

RECENT ADVANCES IN THE MANAGEMENT OF MÉNIÈRE'S DISEASE

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Ménière's disease is a commonly diagnosed condition. The symptoms of tinnitus, vertigo, hearing loss and fullness in the ear do significantly affect a patient's quality of life. Currently, the management of Ménière's has exciting new options available. These options have been reviewed in special study modules by Lancaster University Medical students and provide an excellent evidence-based review of these management options.

INTRODUCTION

The ear is a remarkable organ which plays a vital role in the maintenance of balance; the membranous labyrinth of the inner ear houses areas of neuroepithelium which detect movements of the head. Sensory information from the eyes and proprioceptors is also required to sustain overall equilibrium. Disease of the vestibular apparatus gives rise to hallucinatory sensations of movement known as vertigo. One such condition is Ménière's disease, which features episodic attacks of vertigo, fluctuating tinnitus, sensorineural low frequency hearing loss, and aural pressure. The term Ménière's syndrome refers to symptoms associated with another condition. Table 1 outlines the differential diagnosis between Ménière's disease and other conditions causing vestibular disturbance as well as tinnitus. Fullness or pressure in the ear is specific to Ménière's.

Anatomy and physiology

The ear is divided anatomically into three sections - the external, middle and internal ear. The internal ear is the organ of balance or equilibrium.

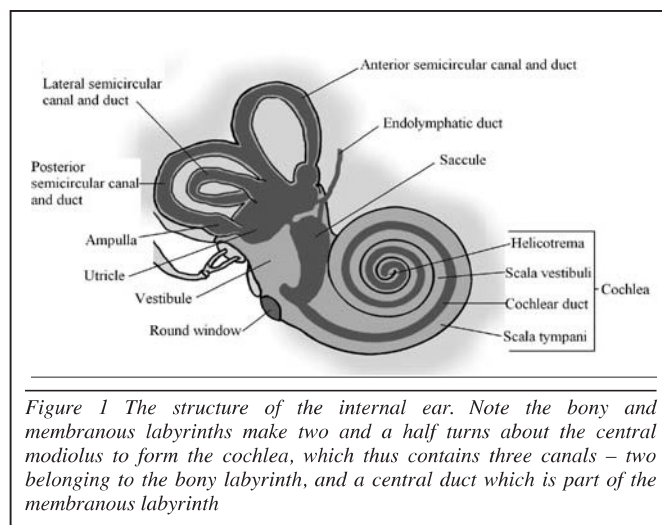


Figure 1 The structure of the internal ear. Note the bony and membranous labyrinths make two and a half turns about the central modiolus to form the cochlea, which thus contains three canals – two belonging to the bony labyrinth, and a central duct which is part of the membranous labyrinth

The internal ear consists of a cavity in the petrous temporal bone known as the bony labyrinth, and a series of ducts within this called the membranous labyrinth. The

membranous labyrinth is filled with endolymph, and surrounded by perilymph. Figure 1 shows the structure of the internal ear.

The bony labyrinth is continuous; the ampullae of the semi-circular canals form five communications with the vestibule (the anterior and posterior canals share a communication) and the scala tympani and vestibuli are joined at the helicotrema. The scala tympani ends at the round window, and the scala vestibuli at the oval window.

The membranous labyrinth is also continuous, but does not communicate with the bony labyrinth. The utricle and saccule are connected by the utriculosaccular duct, from which the endolymphatic duct arises. This passes through the vestibular aqueduct, to the posterior of the petrous bone, before forming the endolymphatic sac. Endolymph, produced by blood capillaries in the membranous labyrinth, is absorbed in the endolymphatic duct and sac.

The bony labyrinth is concerned with hearing; the organ of Corti, which contains the receptors for sound, is found in the bony cochlea, on the basilar membrane which separates the scala tympani from the cochlear duct.

The neuroepithelium concerned with equilibrium is located in the membranous labyrinth. It consists of five parts – one in each of the semi-circular ducts and one, of a slightly different structure, in both the utricle and saccule. These latter two epithelial areas are known as the maculae, the epithelial areas of the semicircular canal ampullae being known as the crista. Each neuroepithelium consists of hair cells covered in a sensory array of stereocilia embedded in a glycoprotein or gelatinous membrane in which are embedded otoliths.

The maculae are responsible for providing awareness of the position of the head in space, and detecting its linear movements. The maculae of the utricles are positioned horizontally, and so are able to detect sideways tilting movements of the head, whilst the vertical saccular maculae sense forward and backward tilts.

Whilst the vestibular complex contributes to the maintenance of balance, it is not solely responsible for it; sensory information from the eyes and proprioceptors is also required in order to sustain equilibrium. Defects in any of these organs can cause imbalance or dizziness, as can deficiencies in other body systems, such as the cardiovascular system, eg in postural hypotension. The hallmark of pathology of the vestibular system is a hallucinatory sensation of movement, known as vertigo.

Table 1 lists five common causes of vertigo and their aetiologies.

| Cause of vertigo | Origin |
|---|--|
| Ménière's disease | Secondary to head trauma, idiopathic hydrops, post herpes simplex virus or possible autoimmune |
| Benign paroxysmal positional vertigo | Peripheral: otoliths from the maculae are displaced into the semi-circular ducts, inappropriately stimulating the crista |
| Labyrinthitis | Peripheral: middle ear infection spreads to the inner ear causing inflammation of the labyrinth |
| Vestibular failure | Peripheral: end-organ failure due to occlusion of end-arteries supplying the inner ear |
| Compression of vestibulocochlear (VIII) nerve | Central: due to tumour, eg in cerebellopontine angle |

Table 1 Common causes of vertigo

MÉNIÈRE'S DISEASE: THE CLINICAL PRESENTATION

Ménière's disease is characterised by episodic attacks of acute rotatory vertigo, unilateral, a predominantly low tone fluctuant hearing loss and roaring tinnitus. The hearing loss and tinnitus may become continuous and together with sensation of fullness in the ear, these symptoms may heighten before an attack of vertigo. Attacks typically last for several hours and the occurrence varies from as few as several attacks a year to several in a month. On the background of this is a fluctuating but ultimately progressive hearing loss. Other patients may not have the full triad of symptoms and present with either cochlear or vestibular symptoms alone. Drop attacks occur in 2-6% of patients and this has been attributed to acute utriculosaccular dysfunction and is often called 'otolithic crises of Tumarkin'. Ménière's disease affects about 157 persons per 100,000 in the UK and may eventually affect both ears in up to 42.5% at 20 years.^(1,2)

Histopathophysiology

Ménière's disease is an idiopathic condition in about 75% of patients. In 25% of cases an identifiable cause is found. Aetiologies include trauma, viral or bacterial infection or chronic suppurative otitis media. In recent years a few cases have been associated with syphilis. Excess endolymph volume (endolymphatic hydrops) is a characteristic finding, but it is uncertain if the pathological process is due to overproduction or inadequate resorption. Endolymphatic hydrops tends to affect the cochlea and saccule more than the utricle or semicircular canals. A distended saccule wall in contact with the oval window may induce vertigo when the external auditory canal is pumped. This is Hennerbert's sign and is present in 30% of Ménière's patients. In the cochlear, Reissner's membrane is typically bowed into the scala vestibuli. Microruptures and subsequent healing allows the neurotoxic potassium-rich endolymph to depolarise cells in the perilymph, thus explaining some of the Ménière's symptoms. A reduction in afferent nerve endings of the cochlear and type II hair cell in the vestibule has been found on electron microscopy.^(1,3)

Diagnosis

There is no diagnostic test for Ménière's disease. Neither are there any pathognomonic features in the history or examination. Investigations are used to aid diagnosis and exclude other causes. An audiogram establishes baseline hearing and may show a predominant low-frequency fluctuating hearing loss. Ménière's is a clinical diagnosis and seldom needs haematological support. However, in bilateral disease there may be reason to test for syphilis. Where the symptoms are not characteristic, imaging the cerebellopontine angle may be necessary to exclude lesions there. To help diagnosis, the American Association of Otolaryngology (Head and Neck Surgery) has devised a diagnostic scale. Definite Ménière's requires two or more episodes of vertigo of at least 20 minutes, audiometrically documented hearing loss, with tinnitus and aural fullness.^(1,4)

Disability and management

Ménière's disease causes significant disability and reduction in quality of life. The unpredictable attacks place restrictions on employment, limit social interactions and can produce a profound sense of loss and grief. There is no known cure. A management plan should include a multidisciplinary team approach and coping strategies for patients. Medical management includes drugs such as prochlorperazine and cinnarizine to control acute vertigo, while betahistine, diuretics and salt restriction reduces frequency and severity of attacks. Surgical forms of management include gentamicin labyrinthectomy and saccus decompression. An alternative to these surgical options is the relatively recent addition of the Meniett® therapeutic device.^(2,5)

This article will now review the literature available for the two non-surgical options of management of the endolymphatic hydrops Ménière's:

1. The gentamicin transtympanic injection, and
2. The Meniett® device

GENTAMICIN TREATMENT OF MÉNIÈRE'S DISEASE

Gentamicin treatment is considered when conservative management is ineffective. It is vestibulotoxic, so causes hair cell damage and reduced endolymph production, therefore inducing vestibular hypofunction in the affected ear. This reduces the number of vertigo attacks. Gentamicin causes fewer cochleotoxic side effects when compared to other aminoglycoside antibiotics.

Vestibular hypofunction is measured by electronystagmometry, but studies have shown that there may be no correlation between recoveries from vertigo and reduced caloric responses.⁽⁶⁾ This indicates the importance of asking patients about symptom changes and quality of life throughout treatment.

The popularity of this treatment increased during the 1990s and has been reported to successfully treat vertigo in 71.4-100% of Ménière's patients.⁽⁷⁾ Administering gentamicin directly into the affected ear means no systemic side effects occur. Methods of application vary, but the two main methods located in the literature are intratympanic injection, and transtympanic perfusion.

Intratympanic injection

Gentamicin can be injected blindly or via a tympanostomy tube over the round window niche.⁽⁷⁾ Fluid can be lost through the eustachian tube, which raises issues of drug doses reaching the inner ear. Additionally, initial periods of high concentration with short-term potent ototoxicity increases the risk of hearing loss.

Under local anaesthetic (LA), Dry Gelfoam™ is inserted onto the round window membrane, which is then saturated with gentamicin solution. This allows slow influx at a steady concentration which minimises hearing loss risks.⁽⁷⁾

The optimal concentration to use, or whether it should be a single or multiple injection therapy, is unknown and studies are contradictory. Some conclude that there is no direct correlation between gentamicin concentration and hearing loss,⁽⁸⁾ whereas others concluded that there was increased hearing loss with large doses of gentamicin.⁽⁹⁾ Studies are positive with vertigo control in 83.1% patients; 76.5% patients had vertigo relief after another course, but hearing loss occurred in 66.6% patients.⁽¹⁰⁾

Transtympanic perfusion

This technique avoids peaks in concentration by allowing continuous perfusion. It is now accepted practice to administer gentamicin via two main methods:

- A microcatheter is placed at the round window niche under general anaesthetic (GA) and attached to the external ear via an expandable sponge. Gentamicin is then pumped or titrated through the catheter into the inner ear.⁽⁷⁾ In one study, patients were treated with 10mg/ml three times daily for 1-4 weeks. Eighty-five percent had relief from vertigo and the overall incidence of hearing loss was 36%.⁽¹¹⁾ A study in 2001 found only one patient out of 11 had preserved hearing after treatment.⁽¹²⁾ They concluded there was no advantage in using the microcatheter compared with other methods when considering hearing loss.⁽¹²⁾
- The Silverstein MicroWick™, consisting of an absorbent sponge and grommet, can be inserted under GA or LA.⁽¹³⁾ When positioned, the microwick is primed with gentamicin and anchors itself at the round window. Gentamicin can then diffuse through into the labyrinth. The patient must then administer gentamicin drops three times daily for two weeks.⁽¹³⁾

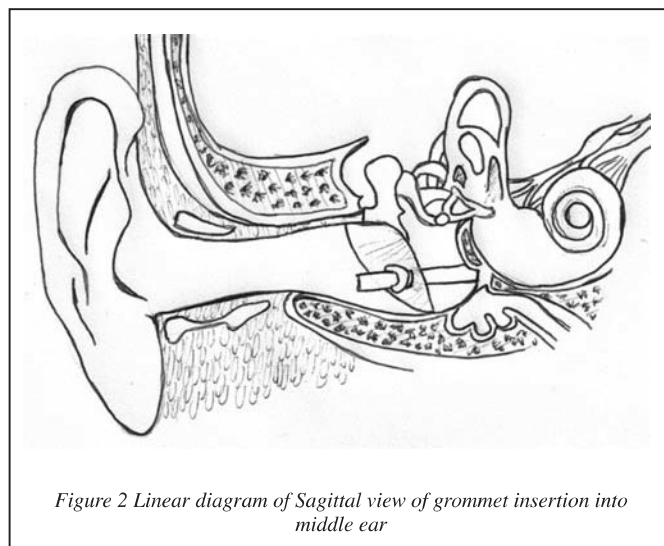


Figure 2 Linear diagram of Sagittal view of grommet insertion into middle ear

The studies of this method have demonstrated 100% initial recovery, which then reduced to 80% with complete control of their vertigo longterm, with only 26% of patients experiencing secondary hearing loss.⁽¹³⁾ Another study using the titration method showed that 85% gained vertigo control and 37% suffered hearing loss.⁽¹¹⁾ This method is popular due to the relative reduction in distress and imbalance in the postoperative recovery period.⁽¹³⁾

Discussion

This article has reviewed methods of treating Ménière's disease with gentamicin. Its success is heavily based on epidemiological evidence, but developing an understanding of the exact modes of action has largely been ignored. The studies that have been done to understand the mechanism of gentamicin action have used animal models, and although birds have been shown to regenerate hair cells after gentamicin application,⁽¹⁴⁾ would this still be the case for humans? Nevertheless, if hair cells do follow these findings there would be scope for longterm monitoring of patients post-treatment, as subsequent applications may be needed. The longterm effects of the treatment have not been analysed fully. This is worrying due to the popularity of gentamicin treatment, suggesting a need for further research.

The best method appears to be the Silverstein MicroWick™ method, as this has the greatest prognosis in hearing maintenance, is a painless procedure and, unlike the microcatheter, can be placed under LA. It avoids peaks of concentration and allows the patient to self-medicate after the procedure, giving the patient a role in their treatment. However, only two papers could be found describing this method,^(13,15) one of which was carried out by Silverstein himself, suggesting further investigations are required.

More research should be carried out comparing modes of application, as few studies were found to do this. There were many papers describing transtympanic injection, but few describing transtympanic methods, so, although it seems to be the preferred method currently, subsequent research may reveal hidden flaws.

When using gentamicin in the treatment of Ménière's disease, the risk of hearing loss is greater than in surgical treatments. The lowest percentage of hearing loss found (26%)⁽¹³⁾ was quite high and would have implications for the patients quality of life, even if vertigo was controlled. Gentamicin could also be more appropriate for all age groups, as invasive surgical treatments can result in acute loss of vestibular function, increasing the likelihood of dangerous falls, as well as being poorly tolerated. Exploration into the age boundaries, as well as the degree of disabling vertigo, is required to demonstrate that gentamicin treatment can be more beneficial than, for example, saccus surgery.

The patient should be told about the high risk of hearing loss, and treatment should only be considered if the patient has normal hearing function in the affected ear. This is less likely to be the case in the elderly population, due to natural degeneration of hearing function; therefore, the number of patients eligible for this treatment may be reduced.

All studies have been small scale with a maximum number of subjects being 93.⁽⁶⁾ Therefore, conclusions drawn from the studies may not be true representation of the Ménière's disease population. This is important, as the treatments for Ménière's disease are based on epidemiological evidence.

In conclusion, the lack of guidelines about the optimal concentration, dosage, method of gentamicin application and age at which it should be an option is profound. Too much pressure is being placed on specialists in this area to provide gentamicin treatment without the appropriate support to backup its usage, and this needs to be addressed urgently.

MÉNIÈRE'S DISEASE AND THE MENIETT® DEVICE

The Meniett® device

The Meniett® device is a relatively new treatment option for Ménière's disease, based on the theory that symptoms are caused by an excess of endolymph within the inner ear. More sophisticated than pharmaceutical management, yet more conservative than saccus decompression or neurectomy, the Meniett® device is considered to hold an intermediate position between medicine and surgery on the Ménière's treatment ladder. It is easy to use, portable and non-invasive. However, use of the



Figure 3 The Meniett® device⁽¹⁶⁾

device in the UK is limited, as it is currently unavailable on the NHS.

How it works

The earpiece of the Meniett® device is positioned in the ear canal, where it transmits low-frequency pressure pulses to the middle ear, via a grommet in the eardrum. It is not clear exactly how this works, but it is thought to improve disease symptoms by reducing the volume of endolymph in the inner ear; the action of the pressure waves on the round and oval window is believed to force endolymph into the endolymphatic sac, where it is absorbed.⁽¹⁷⁾ The treatment is self-administered, usually for a five minute period three times a day.

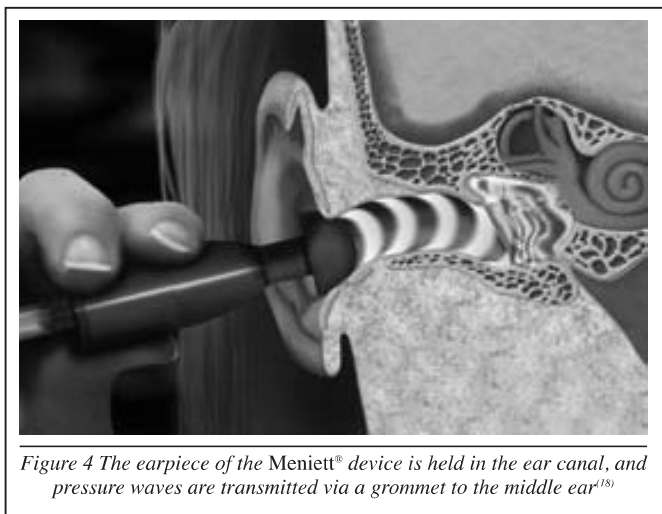


Figure 4 The earpiece of the Meniett® device is held in the ear canal, and pressure waves are transmitted via a grommet to the middle ear⁽¹⁸⁾

The evidence

Studies examining the efficacy of the Meniett® device in the management of Ménière's disease have produced conflicting results. A study in 2004 found that both the frequency and severity of vertigo attacks were significantly lower amongst patients who used the Meniett® device for four months, than those who used a placebo device.⁽¹⁹⁾ A further trial by the

same researchers also demonstrated the longterm efficacy of Meniett® therapy; two years of treatment with the Meniett® device led to disease remission or improved symptoms in 67% of study participants.⁽²⁰⁾ Conversely, a 2005 study conducted a trial involving patients who had been referred for ablative therapy which found no improvement in patients' functional levels or their perception of dizziness handicap after three months of treatment with the Meniett® device.⁽²¹⁾

An interesting conclusion of the studies is the indication that there may be a subgroup of patients with Ménière's disease who could potentially benefit the most from Meniett® therapy. The 2004 study recruited patients with unilateral disease only and found that the Meniett® device had a greater efficacy amongst patients who had higher baseline levels of vertigo,⁽¹⁹⁾ and the 2005 study suggests that their trial may have shown negative results as the study cohort was more resistant to medical therapy (as evidenced by their referral for an ablative procedure) than cohorts used in other studies.⁽²¹⁾

Future use of the device

Further studies are clearly indicated to explore the use of the device in subgroups of patients. If such a group who may be most likely to benefit is identified, it may well be appropriate for their treatment to be funded by the NHS. In the meantime, the device continues to be available privately, and it is arguable that a financial investment may act as a placebo to improve patients' symptoms.

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