménière was a French physician who identified the inner ear as the source of the symptoms of vertigo, tinnitus, and hearing loss. At the time, cerebellar disorders were considered to cause these symptoms. His patient, the subject of a famous report to the Royal Academy of Medicine of Paris at its weekly meeting on January 12, 1861, actually had bilateral cochlear hemorrhages of unknown cause. Thus, even Ménière's patient did not have what we now view as Ménière's disease. Nonetheless, he is properly credited with making an important advance in knowledge of cochlear pathology and function.

A PubMed search done during the writing of this review using "Ménière's" as the keyword returned a list of 5,675 citations, which suggests that investigators are continuing to pursue ways and means to unravel the complex web of theories and counter-theories proffered to explain this enigmatic disorder. The final answers to the many questions about etiology, pathophysiology, and therapy have yet to be found. Nonetheless, an analysis of the current theories is appropriate and potentially useful. Time and space do not permit an exhaustive review. Therefore, only those areas that have received recent attention are discussed in any detail.

CLINICAL FEATURES

Classic Ménière's disease (MD) is manifested clinically by the symptoms of episodic vertigo associated with fluctuating hearing loss, tinnitus, and fullness all in the same ear. Variant forms of the disease (MD without hearing loss, MD without vertigo) have been postulated. This review focuses on classic unilateral MD.

Vertigo, from the Latin "I turn," is a sensation of motion of the individual or the environment associated with nystagmus, the rhythmic back and forth eye movement that has both a slow and a quick component. Vertigo associated with MD is irritative in nature, that is, the slow component of the nystagmus is away from the affected ear during an attack. However, since nystagmus is named according to its quick component, the direction of irritative nystagmus is toward the affected ear. Typically, the vertigo begins fairly quickly and builds in intensity over minutes to hours. When severe, nausea and vomiting may occur. Movement during a vertigo attack worsens the nausea, so patients learn quickly to stay motionless during an attack. The vertigo usually lasts more than 20 minutes and rarely more than 24 hours.

MD affects both genders equally and is most common in 40–55 year olds, with a median age of onset of 51 years. The yearly number of new cases was estimated at from 15/100,000 in 1984 in Rochester, Minnesota (Wladislavosky et al, 1984) and 17/100,000 population in Japan (Watanabe, 1995) to 46/100,000 in Sweden.(Stahle et al, 1978) Based on the estimate from Rochester (Wladislavosky et al, 1984), about 46,000 new cases develop annually in the United States. Ménière's disease is encountered worldwide. Because the vast majority of people have no ear-related symptoms prior to the onset of the disorder, MD has all the epidemiologic hallmarks of an acquired disorder. Putative theories of etiology must take this fact into account.

The clinical course for any given patient is unpredictable, reflecting the capricious nature of the disorder. About 70% of patients respond to conservative medical management (Torok, 1977); 30% respond poorly and often require surgical therapy to control symptoms (Torok, 1977). The long-term treatment results are generally acceptable for the majority of cases, but the indications for, and methods of, medical and surgical therapy vary widely.

Although MD is nonfatal, it results in reduced activity, time lost from work, and diminished quality of life. During major vertigo attacks, the MD sufferer is unable to perform any productive activity and usually has to lie down for several hours until the attack subsides. Treatment costs for MD are unknown but are clearly nontrivial owing to the many complex procedures used for symptom control.

Diverse theories exist to explain the pathophysiology of MD. Expansion of the endolymphatic spaces (hydrops) has been observed in the temporal bones of people having symptoms and signs of MD (Hallpike and Cairns, 1938; Yamakawa, 1938). Indeed, hydrops is both the histologic hallmark of MD and the working concept of its pathogenesis. Paradoxically, not all people with symptoms of MD have hydrops, and not all people with hydrops discovered at autopsy had symptoms during life. Numerous investigations have suggested that the symptoms of MD originate from a disturbance

in the volume/pressure relationship of the endolymph. It is not known whether hydrops is the cause of the symptoms or simply a side effect of the disorder.

The mechanism whereby hydrops produces symptoms is controversial (Gibson and Arenberg, 1997). The increased volume of endolymph is likely due to fluid overproduction; however, deficient absorptive mechanisms have also been considered. The classic animal model of hydrops developed by Kimura (1976), which relied on surgical obstruction on the endolymphatic duct, implied that blockage of endolymph "flow" was a factor. However, this animal model does not result in anything resembling attacks of vertigo, even though a predictable low-tone hearing loss occurs. This concept also requires that endolymph is produced in the cochlea and semicircular canals and is resorbed in the endolymphatic sac. Salt has shown that endolymph does not flow longitudinally from source to sac under normal conditions (Salt and DeMott, 1994), but endolymph will flow into the endolymphatic sac under abnormal conditions. In other words, normal endolymph production and resorption is radial rather than longitudinal. Thus, theories of pathogenesis based on the concept of endolymph flow must be reexamined in the light of this new evidence.

Many etiologic theories of MD and many experimental models have focused on dysfunction of the endolymphatic sac as the cause of the hydrops. Given that the vast majority of cases of MD are unilateral and nonfamilial, it is likely that some extrinsic event precedes the onset of the disorder. Viral infection of endolymphatic sac was proposed by Shucknecht (1975) as the trigger event that disrupts the normal endolymphatic fluid control mechanisms. Indeed, this theory accounts for more of the clinical findings than any other. Metabolic, hormonal, allergic, genetic, and stress factors have also been implicated over the years, but direct evidence for how these agents act in a unilateral fashion is sparse. These are generally regarded as stressors rather than etiologic agents. Considering the common observation that the endolymphatic sac on the affected side is small and inferiorally displaced (Paparella, 1985), it may be the case that the anatomic variation is a precondition for the development of symptoms from an acquired trigger event. In the vast majority of cases, no clear etiology is found, and the diagnosis of idiopathic Ménière's disease is made by exclusion.

Other disorders have symptoms similar to those of classic Ménière's disease. Basilar migraine is a common imitator (Baloh, 1997). Vascular loops in the internal auditory canal may cause imbalance but seldom results in vertigo similar to MD (McCabe and Harker, 1983). Autoimmune inner ear disease is also associated with bilateral fluctuating hearing loss and vertigo.(Hughes et al, 1983). However, Rauch and colleagues (Rauch et al, 2000) found no convincing evidence for autoimmunity as a factor in Ménière's disease. The similarity of symptoms among these disorders does not infer commonality of causation. Rather, they attest to the limited symptom set associated with the vestibular labyrinth and its central connections.

The issues related to the etiology of bilateral Ménière's disease have not been resolved. It may be the case that some individuals do develop a true autoimmune process in the second ear. It is also the case that there is a positive family history in 5% of cases (Morrison et al, 1994). These cases may be considered as the exception rather the rule for typical MD and, possibly, the manifestation of a different disorder. It is entirely plausible, but unproven, that several underlying conditions may result in a common final clinical pathway.

The function of the endolymphatic sac is not fully understood. Many have hypothesized that the sac exists primarily to resorb fluid. Although some have noted the absence of cytologic features normally associated with fluid resorption (Stankovic et al, 1995), recent work indicates the presence of aquaporin receptors in the lateral wall fibrocytes (Stankovic et al, 1995) and in the endolymphatic sac (Couloigner et al, 2004). Hydrops has been noted after chronic administration of vasopression, which suggests an alternative mechanism (Naftalin, 2001).

Qvortrup and colleagues (Qvortrup et al, 1996) noted histologic features of the sac that resembled endocrine organelles. They then demonstrated the presence of a naturietic hormone in the rodent endolymphatic sac, which was termed "saccin." The chemical nature of this hormone has yet to be established, but the histologic criteria for designation of the sac as an endocrine gland have been fulfilled (Qvortrup et al, 1999). If, as postulated, the

endolymphatic sac participates in the central regulation of serum sodium concentration, then the effect of sodium reduction therapy for people with Ménière's disease may, at last, have a logical explanation of effect. This finding, and the thesis of Gulya and Schuknecht (1982) that viral infection affects the endolymphatic sac, are compatible with the following hypothetical scenario: (1) excessive dietary intake stimulates saccin production; (2) the injured sac leaks saccin, which can diffuse upstream into the vestibular and cochlear areas (such as the stria vascularis) responsible for endolymph production; (3) the cells in the stria vascularis, being functionally similar to renal tubular epithelia, might respond to this adventitious saccin stimulation to excrete sodium into the endolymph; (4) fluid shifts would follow the ion transfer resulting in increased endolymph volume (hydrops). The generally beneficial effect of surgery on the endolymphatic sac, especially excision, might also be explained by physical down-regulation of saccin production.. Of course, such speculation remains conjectural and unproven. It is lamentable that further reports about saccin have not been made, which leaves this promising line of research in limbo.

CLINICAL EVALUATION

The diagnosis of Ménière's disease is made by a physician in view of the history, physical examination, and the results of clinical tests done to include Ménière's disease and exclude conditions that mimic Ménière's disease.

The history of typical spells of vertigo associated with increased aural symptoms (hearing loss, tinnitus, pressure) is essential for the diagnosis. In many early cases, the history is the sole clinical manifestation of the disorder. Atypical forms of Ménière's syndrome have been suspected on the basis of fluctuating hearing loss (cochlear hydrops) or episodic vertigo (vestibular hydrops). In some instances, the full-blown tetrad of symptoms occurs months or years after an atypical onset. Excluding other conditions (e.g., migraine) is important in people with atypical history.

Two stages of MD are recognized, an early fluctuant stage in which the hearing improves after an attack, and the late, so-called neural stage, where the hearing loss is more or less fixed at a moderate hearing loss level or worse. As a general rule, people in the fluctuant stage tend to respond favorably to medical therapy whereas those in the neural phase generally require more invasive therapy.

Audiometry in the early stages of MD usually reveals a low-frequency sensory hearing loss with recruitment, high Short Increment Sensitivity Index (SISI) scores, diplacusis, and normal stapedial reflex thresholds. The Alternate Binaural Loudness Balance test (Fowler test) is classically positive in MD cases. In between attacks, the hearing may return to normal or improve substantially. As the disorder progresses, hearing thresholds typically no longer fluctuate and remain poor. Dehydration testing with oral glycerol ingestion may show a >15% increase in word-recognition scores or >10 dB improvement in the pure-tone thresholds in about 50% of cases.(Morrison et al, 1980) Repeated audiograms showing fluctuation or a positive glycerol test are held to be evidence of cochlear hydrops. Glycerol testing is generally done only for cases in which the diagnosis is in doubt. The bad taste of the glycerol and the accompanying headache limit its acceptance. More importantly, the low sensitivity of the test (50%) leaves much to be desired for its use either as a confirmatory or a screening test.

Electrocochleography (ECochG) shows an elevated click-evoked summating potential in relation to the action potential (SP/AP) ratio of 0.4 or greater in about 50% of cases (Gibson and Prasher 1983) as well as a large proportion of normal subjects (Campbell et al, 1992) Tone-burst ECochG with transtympanic electrodes are held to be more sensitive and specific (Conlon and Gibson, 2000). However, tympanic membrane electrodes are easier to use and provide excellent recordings (Margolis et al, 1995)

Distortion-product otoacoustic emissions (DPOAEs) are objective measures of outer hair cell status. DPOAE audiometry is normal in about one-quarter of patients with MD and absent in late stage cases (van Huffelen et al, 1998). Human DPOAE in the hydropic ear is very sensitive to the effects of ingested glycerol and change from baseline more than the normal ear, and, in addition, the rate of change is earlier than the change in pure-tone thresholds or word recognition (Magliulo et al, 2001). However, not all hydropic ears showed change in DPOAE function after

glycerol ingestion.

Standard auditory brainstem responses (ABR) generally reflect the status of the pure-tone thresholds. Recently, Don has devised a new test paradigm, the High-Pass Noise-masked ABR (Don et al, 2005). This test measures the difference in wave V latency in the response to clicks presented alone and to clicks in the presence of high-pass pink masking noise. In the normal ear, there is a latency shift as more and more of the higher frequencies are masked by the pink noise. However, in the Ménière's ear, no such latency shift occurs, that is, there is undermasking. The sensitivity and specificity of this test in contrasting normal controls from Ménière's cases is very high, approaching 100% each. The test has not been evaluated in people with low-frequency hearing loss not due to Ménière's disease.

Vestibular testing is normal initially between attacks, but there is a gradual loss of sensitivity with repeated episodes. Spontaneous remission of vertigo spells is often associated with declining vestibular sensitivity in the affected ear. Radiographic examinations may show an abnormal vestibular aqueduct in the affected ear (Yazawa and Kitahara, 1994). Correlation of objective testing (ECochG, dehydration, CT findings) with prognosis has not been documented. The search for validated predictors of outcome continues. We found that an abnormal ENG (canal weakness of 30% or greater on bithermal caloric stimulation) is a predictor of subsequent decrease in vertigo (Gates et al, 2004)

TREATMENT

Treatment of MD is aimed primarily at control of vertigo attacks. All the procedures described below are mentioned from this perspective. While some patients note improvement in hearing as their vertigo improves, this is not predictable. Amplification therapy for the hearing loss of MD is outside the scope of this discussion. Fortunately, fully digital aids, which limit overstimulation, are reasonably effective in ameliorating the effects of loudness recruitment while compensating for the elevated thresholds of the affected ear.

The rationale for medical treatment of MD is based on the idea that decreasing the endolymphatic hydrops can be achieved by dietary sodium restriction, by diuresis

induced by diuretic drugs, or both. Additionally, efforts to limit caffeine intake and reduce stress are recommended by many physicians. While there is copious anecdotal evidence, the true success of salt restriction is unknown. The evidence of effectiveness of diuretic therapy is based on studies from the 1960s that have not been replicated with modern methods. Indications for surgical treatment are variable, and choice of which treatment to use is nonstandard. Although almost all physicians use medical therapy initially, there are no guidelines for duration or intensity of that therapy, nor are there generally accepted second-level treatments for those who fail the first-line treatment. Thus, there is considerable art in the medical management of people with MD.

Medical Therapy

A low salt diet has been the mainstay of therapy since 1931 when first advocated by Dederding of Copenhagen (1929), a female otolaryngologist who suffered from MD. However, the efficacy of this regimen has not been validated. Most physicians recommend a daily sodium intake not to exceed 1.5 gm. Although some patients report increased symptoms following salt ingestion, many do not. Sodium retention may result from endogenous hormonal responses to stress (Proctor et al, 1992). A 6 feeding diet to limit hyperinsulinism, with its secondary fluid retention, has been advocated (Proctor and Proctor, 1981).

Furstenberg and Lashmet (1934) recommended the low salt diet and ammonium chloride. Diamox has been evaluated several times with contradictory results (Varga et al, 1966; Brookes et al, 1982; Brookes and Booth, 1984). It is used less often now because agents that do not exhibit tachyphylaxis are available. Klockhoff and colleagues (Klockhoff et al 1974) compared the effect of hydrochlorthiazide versus placebo in 26 patients using a double-blind crossover trial. Their analysis showed a significant improvement in vertigo, tinnitus, and well being (general condition) with diuretic therapy. However, they did not measure the magnitude of the effect; rather, they used the patient's judgment of symptoms during each three month period as to improved, same, or worse. van Deelen and Huizing (1986) used the same study

methodology to compare the combination of hydrochlorthiazide and triamterene (Dyazide) to placebo, and they also noted a significant reduction in vertigo during the diuretic therapy as compared to the placebo. The use of three categories (better, worse, same) in these studies, rather than two (better, not better), introduces a measurement bias, because outcomes where placebo and treatment are comparable may, in fact, represent failure (Ruckenstein, 1991). It is fair to question whether these levels of evidence would be persuasive if they were to be submitted to regulatory agencies today for consideration of adding Ménière's disease as an indication for diuretic therapy. At present, such use is off-label.

A number of other agents have been used, including intravenous histamine and an oral histamine analogue, betahistine (Wilmot, 1972). Such therapy is not approved by the U.S. Food and Drug Administration. More recently, injection of corticosteroid into the middle ear has been advocated (Arriaga and Goldman, 1998). However, the true value of this therapy is unknown since the reports lack controls for comparison. As will be discussed next, determining effectiveness in a disorder that is variable and unpredictable is difficult at best and impossible without the use of controls. The apparent rationale for intratympanic steroid therapy is a possible immune disorder. Although the corticosteroid enters the perilymph via the round window membrane, distribution of the agents within the endolymphatic space is uneven and unpredictable. Salt has demonstrated that agents placed directly into the endolymph do not diffuse appreciably (Salt and DeMott, 1994), so it is likely that the effect of the corticosteroid would be confined to the area around the round window.

Placebo Effect

The cyclic nature of MD causes difficulty in evaluating the response to therapy. Torok (1977) suggested that most forms of therapy have only a placebo effect and that the response to therapy simply manifests the natural history of the disease. Thomsen et al (Thomsen et al, 1981) ascribed the action of a surgical placebo effect in their randomized, double-blind trial of endolymphatic sac surgery. However, they did not evaluate the effects of anesthetic agents, which are known to affect vestibular function (Boedts and Vandenhove, 1969; Johnson et al, 1985), and may well have explained their findings. Subsequent reports have emphasized the "nonspecific" nature of endolymphatic sac surgery (Thomsen et al, 1986). It is important to separate conceptually the placebo response, which is less than generally believed (Hrobjartsson and Gotzsche, 2001), and the natural history of the disease. They are not equivalent concepts.

My colleagues and I (Gates et al, 2004) have documented the time-course of vertigo decrease in a control group of subjects. As with most studies, subjects are recruited during an active stage of the disorder. Torok's "law" indicates that a majority of these subjects, if untreated, will improve with time. Statisticians refer to this phenomenon as regression to the mean. It also typifies the natural history of the disorder.

SURGICAL THERAPY

Surgical therapy of MD is indicated for those patients who fail medical treatment. Surgical treatments are directed at relief of the putative cause (endolymphatic sac) or at deafferentation of the affected ear (vestibular nerve section, labyrinthectomy [surgical or chemical]). The procedures are discussed in order of increasing invasiveness and complexity.

Tympanostomy Tube Insertion

Montandon et al (1988) advocated tympanostomy tube insertion as a prophylactic measure for MD vertigo and showed anecdotal evidence of success. The mechanism for this treatment approach is not established nor has the therapy been evaluated in a controlled study. We compared vertigo frequency for the two weeks before and after tube insertion and found no effect (Gates et al, 2004).

Meniett Therapy

Some people with MD note temporary improvement in symptoms when traveling to higher elevations or with weather changes. Research, primarily in Scandanavia, indicated that the relative positive pressure in the middle ear during the transition to higher altitude is responsible for this effect. These

experiences suggested a new approach to therapy (Densert and Densert, 1982). Subsequent research has shown that intermittent application of positive pressure micropulses to the inner ear (via a tympanostomy tube) is associated with improvement in symptoms in active MD cases (Odkvist, et al, 2000). Two additional studies of efficacy have been conducted with the same results: Gates et al (Gates et al, 2004) and Thomsen et al (2005). However, acceptance of this treatment approach has been slow because of cost and uncertainty about its long-term effectiveness. Densert and Sass (2001) found that over 90% of their subjects had excellent to good vertigo control over two years. Our two-year follow-up is nearly complete, and we reported interim results of 75% excellent to good vertigo control at the 5th International Symposium on Ménière's Disease (2005). Thus, there is now sufficient evidence to address both the short-term and long-term outcomes of use of the Meniett device.

The mechanism whereby external applications of intermittent pressure change labyrinthine physiology is incompletely understood. Static pressure changes transmitted to the inner ear fluids equalize within seconds (Densert et al, 1979), but intermittent pressure pulses reduce experimental hydrops (Densert et al, 1986). It was inferred that a positive pressure change in the inner ear compartment may lead to a reduction in the endolymphatic fluid volume via the inner ear pressure communication routes. Changes in endolymph sac potassium levels have been demonstrated in the guinea pig in response to low-frequency alternating pressure, suggesting a functional one-way valve (Salt et al, 2004). Alternative explanations involving oxygenation, hormones (atrial natriuretic peptide), and down-regulation of fluid production have been offered (Sakikawa and Kimura, 1997). The effect of tympanostomy tube placement alone was not evident in the short term (Odkvist et al, 2000).

Odkvist et al (2000) demonstrated relief of vertigo and improved hearing in 31 patients with symptoms of Ménière's disease, but not in 25 control patients, after application of intermittent overpressures in the middle ear using the Meniett-20 device in a two-week randomized, placebo-controlled clinical trial. Densert and Sass (2001) reported the two-year follow-up of the participants in the Odkvist et al (2000) study and noted that the improvement was maintained for the two years in the vast majority of cases.

In December 1999 the U.S. Food and Drug Administration cleared the 510k application of Pascal Medical AB to market the Meniett-20 as a Class II device for the symptomatic treatment of Ménière's disease. The treatment involves placement of a tympanostomy tube in the tympanic membrane. There are many unresolved issues regarding the Meniett-20. First, the mechanism of its effect is incompletely understood. Second, tympanostomy tube placement for Ménière's disease is not recognized as an indication by insurers in the United States. Third, few insurers know about the device, and fewer still have made provision for payment. On the plus side, the device has essentially no side effects; it is portable and easy to use; it gives patients a sense of control over their condition; and the results have been encouraging.

We recently completed a randomized, double-blind, placebo-controlled multicenter clinical trial of the Meniett device in 67 volunteer patients with classic unilateral cochleovestibular MD (Gates et al, 2004). Over a four-month period of use, the vertigo scores of the Meniett device users was significantly reduced compared to the vertigo scores of the placebo device users even though vertigo scores fell in both groups. There was no effect on hearing. We concluded that the Meniett device is a safe and effective treatment for people with classical MD who had failed conservative medical therapy. The results of our two-year follow-up study will be reported in the near future.

We also demonstrated that outcome is influenced by the severity of symptoms at the beginning of therapy and by vestibular status. People who did poorly had high levels of vertigo and normal vestibular function, whereas those that did well had less severe vertigo at entry and abnormal vestibular function. We interpreted these findings as suggesting that normal vestibular function is associated with the early stage of the disease and with high symptom levels, and that as the disorder "burns out" over time, the progressive loss of vestibular function is associated with less vertigo. Given that Menieriform vertigo appears to result from acute temporary denervation of the vestibular labyrinth (through mixing of endolymph and

perilymph), the higher the resting levels of vestibular function, the greater the intensity of the symptoms.

Intratympanic Gentamicin

Over the past decade, chemical labyrinthectomy has become increasingly used because of low cost and low risk (Pender, 1985). Intratympanic gentamicin reduces vertigo by decreasing peripheral vestibular function on the affected side but with a 30% risk of hearing loss (Blakley, 2000) Two schools of thought regarding unilateral chemical labyrinthectomy have evolved: the ablative school (Nedzelski et al, 1992) and the titration method (Odkvist et al, 1997). The reader is encouraged to review these philosophic approaches. Most authors have used a buffered solution to achieve pH neutrality, which results in a gentamicin concentration of <30 mg/cc. The unbuffered 40 mg/cc solution also produces a substantial decrement in vestibular function with a single dose, thereby combining, perhaps, the advantages of both approaches. Today, most patients are treated with a single injection and reevaluated at one month. Most achieve a desirable reduction in vertigo symptoms. Those that do not are offered repeated injections to achieve the desired effect. It is not necessary to ablate all vestibular function to control symptoms.

Gentamicin therapy is associated with worsening of the hearing in up to 30% of cases. The loss may be total and is unpredictable. The greater the dose of gentamicin, the larger the probability of loss. Many patients are willing to sacrifice their hearing, particularly when it is poor to start with, in exchange for relief of vertigo. For those who are unwilling to risk further hearing loss, alternative surgical therapy should be considered.

Invasive Surgical Procedures

Nondestructive

Endolymphatic sac surgery remains controversial. The pros and cons of this approach have been reviewed (Smith and Pillsbury 1988). The procedure has a long history beginning with the decompression and drainage procedure of Portmann (1926), the endolymphatic-subarachnoid shunt made popular by House (1965), endolymphatic-mastoid shunt (Goldenberg and Justus 1983), endolymphatic sac enhancement (Paparella and Sajjadi 1994), endolymphatic sac excision (Gibson, 1996), and, finally, sac and sigmoid sinus decompression without drainage (Gianoli et al, 1998). Taken at arms length, the results of all of these procedures is similar. Although short-term vertigo control for endolymphatic sac surgery is reported to occur in about 80 to 90% of cases (Huang et al, 1991), the long-term vertigo control rate appears to be closer to 60% of cases (Telischi and Luxford, 1993).

The famous Danish study (Thomsen et al, 1981) of endolymphatic sac-mastoid drainage was begun in Copenhagen in the late 1970s. The study participants were 30 adults with active Ménière's disease randomly assigned to receive an active or a sham procedure. This was a bold study with careful controls to minimize bias. Patients at hospital A had their surgery at hospital B and returned to their primary hospital for follow-up evaluation. None of the surgeons or patients was aware of the treatment assignment. The participants rated the vertigo level each day on a 0–3 scale with "2" indicating a significant attack of vertigo lasting 20 minutes or more, "3" a severe attack, and "1" a mild attack that did not impact on their planned activities for the day. For the three months prior to operation, the average monthly vertigo score was 30 for both groups. This would correspond to an average of 10 days/month with severe (i.e., level 3) vertigo, 15 days/month of level 2 vertigo, or 30 days per month with level 1 vertigo. After the surgery, the average monthly score over 12 months fell to 3 per month for the active surgery group and to 9 per month for the sham surgery group. In other words, both groups of subjects had improvement, significantly more (at the $p < 0.05$ level, but not at the $p < 0.01$ level) for the treatment group. These results led the investigators to deny any effect of the surgery (Thomsen et al, 1981). Later they acknowledged the nonspecific effect of general anesthesia and surgical manipulation of the temporal bone upon the endolymphatic system. Even today, the merits of this study and its conclusions are discussed. My personal opinion is that there is more to surgery than removal of bone, including powerful anesthetic agents, for example, and that the

significant improvement in the sham surgery group was a combination of the procedure and the natural history of the disorder. Finally, a difference between groups in a clinical trial that has a probability of an alpha error of $p < 0.05$ must be recognized as meeting the conventional standards of statistical significance. Thus, I interpret the study as showing a moderate improvement from the sac surgery, over and above the improvement due to the other factors.

Use of endolymphatic surgery continues. To me, the ideal candidate is one early in the course of the disease with frequent and severe vertigo attacks, normal ENG function, and fluctuation of hearing. Given that the procedure is safe, is done as an outpatient, and is rarely associated with hearing loss or vestibular loss, it remains a valuable choice for some patients. Even if the long-term success is 50% remission, a six-month remission rate of 75% with minimal complications has value.

Destructive Surgical Procedures

There is general agreement that people with MD who have failed medical therapy, Meniett therapy, or sac surgery can expect cessation of vertigo attacks after vestibular nerve section or labyrinthectomy. In general, younger people with intractable vertigo in my practice opt for nerve section because hearing preservation and vertigo control are predictable. Older patients, particularly those with nonserviceable hearing, tend to opt for labyrinthectomy because of safety and simplicity. In either case, the patient exchanges the disability from recurrent vertigo for the disability attendant to loss of vestibular function in one ear. Fortunately, central compensation—either spontaneous or assisted by vestibular rehabilitation therapy—restores balance function satisfactorily in most, but not all, cases.

Labyrinthectomy in experienced hands is a very short, outpatient procedure that is ideal for the older person or one with some anesthetic risks. Both hearing and vestibular function are lost in the affected ear. Most candidates have lost considerable hearing and balance function prior to surgery so the subsequent removal of remaining function is generally well tolerated. These have been very grateful patients in my experience.

For younger people with good hearing, vestibular nerve section is a reasonable choice. Because the intracranial cavity is opened, the risks of severe operative complications are higher than with procedures on the inner ear. However, in experienced centers, where the otologic surgeon and neurosurgeon collaborate, or where the otologic surgeon has substantial neurosurgical training and experience, these complications are uncommon. Nonetheless, the procedure is stressful, there is a several-day hospitalization, and a program of active vestibular rehabilitation is advisable to facilitate central compensation. Recurrence of vertigo after vestibular nerve section is rare, hearing loss is uncommon, and the long-term vertigo control results are excellent. Compensation for the loss of vestibular function is a consideration for older patients.

SUMMARY

Ménière's disease continues to present problems in management. The lack of a universal standard for diagnosis, the lack of uniformity in treatment methods and indications, and inconsistent outcome measures make direct comparisons of the various options difficult to interpret. Treatment trends are moving away from surgically invasive therapy to minimally invasive therapy with newer technology and agents. However, the final chapter on this problem has not been written. The Meniett device offers symptom control with little risk for those who have failed medical therapy. Gentamicin injection into the middle ear offers a safe and reasonably effective method for chemical labyrinthectomy for people with intractable vertigo willing to risk hearing loss. Vestibular nerve section controls vertigo with minimal risk of hearing loss. Labyrinthectomy is effective in controlling vertigo and is useful for older people with nonserviceable hearing.

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