

Surgical treatment of Ménière's disease

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Purpose of review

This review comprises new insights from and discusses the impact of recent medical publications on the surgical treatment of Ménière's disease.

Recent findings

Refining surgical indications through recognition of clinical conditions with similar symptoms and through a more precise estimation of the degree of disability will improve the process of decision making for surgery. Further high-level evidence-based medical data supporting the effectiveness of intratympanic gentamycin has become available. Physiopathological progress, based on animal experiments, towards surgically applied intracochlear drug delivery is addressed.

Summary

Studies using level 1 or 2 evidence-based medicine must be conducted to enable better decision making, such as in the application of intratympanic gentamycin or micropressure Meniett therapy at an earlier stage of Ménière's disease. If the results of such studies are conclusive for surgery, this will lead to a shorter duration of discomfort for patients before being offered the possibility of surgery.

Keywords

diagnosis, intratympanic gentamycin, Ménière's disease, Meniett, selective vestibular neurectomy, surgical treatment

Introduction

Ménière's disease is the idiopathic disorder of the cochlea and labyrinth caused by endolymphatic hydrops [1]. It is a fairly frequent life-long disorder affecting the patient's quality of life and work performance, with an estimated annual incidence of about 5/10 000. Ménière's disease is probably the most frequent etiology of recurrent vertigo. A recent review by Minor *et al.* [2**] gives an excellent overview.

In the majority of patients, symptomatic relief can be achieved by salt restriction, avoidance of caffeine, alcohol, tobacco and stress, and medication (mainly diuretics and betahistine).

For the estimated 20% of patients in whom conservative treatment fails, a surgical treatment may offer relief. Various surgical procedures have been advocated but some are subject to great controversy; for example, endolymphatic sac surgery since Thomsen *et al.* [3] found no difference from a sham procedure.

During the last year, new data have been published influencing the surgical management of Ménière's disease in its different phases, including differential diagnosis, counselling, assessment and outcome measures, surgical techniques, and postoperative rehabilitation. In particular, intratympanic gentamycin (ITG) treatment acquired greater evidence-based medical support from the first prospective controlled, randomized trial [4**], and from a comprehensive meta-analysis [5**]. The authors aim at highlighting the relevance of these new findings to their surgical approach for Ménière's disease.

Definition and physiopathology of Ménière's disease

Endolymphatic hydrops (ELH) is the inner ear condition in which a hydropic distention of the endolymphatic system occurs [1]. The clinical expression of the occurrence of ELH comprises recurrent spontaneous episodic rotatory vertigo spells, hearing loss and tinnitus, with or without aural fullness on the affected side. The AAO-HNS proposed a diagnostic scale based on clinical criteria. An important consequence of these AAO-HNS guidelines was the increased comparability of studies dealing with Ménière's disease.

ELH develops when there is a mismatch between endolymph production and resorption. The hypothesis that there is an increase in endolymph pressure in this

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Abbreviations

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|----------------|--|
| AAO-HNS | American Academy of Otolaryngology and Head and Neck Surgery |
| ELH | endolymphatic hydrops |
| ITG | intratympanic gentamycin |
| NVC | neurovascular conflict |
| QOL | quality of life |
| SNHL | sensorineural hearing loss |

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condition was not supported in a recent animal experiment. During the infusion into the scala media of artificial perilymph Warmerdam *et al.* [6] found no pressure increase as assessed by direct endolymphatic pressure measurements. The investigators showed that the build up of endolymph resulted in a distension of the endolymphatic compartment due to the high compliance of the membranous inner ear structures. It was further concluded that future treatments should not primarily be directed towards the relief of increased pressure, such as in our opinion shunt-type operations.

A second remarkable finding of the Groningen research group using their animal model concerned the cochlear duct patency for perilymph being controlled by the round window membrane position [7]. This finding might explain the effect of pressure changes on the symptoms of Ménière's disease, whether due to external factors such as ambient air pressure, to middle ear aeration difficulties, or a therapeutic action such as micropressure Meniett treatment [8,9] or alternating hyperbaric pressure treatment [10]. It is as yet too early to make conclusions concerning the effect of surgery on the round window membrane, such as obliteration of the round window for an alleged perilymphatic fistula.

Natural history of Ménière's disease

Counselling on treatment options, especially surgical treatment, is based in large part on knowledge of the natural history of Ménière's disease. Although earlier reports suggested that symptoms will decline with time and that the disease leads to a 'burn-out' of the inner ear, Havia and Kentala [11**] demonstrated a progression of vertigo symptoms in the course of Ménière's disease. In a prospective study of 243 consecutive patients they found that the proportion of patients reporting severe or very severe attacks increased with the duration of symptoms. The frequency of attacks was highest among patients who had suffered symptoms for more than 20 years. Nausea was also more common later in the disease than at the beginning. Even after 20 years of suffering from the disease, 21% of the patients reported continuous vertigo. The study did not estimate recovery rate, but stressed that patients with Ménière's disease can have severe symptoms of dizziness even after a 20-year disease history.

This report may lead to an increase in advocating surgical options, especially in patients with a long history of the disease on one side and undergoing severe attacks.

Incapacitating vertigo in Ménière's disease: when to operate?

Most patients consider vertigo to be the most problematic symptom [12], as it may cause significant disability and negatively affect the patient's quality of life and work

performance. Absenteeism at work and increased consumption of health-care facilities result in an additional economic burden. Making the case for surgical treatment of vertigo involves estimating the degree of disability up to the point of incapacity. This is done by self-appraisal of the patient as to whether they consider themselves incapacitated or suffering to an extent that they do not want to rely any longer on conservative measures only. Estimation of this suffering can be by registration of the number and duration of vertigo spells or by assessing the impact on vertigo-specific quality-of-life (QOL) measures such as the dizziness handicap inventory [13].

Starting from this information, the benefits and disadvantages of the surgical procedures can be discussed with the patient. It is at the end of this stage of guiding the patient that he is able to make the decision. Aspects contributing to the decision making by the patient for surgery are diverse, comprising characteristics of the vertigo such as intensity, duration and frequency of spells [14], as well as impact on their social activities and on their work conditions. For the elderly, their autonomy and the risk of falls and hip fracture [15] can constitute an element leading to surgical indication.

Earlier, Kerr and Toner [16] reported that half of the patients to whom selective vestibular neurectomy was offered, indicated after 6 weeks of wait-and-see policy that the vertigo had improved to a degree that no longer warranted surgery. It also can be speculated that the treating physician estimated the degree of incapacity higher than the patient.

Outcome measures

The AAO-HNS [1] has set the standard guidelines for a multidimensional description of Ménière's disease to be used in reporting treatment outcomes. The elements involved are a four-frequency average hearing threshold, word recognition, number of vertigo spells of longer than 20 min, and finally disability estimated using a 6-grade functional test. Additional reporting systems may comprise tests of the vestibulo-spinal system and postural stability during gait, such as the dynamic gait index, and a disease-specific QOL questionnaire for sufferers of vertigo, such as the dizziness handicap inventory, tinnitus handicap inventory or tinnitus questionnaire.

Kato *et al.* [17*] proposed an 18-item QOL questionnaire specific for Ménière's disease. They applied this questionnaire in a retrospective study of 159 patients who had been operated on using an endolymphatic sac procedure, demonstrating a clear improvement with this newly developed instrument.

The full implementation of multidimensional evaluation, including the AAO-HNS recommendation to assess

treatment outcome at 2 and 4 years, is essential for making the best choice of treatment.

Diagnosis

Diagnosis of Ménière's disease implies the exclusion of other causes demanding a comprehensive diagnostic assessment including history taking, audiological and vestibular testing, clinical biology tests, and imaging. The association of vertigo (the disease) with migraine gained attention leading to therapeutical approaches similar to those for migraine [18]. Migraine-associated vertigo has to be considered especially when patients have experienced continuous vertigo lasting 1–5 days or longer [11**].

The positive diagnosis of ELH using electrocochleography gained further support and the recommendation to ascertain this diagnosis [19]. Chung *et al.* [20] reported a sensitivity of 71% and a specificity of 96% using an extratympanic recording with a click-evoked stimulus at an 8.1-Hz repetition rate and a cut-off SP/AP (summing to action potential ratio) set at 0.43%. We further advocate the use of high-frequency repetition rates (>30 Hz) with toneburst stimulation, as more pronounced effects have been recorded with higher stimulation rates [21].

The effect of conditions such as thyroid disorder, in particular corrected hypothyroidism [22], and autoimmune disease [23] on the treatment of Ménière's disease attracted further attention. Evaluation protocols should take these aspects into consideration.

Improved imaging may lead to the detection of a dehiscence superior semicircular canal, presenting with Ménière-like symptoms and low-tone hearing loss [24]. This can be treated by plugging the dehiscence using a surgical middle fossa approach [25,26].

Imaging can also diagnose conditions of the central nervous system which can mimic Ménière's disease, such as brain tumours [27] or cerebellopontine angle tumours. Specific attention has been focused on differential diagnosis with neurovascular conflict (NVC). Fly-through virtual endoscopy software applied to T2-weighted magnetic resonance imaging (MRI) of the pontocerebellar angle allows visualization of NVC [28*]. The glial part, also called the root entry zone, of the cranial nerves in the pontocerebellar angle is considered to be particularly vulnerable to this condition. Based on the length of the root entry zone of N VIII, De Ridder *et al.* [29] estimated the incidence of NVC to be one third of the incidence of Ménière's disease. Correlating audiological findings on the one hand with preoperative findings of NVC localization during decompression surgery [30] and on the other hand with MRI assessment of the

localization of NVC [31] gave further evidence of the clinical existence of NVC, and resulted in a proposal of tonotopical organization of the cisternal segment of the cochlear nerve.

Surgical treatment: rationale

The aim of surgical treatment can be threefold.

The first and most important goal is to stop the unpredictable vertigo spells of high intensity and long duration by reducing or abolishing peripheral vestibular afferent stimulation. In the next phase after surgical deafferentation, central vestibular compensation for the asymmetrical vestibular input must be achieved by labyrinthectomy, ITG or selective vestibular neurectomy.

Second, surgery can influence the physiopathological process of ELH itself by promoting resorption or reducing endolymph production. Endolymphatic sac surgery with shunt implantation is aimed at the former, while ITG can achieve the latter by downregulating the endolymph-producing dark cells around the cupolas and in the stria vascularis [32]. A new development in this respect is the use of the inner ear spaces as the surgical approach in order to improve control of drug dosage in the endolymph or perilymph. This development could overcome the current inability to control or even estimate the rate of diffusion of drugs through the round window membrane due to the great variability in transfer when applying drugs in the middle ear [33]. Also, greater insight into intralabyrinthine fluid dynamics may play a role in the ability to deliver drugs locally to the inner ear through the middle ear [34]. The drugs that can be used cover a variety of options and are directed to the different inner ear structures addressing inflammation [35], apoptosis [36*], neurotransmitter control [37], ion channel regulation [34,38], ototoxicity protection [39] and neurotrophic factors [40]. The use of corticosteroids during endolymphatic sac surgery [41] or in relation to the round window membrane can be classified in this category.

Third, surgery can aim at stabilizing or improving hearing. Up to now, there is not a single therapy, conservative or surgical, that could provide an evidence-based means of achieving this goal at long term. Ménière's disease patients developing a bilateral progressive, severe or profound sensorineural hearing loss (SNHL) appear to be a good indication for cochlear implantation and this treatment option has to be proposed to these patients [42*].

Surgical treatment: a last resort?

Intermittent pressure treatment using the Meniett device in 10 intractable Ménière's disease patients over a period of 11 months resulted in significant control of the

vertigo attacks, a reduction of the spells of long duration and a 6 dB hearing gain [8]. This treatment is recommended before trying an ablative procedure. The reduction of the mean duration of vertigo attacks was confirmed by Boudewyns *et al.* [9], but in their study population of 12 patients with a mean follow up of 12 months, they could not confirm that Meniett therapy can replace surgical ablative therapy as the improvement was not enough to alleviate the need for surgery. At the end of the study two of the 12 patients were still under Meniett therapy. Analysing differences between populations under study, Boudewyns *et al.* concluded that the less favourable outcome could be related to the more advanced stage of disease in their population.

Intratympanic gentamycin application

Intratympanic application of gentamycin is the least surgical invasive method of partial ablation of the vestibular end organ. The mechanism of action consists of the passive diffusion of gentamycin through the round window membrane, absorption into the inner ear structures, for example the hair cells and dark cells, and initiation of apoptosis or downregulation and decrease of function. This mechanism implies a delayed action between application and full effect [43]. The mechanism also is influenced by the antagonistic action of free-radical scavengers and antioxidants such as acetylsalicylic acid and vitamin E. Among the several reports on the effect of ITG, two studies have contributed substantially towards evidence at level 1 EBM (evidence-based medicine) of the effectiveness of ITG.

The first study by Stockroos and Kingma [4**] is a prospective double-blind randomized trial of ITG versus intratympanic application of buffer solution (placebo) in a low-dose regimen comprising 22 patients with Ménière's disease and a follow up period of between 6 and 28 months. The authors demonstrate a significant reduction in the number of vertiginous spells without the occurrence of SNHL.

The other study is a comprehensive meta-analysis of the effectiveness of the different techniques of ITG application [5**]. The authors analysed vertigo control and the incidence of SNHL following ITG. The overall control of vertigo was 92.2%. There was no statistically significant correlation with the post-ITG decrease in vestibular response to caloric stimulation. They concluded that the titration method, consisting of daily to weekly applications until the onset of audiological or vestibular symptoms or a change in vertigo, demonstrated the best vertigo control of 96.3%. The low-dose method of delivery, that is one or two injections with re-treatment for recurrent vertigo, had the lowest control of 86.6%. The multiple daily dose method, with three applications a day for 4 or more days, resulted in more SNHL (34.7%). The weekly

dosing scheme was associated with 12.3% SNHL. In their meta-analysis Chia *et al.* found no difference in profound hearing loss between groups.

When we consider profound hearing loss after continuous microcatheter ITG delivery between some studies the variation is striking, ranging from 3% SNHL [44] to over 25% SNHL [45,46] to 90% SNHL [47]. As in the case of Meniett therapy, populations treated might differ in stage and age; presumably the earlier the stage and the younger the patient group, the less risk of SNHL. This suspicion has to be tested, especially considering the reported increased intensity with duration of disease [11**].

It should be noted that the above-mentioned studies did not assess long-term outcome; only a few studies have done so [48,49]. Also, overall disease-specific QOL outcomes, comparing the treated patients with a group not treated with ITG, are not available.

Selective vestibular neurectomy

Selective vestibular neurectomy as described for example by Silverstein *et al.* [50] is considered as the most efficient way of controlling recurrent vertigo attacks in Ménière's disease. At the same time it is the most invasive therapy as it necessitates a craniotomy, and a few cases of facial nerve palsy have been reported in the past. The procedure involves complete deafferentation of the vestibular end organ, including the input from Scarpa's ganglion as reviewed earlier [51]. The main concern is appropriate selection of the patient, taking into consideration the disequilibrium and oscillopsia that might provoke disability, as reported by Nguyen *et al.* [52]. This view has not changed substantially over the last 10 years, although the more widespread use of ITG has significantly reduced indications for selective vestibular neurectomy [53]. Some retrospective reports of small series confirm these findings [54].

Earlier overview studies on NVC showed a risk of SNHL of less than 10% offering the best preservation of hearing, although the natural progression of the disease is not improved [55]. Disadvantages of labyrinthectomy over selective vestibular neurectomy are the complete loss of hearing, the loss of the option to perform a cochlear implantation, and the remaining risk of recurrent vertigo resulting from remaining sensory input from remnants of the macular, utricular or ampullar vestibular epithelium, and from the neurons in Scarpa's ganglion. The role of residual end-organ dysfunction in provoking recurrent vertigo attacks was ascertained by impulse tests in eight patients with recurrent vertigo after selective vestibular neurectomy [56].

In a retrospective study, 25 patients treated with ITG and showing 20% SNHL of more than 30 dB and 80% vertigo

control were compared with 39 patients treated with selective vestibular neurectomy showing 3% SNHL of more than 30 dB and 95% vertigo control [57]. No additional data were presented concerning the likelihood of performance of an additional neurovascular decompression when a NVC was seen proximal from the selective vestibular neurectomy site during surgery. Inspection of the root entry zone using endoscopes was advocated [58].

Vestibular rehabilitation after unilateral deafferentation

Providing vestibular rehabilitation after an ablative vestibular procedure is 'state of the art' for enhancing the adaptive processes. Rehabilitative efforts result in reducing the sensation of instability. Two studies further elaborate on the static and postural outcome of rehabilitation.

The first study by Hall *et al.* [59] demonstrated an equal gain in gait test scores for patients under and over 65 years, albeit that a significantly greater proportion amounting to 45% of the older adults remained at risk of falls even at the end of the rehabilitation programme. An important finding is that the time between onset of unilateral hypofunction and the start of vestibular rehabilitation did not influence the improvement. This means that patients who still have an increased fall risk after having undergone a vestibular ablative procedure can still benefit from a rehabilitation programme. The authors warn that women improved less than men.

Borel *et al.* [60] found that even after 3 months all patients having undergone a selective vestibular neurectomy remained uncompensated, especially in fast walking with eyes closed. Also deviation towards the operated site when walking in the dark persisted after 3 months.

Comments and current practice

Aside from the correct technical performance of a surgical procedure, there must be a precise surgical indication, and therefore a correct diagnosis must be made. New insights differentiating Ménière's disease from migraine and neurovascular conflict have been developed. We stress the need for actually performing the multidimensional functional assessment, as the tools are available.

Although we achieve further physiopathological insights into what is happening in Ménière's disease by using the surgical approach to the inner ear in order to apply different types of drug, the main current surgical aim is to downregulate permanently or totally ablate the vestibular end organ. Substantial progress has been made recently in increasing our knowledge of ITG therapy. Selective vestibular neurectomy remains the last resort for incapacitating vertigo when ITG fails. Finally,

attention is being drawn to meticulous follow up after surgery and fall-risk prevention, including vestibular rehabilitation.

Studies to level 1 or 2 EBM need to be conducted to allow better decision making regarding the application of ITG or Meniett therapy at an earlier stage of Ménière's disease, resulting in a lesser degree and shorter duration of discomfort for patients before being offered the possibility of surgery.

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