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# Ménière's disease pt. 2. Treatment options and therapeutic strategies. Commentary to the current recommendations and own experience

## Choroba Ménière'a cz. 2. Możliwości leczenia oraz strategie terapeutyczne. Komentarz do aktualnych zaleceń i doświadczenia własne

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**SUMMARY:** We present an overview of current diagnostic and therapeutic guidelines on Ménière's disease. Over the last five years, several guidelines and studies on this subject have been published, including *The International consensus (ICON) on treatment of Méniere's disease of 2018*, *The European Position Statement on Diagnosis, and Treatment of Ménière's Disease*, *The Diagnostic and therapeutic strategy in Menière's disease. Guidelines of the French Otorhinolaryngology-Head and Neck Surgery Society (SFORL) of 2017*. Consequently, also the "American Academy of Otorhinolaryngology, Head and Neck Surgery" (AAO-HNS) published updated recommendations on the subject in April 2020. On the basis of these studies and a literature review, the main treatment methods used in Ménière's disease and an assessment of their effectiveness were presented. The current recommendations, as well as own experience of the Clinic of Otorhinolaryngology, Head and Neck Surgery of the Medical University of Warsaw, gave grounds for proposing a therapeutic scheme.

**KEYWORDS:** endolymphatic hydrops, guidelines, Ménière's disease, neurotology, vertigo

**STRESZCZENIE:** Autorzy przedstawiają kontynuację przeglądu aktualnych zaleceń i najnowszych badań dotyczących choroby Meniere'a. W ostatnich latach ukazały się międzyośrodkowe opracowania na temat strategii terapeutycznych, w tym: *International consensus (ICON) on treatment of Méniere's disease 2018*, *European Position Statement on Diagnosis*, and *Treatment of Meniere's Disease, Diagnostic* and *therapeutic strategy in Menière's disease. Guidelines of the French Otorhinolaryngology-Head* and *Neck Surgery Society (SFORL) 2017*. W konsekwencji również „Amerykańska Akademia Otorynolaryngologii, Chirurgii Głowy i Szyi" (AAO-HNS) opublikowała w kwietniu 2020 r. zaktualizowane wytyczne na ten temat. Na podstawie wymienionych opracowań oraz przeglądu literatury, przedstawiono główne metody leczenia stosowane w chorobie Meniere'a oraz ocenę ich skuteczności. W oparciu o aktualne zalecenia, a także doświadczenia własne Kliniki Otorynolaryngologii, Chirurgii Głowy i Szyi Warszawskiego Uniwersytetu Medycznego, zaproponowano schemat terapeutyczny.

**SŁOWA KLUCZOWE:** choroba Ménière'a, otoneurologia, wodniak śródchłonki, zalecenia postępowania, zawroty głowy

## ABBREVIATIONS

**AAO-HNS** – American Academy of Otorhinolaryngology, Head and Neck Surgery
**ChM** – Ménière's disease
**CPAP** – Continuous Positive Airway Pressure

## INTRODUCTION

Ménière's disease (ChM) constitutes a group of symptoms caused by hydrostatic and osmotic imbalance between the endolymph and perilymph, resulting in endolymphatic hydrops [1]. The clinical picture comprises attacks of vertigo, tinnitus and/or ear fullness, and hearing impairment. The natural course of disease also involves periods of exacerbations and remission; however, progression of the disease is associated with increased hearing loss and an elevated risk of developing a disease in the other ear [2].

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Due to the poorly researched etiology of Ménière's disease, the treatment is mainly symptomatic. The main purpose of it consists in decreasing the frequency and intensification of attacks of vertigo with minimal risk of hearing problems. In the light of the applicable recommendations and the latest research, an individual approach to the patient is essential and should assume therapy adapted to the individual clinical picture, as well as psychosocial aspects concerning each individual.

## CONSERVATIVE TREATMENT

In the case of co-existence of other chronic conditions, their treatment is substantial for improving the quality of life of patients suffering from ChM. We should pay close attention to the group of patients with obstructive sleep apnea, in whom the use of continuous positive airway pressure (CPAP) could reduce the severity of balance system ailments.

The applicable guidelines of AAO-HNS recommend early implementation of rehabilitation of the vestibular system in patients with imbalances in the course of the disease, and as a result of ablation therapy. It should be remembered that this procedure should only be included in the period between vertigo attacks.

A major position in the latest recommendations on ChM is gained by psychological support and the use of psychotherapy, particularly in the cognitive-behavioral current. It consists in conduct supporting other treatment options, allowing a better the quality of life and social functioning of patients [8].

Betahistine provides the grounds for pharmacotherapy in Ménière's disease in most European countries, as well as in Japan and Australia. However, it is not registered for treatment of ChM in the USA. As a strong H3 receptor antagonist and weak H1 receptor agonist, betahistine induces at least three processes in the structures of the inner ear: an increase in cochlear blood flow, an increase in histamine reuptake, and a decrease in vestibular excitability. Despite enjoying strong popularity among clinicians, betahistine has so far been the subject of few clinical trials with a high level of reliability. The first multicenter, randomized, placebo-controlled clinical trial (BEMED trial) conducted in recent years did not show a major difference in the incidence of attacks of vertigo between patients receiving betahistine at 2 x 24 mg or 3 x 48 mg and the placebo group [9]. Different conclusions are drawn from the meta-analysis conducted by Nautas [10], which suggest the significant impact of betahistine on the clinical course of Ménière's disease, i.e. the reduction of dizziness with simultaneous good tolerance of medication among patients. The favorable safety profile of the medicine is indicated by studies in which betahistine was administered at doses several times higher and did not cause significant adverse effects [11].

Basing on years of clinical experience, experts in these guidelines recommend using betahistine 24 mg twice a day to treat Ménière's disease. The latest international recommendations also point to diuretics, which have been widely used as first-line pharmacotherapy in ChM for many years. The prescribed diuretics include substances with a different mode of action, which results in a decrease in the hydrostatic pressure and volume of the endolymph. Thiazide diuretics are the most widely used group today.

Experts of these international recommendations also indicate the contraindications to the use of individual diuretics and their possible side effects that should be considered when planning treatment.

The authors of these guidelines have not included oral steroid therapy in the proposed therapeutic recommendations.

In some countries (including Australia and Italy), first-line treatment also involves the use of local therapy with the production of low-pressure pulses (Meniett ®). The pulses are transmitted into the vestibular structures through a ventilation tube previously placed in the tympanic membrane, using a generator that performs three 60-second low pressure cycles, separated by 20-second intervals. Treatments are carried out 3 times a day for 1 to 2 months. In a systematic review published in 2015, van Sonsbeek et al. analyzed 5 studies aimed at assessing the effectiveness of Meniett therapy in the treatment of Ménière's disease. The authors did not demonstrate a beneficial impact of therapy with the production of pulsatile pressure on the frequency of vertigo, while assessing the effectiveness of this method in eliminating other symptoms of ChM was challenging, mainly due to the lack of homogeneous endpoints and consistent criteria for analyzing the effectiveness of treatment in individual studies [17]. The therapeutic scheme proposed by Nevoux et al. in the international consensus of 2018 permits the addition of this therapy due to its low invasive nature and rare adverse reactions. AAO-HNS guidelines do not recommend this type of treatment due to numerous reports about the absence of benefits from its use.

## TRANSTYMPANIC TREATMENT

In the case of ineffective conservative management or contraindications to the use of oral pharmacotherapy, administration of medication into the tympanic cavity should be considered. Drugs used transtympanally involve steroids and aminoglycosides.

Numerous studies compare the effectiveness of medicines administered intratympanically.

Albu et al. [18] compared the efficacy in controlling vertigo between a group of patients receiving dexamethasone injections for 3 consecutive days and a group that additionally took high dose betahistine (144 mg/d). Patients who used a steroid in monotherapy had a significantly less satisfying degree of reduction of vertigo – complete control of vertigo (class A according to AAO-HNS) was only achieved in 44% of patients, compared with 73.3% in the group receiving betahistine. Significant improvement, i.e. in classes A and B combined, was obtained in 65.5% patients receiving steroid only and in 90% individuals from the group subject to combination therapy.

From a retrospective analysis conducted by Naples et al. [19], it resulted that satisfying control of vertigo requires more

steroid injections than with gentamicin. In turn, Patel et al. designed a randomized, double-blind study in which they compared methylprednisolone and gentamycin administered transtympanally for efficiency and safety in ChM therapy. Their results showed comparable effectiveness of both drugs – the average reduction in the number of attacks of vertigo within 18–24 months after treatment compared to 6 months before treatment was 90% for steroid therapy and 87% for gentamicin [20]. A noteworthy conclusion from the aforementioned papers is the lack of statistically significant differences in hearing impairment between the studied groups using transtympanal therapy.

On the other hand, Öztürk and Ata [21] compared the effectiveness of transtympanal mono-steroid therapy with treatment using dexamethasone and gentamycin injections. Two years after finished therapy, the group where the steroid was administered obtained a satisfactory level of reduction of vertigo in 70.6% of patients, while among patients who received combined injections, this percentage was 81%.

According to current recommendations, steroid drugs administered into the tympanic cavity form the grounds of the second line of therapy in Ménière's disease. Of the two available substances, dexamethasone is the more common choice; compared to methylprednisolone, it is less likely to cause an unpleasant burning sensation in the ear after administration. Experts recommend using dexamethasone at a concentration of 4 mg/mL in single injections for 5 consecutive days. It is also possible to use the drug every  days for 2 weeks or every 7 days for 4 weeks. Due to the high effectiveness and also a favorable safety profile for the organ of hearing, intratympanic steroid therapy can also be used in patients with bilateral Ménière's disease.

As an ototoxic antibiotic, in the past gentamicin has been used at high doses and short intervals to induce pharmacological vestibular ablation. In the currently recommended regimen, gentamicin is administered in small doses at larger intervals, which results in satisfactory control of ChM symptoms in the absence of complete vestibular damage and a lower risk of hearing damage. Regardless of the used regimen, the possibility of hearing loss after just one dose of gentamicin should be borne in mind, which is why the recommendations mainly regard patients with substantial hearing loss in the affected ear and those who cannot undergo surgery with the choice of a hearing preserving technique. A contraindication to transtympanal therapy with aminoglycoside is bilateral Ménière's disease, which is particularly relevant given the progressive nature of the disease and the risk of developing symptoms in the other ear intensifying with duration of the condition.

## SURGICAL METHODS OF TREATMENT

Approximately 10–20% of all patients with Ménière's disease do not succeed in achieving satisfactory clinical improvement despite conservative and transtympanal treatment [22]. In such cases we should consider surgical treatment. Potential techniques include treatments aimed at increasing endolymph drainage (drainage or decompression of the endolymphatic sac) and destructive

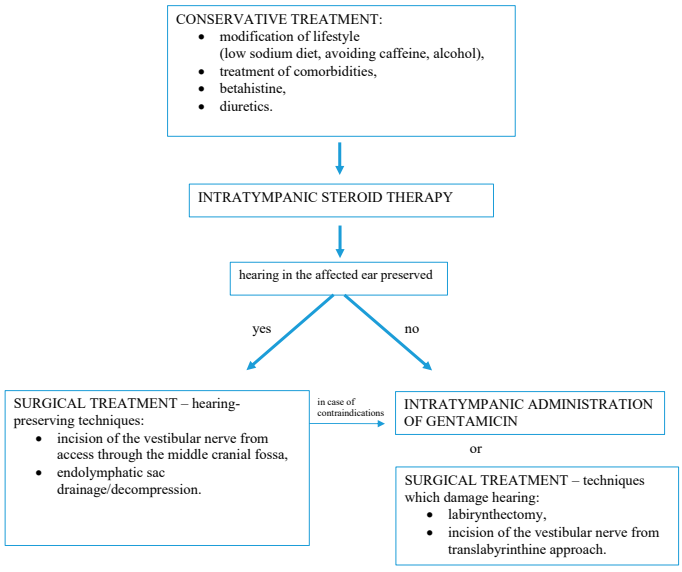


**Fig. 1.** Therapeutic algorithm for escalation of treatment of Ménière's disease – ICON [3], modified and detailed at the Department of Otolaryngology, Head & Neck Surgery of the Medical University of Warsaw.

procedures on structures of the vestibular organ (labyrinthectomy and vestibular nerve section).

Treatments based on increasing endolymph drainage from the endolymphatic sac remain frequently chosen surgical techniques, although their effectiveness in reducing the frequency of vertigo attacks is currently under discussion. Already in the 20th century, Thomsen et al. conducted a study in which they demonstrated that the efficiency of endolymphatic sac surgery is comparable to that of mastoidectomy [23] or placement of a ventilation tube in the tympanic membrane [24]. Given the unpredictable natural clinical course of ChM, caution should be exercised in interpreting the results of performed tests. Assessing the effectiveness of surgical treatment is further complicated by the limited possibility of randomization, blinding and selection of a placebo procedure.

In 2008, Kitahara [25] proposed to modify the procedure of endolymphatic drainage by adding additional dexamethasone to the endothelial sac. In a prospective randomized trial, he assessed the effectiveness of the altered procedure in reducing vertigo, as well as its effect on hearing. Two years of surgery, complete reduction of vertigo was achieved in 88% of patients undergoing classical endolymphatic drainage and in 85.1% of patients who were additionally given a steroid in the endothelial sac, while after 7 years 78.8% and 79.2% of people were in complete remission. Both in 2-year as well as 7-year follow-up, the differences in the efficacy of treatment of vertigo between the groups were not statistically significant. However, it is interesting to note that the group administered dexamethasone intraoperatively experienced statistically significant more frequent hearing improvement (49% of patients after 2 years and 36.5% after 7 years – compared with 31.9% and 8.3% in the group operated classically.

Selective vestibular nerve section with access through the middle cranial fossa allows for successful handling of discomfort with high

safety for hearing and rare complications. Complete resolution of vertigo attacks in long-term postoperative follow-up is possible in more than 90% of patients [26].

Selective neurectomy is particularly recommended for patients with the classical form of the disease, preserved hearing and significant functional limitation (classes IV–VI on the Functional Scale of the AAO-HNS), as well as for people with a history of Tumarkin seizures. The Clinic of Otorhinolaryngology, Head and Neck Surgery of the Medical University of Warsaw recognizes vestibular nerve section with access through the middle cranial fossa as the method of choice in the surgical treatment of advanced Ménière's disease. A retrospective analysis of the results of procedures performed at the Clinic in 2012 demonstrated that it is an effective method for achieving control of vertigo in 98%, hearing preservation in 60% and hearing improvement in 1/3 of patients [28]. In the case of substantial hearing impairment in the course of the disease, vestibular neurectomy by transtympanal access can be performed.

## EVALUATION OF RESULTS OF TREATMENT

To assess the effectiveness of treatment of Ménière's disease, the formula proposed by AAO-HNS is used; according to this formula, the therapeutic effect is assigned to one of six classes (A–F). The basis for classification is the change in the frequency of vertigo in the 18th to 24th month period after treatment in relation to the 6 months before treatment. From the patient's point of view, the essential indicator of the effectiveness of treatment is the improvement of their functioning, which they subjectively evaluate on a six-point scale.

The fluctuating, individually varying natural course of Ménière's disease, which is characterized by periods of exacerbations and spontaneous remissions, is a primary concern for an objective assessment of the effectiveness of any treatment.

## CONCLUSION

The priority in treatment should be to reduce the frequency of vertigo attacks, which is considered the most burdensome aspect of Ménière's disease. The therapeutic scheme should be based upon an individual analysis of the course of disease for a particular patient and should be directed to their main ailments.

Treatment should begin with conservative management and in the absence of clinical improvement, continue by escalation of therapy with the selection of invasive methods. In the absence of improvement despite the use of pharmacological treatment, as well as the occurrence of Tumarkin attacks, an aggressive course of Ménière's disease with frequent, persistent attacks of vertigo constitutes an indication for surgical treatment. In centers with capabilities and experience in performing advanced otosurgical procedures, due to high relevance and a high percentage of hearing preservation after surgery vestibular neurectomy with access through the middle cranial fossa should be considered the treatment of choice for advanced ChM.

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