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Menière's Disease
Pathophysiology and Treatment

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Contents

Abstract

Menière's disease is defined by the association of 4 symptoms: vertigo attacks, fluctuating hearing loss, tinnitus and an auricular plenitude sensation. The pathophysiology is commonly explained by a distension of membranous labyrinth by the endolymph, equally called endolymphatic hydrops. Recent studies also tend to relate the disease to immune mechanisms.

The treatment is medical in the majority of patients but there is no international consensus on the management of the different stages of Menière's disease. Regarding the lack of clinical studies clearly demonstrating the effectiveness of a certain therapy or another, the recommendations are usually based on the empir-

ical experience of practitioners and on the observation of a marked amelioration at 2 years of treatment in the majority of patients.

The treatment of the acute phase of Menière's disease is basically symptomatic. Vestibular suppressant drugs have a well-established record in controlling acute attacks of vertigo. Most have variable anticholinergic, anti-emetic and vestibular sedative effects. If necessary, the administration of benzodiazepines will help to alleviate anxiety.

Long term management of Menière's disease includes a low salt diet, the use of diuretics in the post-crisis phase, and the very common use in Europe of histaminergic agents. Corticosteroids are used in bilateral forms of Menière's disease, particularly if an autoimmune basis is suspected. All authors insist on the interest and the importance of regular follow-up, especially with regard to the psychological status and responsiveness to treatment of the patient.

Surgical indications are rare and the least invasive procedures are used first. The choice of the procedure should take into consideration the need to preserve the auditory function of the patient.

Menière's disease is an idiopathic disorder of the inner ear characterised by 4 associated symptoms: vertigo, tinnitus, aural fullness, and low frequency hearing loss at early stages. It has long been considered to consist of a distension of the membranous labyrinth also called endolymphatic hydrops. More recent findings indicate that in some patients the disease may be linked to immune reactions. Medical treatments produce good results in 80% of patients. Because this pathology is incompletely understood, its management remains widely empirical. Even more, the fluctuating aspect of symptoms combined with an unpredictable evolution of this disease over time explain, in part, the lack of clinical studies performed in this field. Therapy usually includes a mix of dietary recommendations, physiotherapy, psychological support and pharmacological intervention. Despite the variety of regimens used (mainly diuretics and vasodilators but also even anaesthetic drugs such as droperidol/fentanyl), to date none have shown the ability to prevent symptoms in well-controlled studies.

There are 3 steps in the management of patients with Menière's disease.

1. The treatment of the acute phase. Protocols of drugs administered in vertigo attacks differ among medical centres. However, the therapeutic attitude has an ubiquitous goal: to suppress vertigo and associated symptoms (anxiety, nausea, vomiting), without compromising the vestibular compensatory mechanisms. These reflect the capacity of the central nervous system (CNS) to reorganise the neurosensory information responsible for equilibrium control in response to an acute vestibular dysfunctioning.

2. Long term management. The goal is to improve the quality of life by decreasing the recurrence of vertigo crises in the first instance, and secondly to prevent, as much as possible, the deterioration of auditory function. In the majority of patients, medical treatment allows control of disease evolution. Surgical indications are reserved for some disabling forms once medical therapeutic alternatives have proved unsuccessful.

3. Psychological support. This forms an important part of the therapeutic management. The clinician has to offer their patient a positive perspective of the different stages of their disease. The patient needs their disease to be explained in detail, and the absence of an intra-cranial tumour must be clearly stated. Whatever the psychological profile of the patient, they may still be anxious and this may require pharmacological intervention and/or counselling in stress management.[1] A good stress management, e.g. by means of relaxation or cognitive therapy, goes together with a favourable evolution of this disease.[2]

1. Pathophysiological Basis Treatment: Current Knowledge

A major underlying pathophysiological state in Menière's disease is endolymphatic hydrops, which can only be demonstrated with certainty after death by histopathological study of the temporal bones.[3,4] The hydrops is a distension of the membranous labyrinth that begins at the apical part of the cochlea. With time, this process extends to the cochlear aqueduct and the vestibular apparatus (utricule, saccule). For clinical purposes (treatment and reporting), the presence of endolymphatic hydrops can be inferred during life by the presence of the following symptoms: recurrent, spontaneous episodic vertigo; hearing loss; aural fullness; and tinnitus. Either tinnitus or aural fullness (or both) must be present on the affected side to make the diagnosis.

Although Menière's disease is commonly attributed to an idiopathic endolymphatic hydrops, some immune disturbances have also been evidenced in patients with Menière's disease. Furthermore, experimental studies in animals have shown that hydrops do not necessarily lead to Menière symptoms; conversely these symptoms may be found, though rarely, without hydrops.

1.1 Mechanisms of Endolymphatic Hydrops

Different pathogenic mechanisms have been proposed to explain the hydrops. These include the following:

- obstruction of the endolymphatic duct and/or dysfunction of the endolymphatic sac
- dysregulation of endolymph production.

1.1.1 Obstruction of the Endolymphatic Duct and/or Dysfunction of the Endolymphatic Sac

The endolymphatic duct unites the cochlear and vestibular portions of the inner ear at the ductus reuniens, which joins the utricle and the saccule. After passing through the otic capsule, it reaches the endolymphatic sac (fig. 1). The endolymphatic sac is thought to have numerous functions:

- transmission of changes in pressure from cerebrospinal fluid (CSF) to endolymph
- homeostasis of endolymph (resorption/secretion)
- secretion of glycoproteins to increase the longitudinal flow of endolymph by means of an osmotic process
- secretion of a natriuretic hormone (saccin) to increase endolymph production[6]
- removal of metabolic and cellular debris, and immunodefence of the ear.

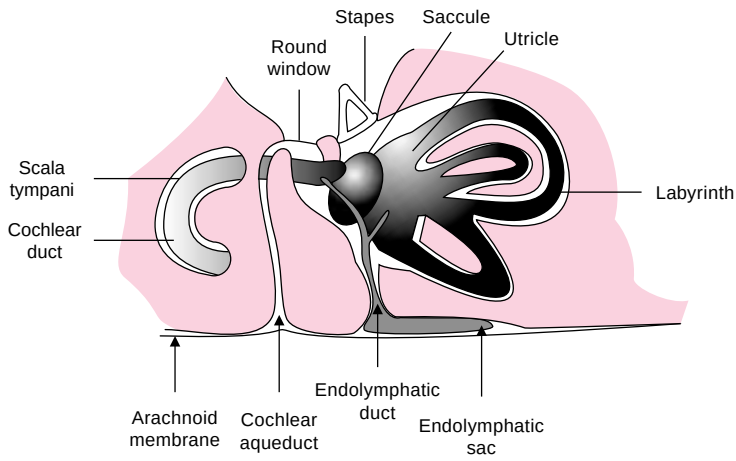

Fig. 1. Schematic of the endolymphatic system (reproduced from Marchbanks[5], with permission).

The duct obstruction or the endolymphatic sac dysfunctioning are considered to be aetiological factors in Menière's disease because hydrops can be created experimentally on animals by procedures which create these same conditions.

1.1.2 Overproduction of Endolymph

The excess of endolymph in temporal bones of patients with Menière's disease could be explained by an overproduction of endolymph. The antidiuretic hormone level has been reported to be significantly higher in patients with Menière's disease.[7]

Sterkers et al.[8,9] have described the presence of two osmotic gradients in the cochlea. The first one is between perilymphatic space and endolymphatic sac, and the second is inside the endolymphatic space between the apex and the base of the cochlea. Any disturbances of these two gradients could result in hydrops.

1.2 Immune Disorders

Although endolymphatic hydrops can be experimentally elicited in animals by obstructing the canal of the endolymphatic sac, the consequences vary depending on species; the hydrops is constant in guinea-pigs, but rare in monkeys. In addition, in no instance did any animal develop Menière's vertiginous spells.[10]

Conversely patients in whom Menière's disease symptoms could be elicited by food allergens did not concomitantly develop hydrops as investigated by electrocochleography.[11]

These observations may suggest that symptoms of Menière's disease may be related to other mechanisms than endolymphatic hydrops, e.g. immune disturbances. Many arguments in favour of an immune aetiology of Menière's disease have appeared in recent years.

These include:

(i) the presence, close to the endolymphatic sac, of a lymphatic vascularisation and immunocompetent cells (T lymphocytes, macrophages);

(ii) the presence of biological signs of immune reactions in patients with Menière's disease, for example, raised immunoglobulin (Ig)M complexes and C1q component of complement;[12]

(iii) the abnormal presence of IgG deposits in the endolymphatic sacs of patients undergoing shunt surgery for Menière's disease;[13]

(iv) the presence of characteristic manifestations of Menière's disease in certain autoimmune diseases (Cogan syndrome, Periarteritis nodosa); and

(v) the presence of autoantibodies directed against endolymphatic sac in the sera of patients with Menière's disease.[14]

1.3 Aetiology of Symptoms

1.3.1 Possible Local Causes

The theory of intoxication by potassium described by Lawrence and McCabe[15] is commonly accepted. Endolymphatic sector hyperpressure would lead to a rupture of the membranous labyrinth, resulting in a blend of perilymph and endolymph fluids. This in turn would produce a decrease of potassium levels in endolymph sector and an increase in potassium levels in perilymphatic sector. This step would be followed by a depolarisation of vestibular nerve fibres, leading to an irritative vestibular syndrome. The absence of repolarisation would explain the decreased vestibular excitability observed secondarily. In Tonndorf's theory,[16] the increase of endolymph volume is the original cause of alteration in inner ear mechanical properties.

1.3.2 Role of the CNS

Vertigo is thought to result from a functional imbalance between the labyrinths of the two ears. Different neurotransmitters are involved in the central compensatory mechanisms, mainly: histamine, acetylcholine and γ-aminobutyric acid (GABA).

To date, 3 types of histamine receptors have been identified in mammals, the post-synaptic histamine H_1 and H_2 receptors[17] and the pre-synaptic H_3 receptors,[18] all of them being present in the vestibular nuclei. Histamine modulates vestibular nuclei neuron activity via H_1 and H_2 receptors.[19] Unilateral vestibular neurectomy in the cat induces

a histamine-led compensatory mechanism: increase in histamine synthesis and release by the tuberomammilary neurons projecting to the vestibular nuclei, promoting vestibular recovery. Since similar effects have been observed after treatment with H_3 receptor antagonists, it has been hypothesised that H_3 receptors could play an important role in such compensation of vestibular disorders.[20]

Cholinergic receptors have been also identified in the vestibular nuclei and the midbrain.[21] During the vestibular compensatory process, a modification of cholinergic brainstem synapses occurs, resulting in new synapses with an asymmetric pattern of distribution in both number and sensitivity. The reafferent neurons fire again at a normal rate under the control of the contralateral non-damaged labyrinth.

At the same time, inhibitory synapses coming from the cerebellar Purkinje cells are mediated, at the vestibular nuclei level, via the neurotransmitter GABA.

Another inhibitory system, under adrenergic control, intervenes in the vestibular nuclei. On the basis of these neuropharmacological data, the effects of the various drugs used in Menière's disease can be better understood.

2 Dietary Manipulations

2.1 Low Sodium Diet

As early as the 1930s, Dederding[22] and Furstenberg et al.[23] advocated a low salt diet (<2000 mg/day) in patients with Menière's disease. To date, the efficacy of this regimen has not been evaluated scientifically.[24] When associated with diuretics, low sodium diets as in the Furstenberg regimen have been reported to bring positive results.[25] Since the sodium levels in endolymph are typically near normal in both animals with induced endolymphatic hydrops and in a limited number of patients from which endolymph was sampled, and since a low-salt diet is known to have extremely little influence on the plasma sodium level, reducing salt intake is likely to have more complex effects than that of simply changing plasma or endolymph sodium levels. Aldosterone secretion induced by dietary salt reduction may affect ion transport processes in the ear, altering regulation of the endolymph.

2.2 Water Intake

Many physicians give little or no guidance with regard to how much water should be consumed. General rules for a healthy diet apply, including eating small, regular meals and keeping water intake up. If the goal of diuretic therapy and a low salt diet is to increase sodium loss from the body, then a normal level of water consumption (8 glasses per day) would help achieve this aim. Some physicians advise their patients to limit water intake, presumably to aid in the dehydrating effect of the diuretic but there are no data supporting either point of view.

2.3 Other

Some patients report that by limiting sugar, monosodium glutamate, caffeine, and/or alcohol their attacks occur less frequently. There is no compelling scientific rationale for why this should be. Therefore, the practitioner should help each individual patient to make their own assessment of dietary changes that most affect the symptoms. The patient may, for example, be asked to keep a diary in which symptoms are rated as objectively as possible.

3. Pharmacological Treatment

3.1 Benzodiazepines

Benzodiazepines are frequently used in the US in the treatment of attacks because of their central vestibular sedative effect.[26-28] Diazepam is the agent most used for this purpose. Benzodiazepines act on the cerebellar GABA-ergic system that mediates inhibition on the vestibular response. They bind to a specific site on the GABA receptor to potentiate the effect of the endogenous ligand.[29] These effects may offer benefits in the treatment of vertigo and emesis.

In other countries, such as France, their use is more limited. Benzodiazepines might impair vestibular compensation.[30] Nevertheless, their anxiolytic properties (specific action on the limbic system) are very useful in acute vertigo when it is particularly associated with anxiety.

Dependence, sedation, hangover, impaired memory and incoordination with ataxia are the main adverse effects of benzodiazepines. Respiratory depression and cardiac arrest have occurred rarely after intravenous administration. Benzodiazepines are contraindicated in patients with chronic obstructive pulmonary disease.

3.2 Antiemetic Agents

While most antiemetic agents are generally aimed at treating the effects of vertigo in Menière's disease, they may also play a role in controlling the disease itself by reducing stress and anxiety. All of them have sedative, anticholinergic and antiemetic properties, although in various proportions depending on the drug.[31]

The antivertiginous and antiemetic effects of meclozine are believed to be linked to a decrease in the excitability of the middle ear labyrinth and an inhibition of conduction in the middle ear vestibular-cerebellar pathways. It has a longer duration of action (24 hours) and a slower onset of action than other antihistamines used in vertigo. The usual dose in this indication is 25 to 100 mg/day in divided doses. Meclozine is known to often induce drowsiness, and somnolence can be significantly accentuated when used in conjunction with any other CNS depressant medication, e.g. narcotics and barbiturates. Meclozine also increases the toxicity of antipsychotics and of anticholinergics.

Dimenhydrinate is an antihistamine used to treat motion sickness, nausea and vomiting. It is especially useful in preventing and treating vertigo associated with Menière's disease, as well as nausea and vomiting, at an oral dose of 50 to 100mg 3 to 4 times daily. It can also be administered intramuscularly or intravenously. Mild drowsiness may occur.

Metoclopramide is an antidopaminergic drug, which does not cross the blood-brain barrier, but exerts its antiemetic property at the area postrema of the brainstem. The versatile administration routes (oral, parenteral, suppositories) makes metoclopramide very convenient for acute treatment at a regimen of 20 to 40 mg/day in 2 to 3 doses. At such low doses, the main adverse effects consist of orthostatic arterial hypotension and drowsiness. As with any antipyschotic, unwanted effects become more serious at higher doses and increase with treatment duration: extrapyramidal syndrome and endocrine disorders.

Promethazine is a phenothiazine with pronounced antihistaminic properties in addition to a strong anticholinergic activity. Moreover, it has significant dopamine blocking activity. The sedative and anti-emetic properties of promethazine, as well as its possible rectal administration, make it a useful treatment for Menière's attacks. The initial dose in adults is usually 25mg, then 12.5 to 25mg every 4 to 6 hours as needed. At these doses promethazine is relatively free of extrapyramidal reactions associated with other phenothiazine derivatives.

Prochlorperazine, also a phenothiazine, is used for the management of psychotic disorders, anxiety and to control emesis by blocking dopamine receptors. The usual dose of this very potent drug is 10mg given orally or intramuscularly every 4 to 6 hours. The frequent adverse effects of prochlorperazine (up to 50% of patients, even at minimum doses) include drowsiness and mild hypotension, and there is a risk of extrapyramidal reactions at therapeutic doses, leading to parkinsonian-like symptoms. Cardiac conduction problems may occur.

Scopolamine is a naturally occurring belladonna alkaloid with anticholinergic properties, used to prevent nausea and vomiting associated with motion sickness in adults. Dry mouth and blurred vision are quite frequent consequences of its anticholinergic effects.

3.3 Vasodilatators

The idea that Menière's disease is associated with ischaemia, a theory that has been never verified, has led to the use of vasodilators. The intravenous injection of histamine has been used for the same purpose but has most commonly replaced by betahistine.

In Europe, betahistine is the preferred anti-vertiginous drug[32,33] (betahistine is available in the US through compounding pharmacies). Apart from blocking H_1 and H_3 receptors,[34,35] betahistine is also reported to increase cochlear blood flow.[36,37] This may contribute in some way to the improvement in vertigo, nausea and vomiting demonstrated in several clinical trials.[38-42] However, long term, longitudinal, uncontrolled trials have failed to show a benefit on hearing loss.[43,44] Betahistine is not sedative[45] but may induce mild stomach discomfort. Because of its positive adverse effect profile and experience with it as a long term treatment, betahistine is used not only in short term treatment of the acute phase, but also, by some, as a maintenance treatment.

Nicotinic acid is given at doses of 50 to 400mg half an hour before meals, to produce a vasodilatation flush. Only limited success has been reported with this treatment, which is uncommonly used nowadays.[46,47]

3.4 Diuretics

For several years diuretics, like sodium depletion, were considered the principal long term treatment of Menière's disease. This recommendation is based on the supposed action of diuretics on the equilibrium of inner ear fluids, leading to a reabsorption of endolymph.[48] Many clinical trials conducted 15 to 30 years ago concluded in favour of diuretics in Menière's disease, whether hydrochlorothiazide (HTCZ), chlorthalidone, or triamterene.[49-52]

The typical adult dosage of HTCZ is 50 mg/day, and triamterene 50mg in combination with HTCZ 25mg is taken as one tablet per day. The main adverse effect of thiazide diuretics is hypokaliaemia and intravascular volume depletion with resulting pre-renal azotaemia, skin rashes, neutropenia and thrombocytopenia, hyperglycaemia, hyperuricaemia and hepatic dysfunction. Furosemide (frusemide) is also used, at a dosage of 10 to 80 mg/day. Furosemide is a potent diuretic, which may lead to excessive hypotension and fluid/ion depletion. Both furosemide and thiazide diuretics require potassium supplementation.

Acetazolamide, a carbonic anhydrase inhibitor, is known to induce diuresis by virtue of a decrease in sodium-hydrogen exchange in the renal tubule, and is used frequently in France. Adverse effects are relatively benign and include paresthesias, gastrointestinal disorders, fatigue, anorexia, drowsiness, and transient myopia. Tolerance may develop on the diuretic action in the long term. The usual oral regimen is 250mg twice daily or 500mg slow-release once daily. In a retrospective cohort,[53] acetazolamide has been found to be as effective as chlorthalidone in controlling vertigo spells and preventing short term loss but neither were able to prevent long term hearing deterioration in patients with Menière's disease.

Long term nonblind trials with diuretics have reported up to 79% improvement of vertiginous symptoms and some improvement in hearing – evolutions that may indeed reflect the natural history of the disease. Indeed most of the trials conducted with diuretics retrospectively, suffer from considerable methodological flaws and it is now difficult to conclude on a clear benefit of these diuretics on symptoms of Menière's disease.[54]

Osmotic diuretics such as glycerol, urea and isosorbide, are known to be effective in reducing hydrops. Clinically, isosorbide is better accepted than urea and glycerol as it tastes nicer and has considerably fewer adverse effects. Moreover, while the effects of urea and glycerol are transitory, making them more useful in diagnosis than as treatment, isosorbide has been reported to improve hearing after an 8-week administration period. In this study,[55] no reduction in vertigo has occurred.

3.5 Calcium Antagonists

Some physicians, especially in Europe, have been using calcium antagonists, such as flunarizine and cinnarizine, as maintenance therapy in Menière's disease. Neither cinnarizine nor flunarizine are presently available in the US, where other calcium antagonists are sometimes used: nimodipine at a dose of 30mg twice daily and verapamil at a dose of 120mg every morning. Exactly how these calcium antagonist influence Menière's symptoms and/or function of the ear is not known. However, they prevent motion sickness and are vestibular suppressants. Vestibular hair cells are endowed with calcium channels. Studies in animals with endolymphatic hydrops have shown the endolymph calcium level to be elevated with cinnarizine. Limited measurements of endolymph sampled from patients with Menière's disease also show a high calcium level. This raises the possibility that a calcium disturbance may contribute to the symptoms of Menière's disease. Flunarizine and cinnarizine may also exert their pharmacological activity thanks to their anti-H_1 receptor and antidopaminergic properties. Whereas flunarizine may induce sedation and bodyweight gain in the short term, and even depression or parkinsonism in the long term, cinnarizine appears to induce fewer adverse effects.[56]

3.6 Aminoglycosides

The ability of specific aminoglycosides to selectively damage the sensory hair cells of the vestibular system is used as a chemical labyrinthectomy, which allows reduction of the sensitivity of the vestibular system. The techniques rely on the fact that for aminoglycosides such as gentamicin, the sensory cells of the vestibular system are more sensitive to damage than are the cells of the cochlea. This gives the opportunity, at the right dose, for vestibular function to be reduced without damaging hearing. The antibacterial is usually injected into the middle ear space through the eardrum, and enters the inner ear through the round and oval windows. This method can be effective, but in practice it is difficult to achieve vestibular ablation without causing some damage to hearing. A number of groups are presently researching the best regimen of aminoglycoside applications. It has been reported that best results were obtained with 2 to 4 applications to the middle ear, with a greater likelihood of hearing loss if more treatments were given.[41] One common approach is to 'titrate' the number of treatments to the patients symptoms, using just enough to alleviate vertigo without necessarily destroying all vestibular function.

Gentamicin is most widely used agent for the selective ablation of the vestibular system of one ear. It is most often administered with a small gauge syringe directly through the tympanic membrane into the middle ear space. From there it diffuses into the fluids of the inner ear. Usually, repeated injections are performed over a period of weeks, which allows hearing function to be monitored to minimise the risk of further hearing loss. The concentration of gentamicin ranges from 26.7 to 40 mg/ml, with similar successful results.[57] At 2 years, gentamicin instillations result in abolition of vertigo in 70 to 80% of patients but in significant hearing loss in a part of the population treated.[41,58]

Parenteral injection of gentamicin or streptomycin at a dose titrated to suppress labyrinthine function, is also a reasonable alternative in patients with bilateral disease. One of the problems associated with bilateral ablation of the labyrinths is oscillopsia, i.e. a perception of oscillation of the visual field, which can be as disturbing to the patient as vertigo. The goal of titration is therefore to reduce the sensitivity of the labyrinths without totally ablating them.[59]

3.7 Others

Acetylleucine has been used to treat vertigo since the late 1950s in some European countries. Although its mechanism of action is not clear, and well-controlled clinical trials are lacking to support its claim of efficacy, acetylleucine exerts a rapid effect on vertiginous symptoms. Often initially injected intravenously in emergencies, acetylleucine

can then be administered orally. Its limited adverse effects include gastritis.

It has been suggested that the improvement seen in patients following ear surgery may be due, in part, to the general anaesthesia used. Furthermore, some patients benefit from anaesthesia without surgery. Gates[60] reported that of the 30% of patients with Menière's disease who did not respond to a low salt diet, diuretics and stress reduction, 60% of these patients gained relief from vertigo after one injection of the anaesthetic combination droperidol/fentanyl (a neuroleptic agent and a narcotic analgesic, respectively). This has been attributed to a long-lasting depression of the vestibular system by some anaesthetics.

The benefit sometimes observed with corticosteroids has been attributed to suppression of an autoimmune response, and has been used to support the concept that Menière's disease may arise from some form of autoimmunity. However, corticosteroids have a vast array of activities, affecting carbohydrate and protein metabolism, lipid metabolism, electrolyte balance, inflammatory responses and immune responses. In addition, glucocorticoid receptors have been demonstrated in tissues of the inner ear,[61] raising the possibility that corticosteroids may have a direct effect on fluid homeostasis in the ear. It is therefore impossible at the present time to know exactly which of the effects of corticosteroids, if any, is important in relieving the symptoms of Menière's disease. Whereas prednisone is administered orally, in order to reach higher concentrations in the cochlea dexamethasone is sometimes given locally as a cochlear instillation[62] in conjunction with intravenous administration.

Other drugs or food supplements are sometimes used in the management of patients with Menière's disease, such as gingko biloba extract or lipoflavins and vitamins. Their mechanism of action in Menière's disease is unknown and their use, although not likely to be harmful, is supported by very little evidence of efficacy.

4. Surgical Treatment

Two types of surgery exist in the management of Menière's disease. The first is represented by nondestructive procedures. These aim on the one hand to act against the supposed mechanism of hydrops and on the other to conserve auditory function. The second type is represented by radical procedures of vestibular deafferentation of the diseased ear, the auditory function not necessarily being conserved.

4.1 Nondestructive Procedures

4.1.1 Endolymphatic Sac Surgery

Under this title, we group several surgical techniques. Endolymphatic sac decompression was first proposed by Portmann in 1927.[63] The current techniques combine decompression and drainage of the endolymphatic sac to the subarachnoid space (endolymph-subarachnoid shunt) or to the mastoid cavity. This drainage is designed to ensure good long term control of endolymph accumulation.

The results of this type of surgery form the subject of several controversies, with the result that the term placebo surgery has been used to qualify it.[64]

4.1.2 Tympanostomy Tube

In 1988, Montandon et al.[65] reported that vertigo in patients with Menière's disease could be controlled by placing a ventilation tube through the tympanic membrane of the affected ear. Since then other reports have supported this observation. Thomsen et al.[66] compared the use of tympanostomy tubes with endolymphatic sac surgery in 2 groups of patients and found no significant differences between the 2 groups, indicating that tympanostomy tubes were as effective as an endolymphatic sac surgery. One reservation in the use of this technique has been the lack of scientific explanation for how it would work. Some physicians remain unconvinced and there is as much controversy on this issue, as there is with endolymphatic shunts. However, as the tympanostomy procedure is a relatively minor procedure – widely used in children for the relief of middle-ear infec-

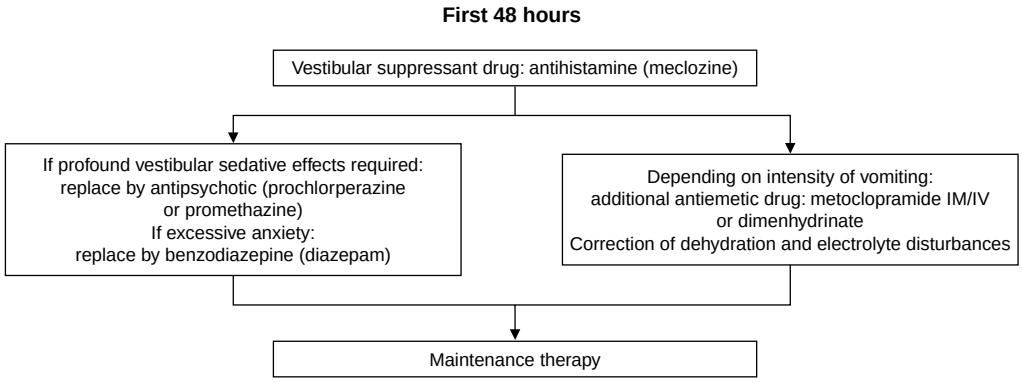

Fig. 2. Symptomatic treatment of acute episode of Menière's disease. **IM** = intramuscular; **IV** = intravenous.

tions – it may be something to consider before other more invasive surgery is considered.

4.2 Destructive Procedures

4.2.1 Labyrinthectomy

The surgical labyrinthectomy permits the vestibular information coming from the pathologically diseased labyrinth to be suppressed definitively. Insofar as the cochlear apparatus is also sacrificed, this kind of surgery is reserved for patients without any beneficial or useful hearing in the ear with hydrops.

4.2.2 Vestibular Neurectomy

Vestibular neurectomy is an otoneurological procedure, which can dramatically cure patients with severe disabling vertigo. The surgery consists of sectioning the vestibular nerve from the vestibular apparatus, while leaving the auditory nerve intact, thereby preserving hearing. During the recovery period, the brain adapts to manage without vestibular input from the operated side, so that normal activity can be resumed.

5. Recommended Therapy

There is no international consensus on how to treat Menière's disease, whatever the stage. In the absence of clinical data clearly establishing the efficacy of one therapy or another, the recommendations are based on the empirical experience of the clinicians and on the clinical observation of a marked amelioration of symptoms at 2 years in the majority of patients. All authors insist on regular follow-up, especially on the psychological aspect and on the response of the patient to treatment. Therapy in Menière's disease must be progressively adapted.

5.1 Acute Episode (First 48 Hours)

The goal of treatment in Menière's disease is to suppress the vertigo sensation and the associated symptoms (fig.2). Vestibular suppressant drugs with or without antiemetics are used in the acute period. Antihistamines such as meclozine (25 to 100 mg/day) have a very well established record in controlling vertigo and nausea. Antipsychotics (e.g. promethazine 12.5 to 25mg 3 times daily) can be used if profound vestibular sedative effects are required. In patients with excessive anxiety, benzodiazepines are useful (e.g. diazepam 10mg intramuscularly or intravenously, once or twice daily for adult patients). In patients with profuse vomiting, a complementary antiemetic agent (metoclopramide intramuscularly or intravenously 10mg once or twice daily, or as suppositories 20mg twice daily) may be added. Antiemetic drugs such as metoclopramide should not be combined with antipsychotics because of the increased risk of ex-

trapyramidal adverse effects. Apart from medication, rest and rehydratation are important adjuvant aspects of therapy.

5.2 Maintenance Therapy

A low salt diet is recommended, as well as avoidance of CATS (coffee, alcohol, tobacco and stress). Patients are requested to observe whether any kind of food precipitates their state.

Immediately after the acute phase, if there is no renal contraindication, a diuretic should be started at a low dose, for example, HTCZ/triamterene (a HTCZ 25mg/triamterene 50mg tablet once daily); this regimen is increased in case of symptom exacerbation (25mg twice daily). Using such a combination of diuretics avoids the need for a potassium supplement, although a measurement before the start of treatment and at 2 weeks is recommended. HTCZ alone must be associated with a potassium supplement and an ionogramme once a week. Blood pressure should be measured every month and controlled.

We use betahistine (16mg 3 times daily in the first 2 months) to prevent recurrence of vertigo. After 2 months' treatment, the betahistine dosage can be decreased to 24 or 32 mg/day.

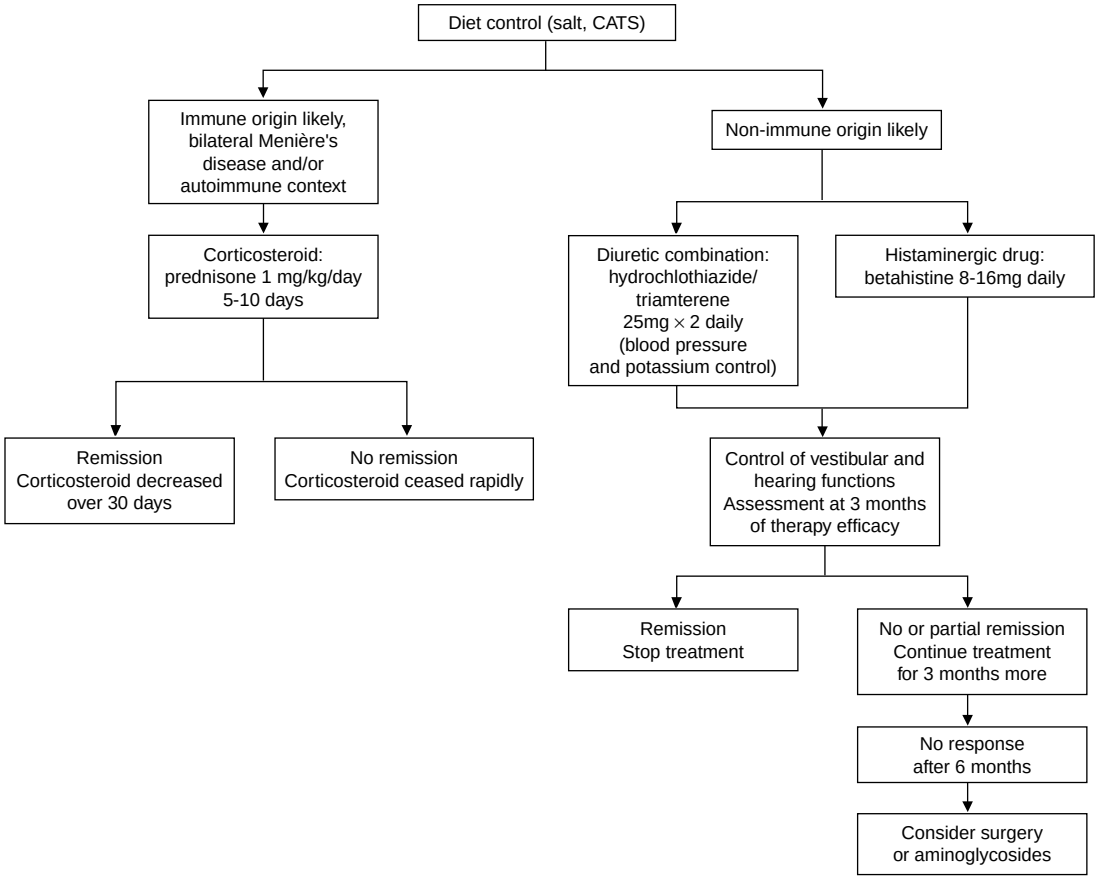

Fig. 3. Protocol recommended for maintenance therapy of Menière's disease. **CATS** = coffee, alcohol, tobacco and stress.

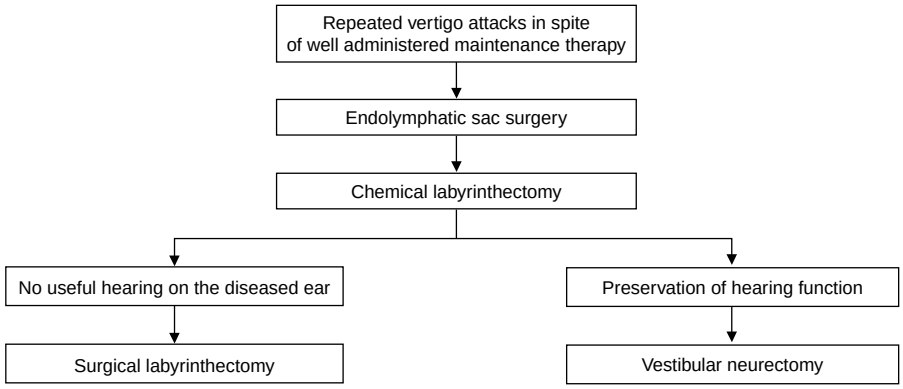

Fig. 4. Ablative therapy and surgical decision for patients with Menière's disease.

Patients should be seen once a month for a clinical vestibular examination and an audiometric control. In bilateral forms evoking an autoimmune origin, the acute phase is commonly manifested by a degradation of the hearing level. These patients may be treated with a corticosteroid (e.g. prednisone 1 mg/kg/day) for 5 to 10 days with the dosage then decreased slowly in remission. Treatment is ceased rapidly if symptoms persist.

The effectiveness of maintenance therapy is assessed every 3 months: in patients with full symptom relief the therapy is stopped. Therapy is continued for a further 3 months in patients with an incomplete response to treatment. In patients with full treatment failure after 6 months, the use of aminoglycosides or surgical alternatives may be considered.

Figure 3 summarises this proposed protocol.

5.3 Surgical Decision

In case of intractable vertigo, resistant to all types of medical treatment, endolymphatic sac surgery may be proposed as the primary surgical option, particularly when attempting to preserve auditory function (fig. 4). An alternative therapy inspired by several recent studies, which is a less invasive procedure often found effective by patients, consists of placing a transtympanic tube. However, this may be a placebo effect.

In patients with no response to any of these procedures, a chemical labyrinthectomy should be proposed while taking into consideration the high risk of hearing loss deterioration. In patients with severe forms of the disease, and after the failure of chemical labyrinthectomy, there are two types of radical surgery. If there is no useful hearing function on the diseased ear, a surgical labyrinthectomy could be proposed as a solution. In the other situation, i.e. patients with useful hearing function, a vestibular neurectomy could be considered.

6. Conclusion

Drug therapy for Menière's disease classically includes vestibular suppressants and drugs acting on the supposed pathophysiological process. Vestibular suppressants are mainly administered as symptomatic treatment for acute vertigo attacks and accompanying nausea and vomiting. They include benzodiazepines, some antihistamines and antipsychotic drugs. Since endolymphatic hydrops is thought to be a prerequisite for developing Menière's symptoms, it provides a basis for the use of diuretics as maintenance therapy. Recently, the possible association between autoimmune inner ear disease and Menière's symptoms has suggested

the use of corticosteroids. It should be noted that betahistine is widely prescribed in Europe as the standard long term oral therapy. This drug, which acts as an H_3 receptor antagonist, is available in the US only through compounding pharmacies.

Apart from drug treatment, techniques for stress reduction, e.g. relaxation therapy, should be proposed to patients who are anxious or depressed.

Among the potential future treatment options, pressure therapy is based on the hypothesis that the inner ear fluid system can be affected by the middle ear static pressure.[33,37] In 1995, Andrews and Strelioff[67] reported that repetitive application of excess pressure to the middle ear through a ventilating tube could induce rapid hearing improvement in Menière's patients. This may account for the alleviation of Menière's symptoms observed after placement of transtympanic drains. To date, pressure therapy still remains to be evaluated as a standardised therapeutic modality.

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