Review Article

Meniere's Disease: A Review on Epidemiology, Aetiology, Diagnosis and Treatment

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Received: 09-02-2022; **Revised:** 24-04-2022; **Accepted:** 30-04-2022; **Published on:** 15-05-2022.

ABSTRACT

Meniere's disease (MD) is a type of peripheral vestibular disease and affects the inner ear. It is characterised by a combination of classic symptoms, including vertigo (spinning sensation), sensorineural hearing loss (SNHL), tinnitus (ear ringing), nausea, and vomiting. The most important histological marker of the Meniere's disease (MD) is endolymphatic hydrops (EH). Different subgroups of patients have different aetiologies, including trauma, viral infection, autoimmunity, allergy, otitis media, and genetic predisposition. MD is most prevalent in European descendants with higher women to men ratio. Recent diagnostic criteria classify MD into definite and probable MD. The treatment consists of non-invasive approaches to surgically destructive methods. The review focuses on epidemiology, aetiology, diagnostic criteria, recent imaging techniques, diagnostic tools, and various treatment regimens.

Keywords: Meniere disease, vertigo, endolymphatic hydrops, vestibular disease, betahistine, labyrinthectomy.

QUICK RESPONSE CODE →

DOI: 10.47583/ijpsrr.2022.v74i01.021

DOI link: http://dx.doi.org/10.47583/ijpsrr.2022.v74i01.021

INTRODUCTION

Meniere's disease (MD) is a disorder of the inner ear that affects balancing and hearing. It is characterised by vertigo, tinnitus, sensorineural hearing loss (SNHL), nausea, vomiting and aural fullness.[1] Prosper Meniere, a French doctor, described this disease in 1861, which consisted of fluctuating hearing loss and episodes of vertigo. He hypothesised that the disease might be due to some malfunctioning or disability in the inner ear.[2] MD can be sporadic MD (SMD) with no prior history in the family or familial MD (FMD). The majority of the cases are sporadic, while familial MD affects 5 to 19 % of all the MD cases.[3]

It's a severe, long-term illness with no apparent cause. Initially, it affects just one ear (unilateral MD) in most cases, while in some cases, it can affect both ears (bilateral MD). Acute episodes occur on average five to ten times a year, followed by periods of remission lasting months or even years. Vertigo is the primary symptom throughout the early stages. In the latter stages, the vertigo spells diminish, and tinnitus becomes prominent and is the leading cause of impairment in MD, causing a major decline in quality of life. In some instances, tinnitus is the first sign of the condition, occurring before hearing loss, vertigo, and aural fullness, which is irregular and arises during vertigo spells. As the disease progresses, tinnitus becomes permanent. [4]

On average, the first symptoms usually manifest at around 42 to 43 years in MD patients. Vertigo with or without tinnitus and aural fullness is usually the first symptom.

Vertigo without hearing loss occurs in 40%, and hearing loss without vertigo occurs in 15% of MD cases as the initial symptoms. In some cases, the time span between the onset of vertigo and hearing loss can be more than ten years.[5]

EH is regarded as the most important histologic marker for the MD. It is the build-up of endolymph in the cochlear duct and sacculus of the inner ear.[6 7] EH is present in 90% of symptomatic cases of MD.[5] Increased cochlear duct pressure has a detrimental effect on the organ of Corti and other inner ear membranes. However, EH alone does not account for vertigo episodes, as histological investigations have revealed EH in patients without MD symptoms.[4]

MD has different aetiology with different mechanisms in different subgroups of patients. The aetiologies behind MD include otospongiosis (otosclerosis), genetic predisposition, viral or bacterial diseases, autoimmunity, trauma, allergy, and other comorbid conditions.[8] Meniere disease (MD) symptoms can also arise due to smoking or even excessive consumption of alcohol. Excessive salt consumption has also precipitated Meniere disease in some patients. Detrimental effects of the Herpes virus have also been the cause of disease in some patients [9]. Numerous studies have indicated that migraine is more prevalent in MD [4].

The prevalence ranges from 34.5 to 513 per 100,000 persons, and the incidence varies from 5.2 to 118.8 per 100,000 persons in different countries. Studies have reported that women get affected more often than men. Mostly Meniere disease is seen to affect adults [10–18].

Current diagnostic criteria given by Lopez-Escamez et al. of the Barany Society have specific criteria to distinguish between probable and definite Meniere disease.[19] Diagnostic investigations include pure tone audiometry (PTA), otoacoustic emissions (OAEs), speech audiometry, caloric vestibular test (CVT), video head-impulse test (vHIT), vestibular evoked myogenic potentials (VEMPs) and electrocochleography (ECochG).[20]

Treatment approaches include a variety of drugs such as diuretics, betahistine, steroids, and anti-emetics. Other treatment approaches include invasive and non-invasive methods.[20]

Clinical Subtypes of MD

Frejo et al. classified unilateral MD and bilateral MD into five clinical subtypes using cluster analysis (Table 1), which would improve MD phenotyping.[21,22]

Table 1 Clinical Subtypes of MD.

Clinical subtypes	Unilateral MD	Bilateral MD
Type 1	Classic MD	Metachronic SNHL
Type 2	Delayed MD	Synchronic SNHL
Type 3	Familial MD	Familial MD
Type 4	SMD with Migraine	MD with Migraine
Type 5	Autoimmune MD	Autoimmune MD

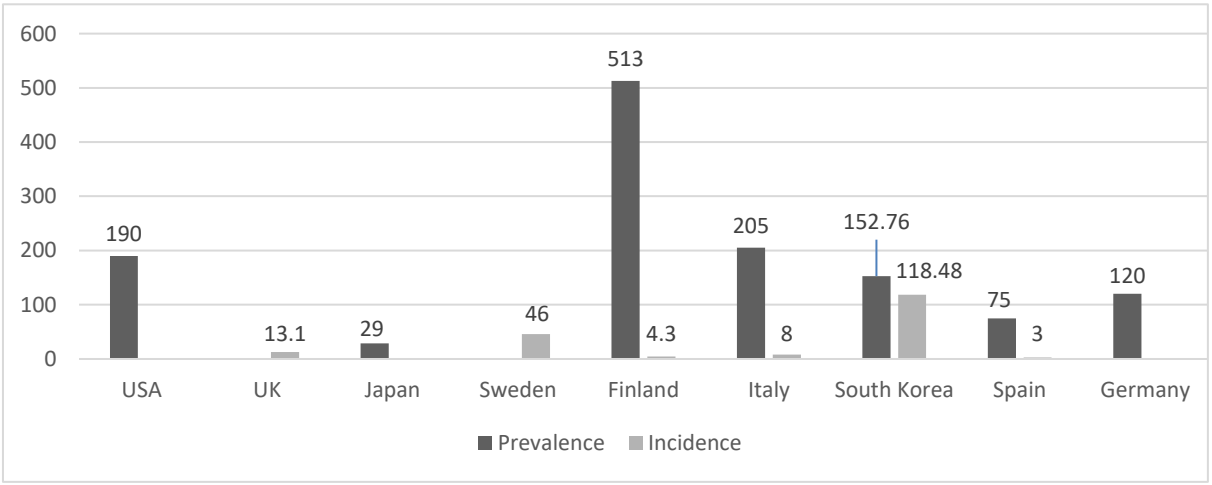

Figure 1: Country-wise epidemiology of Meniere's disease [10–18].

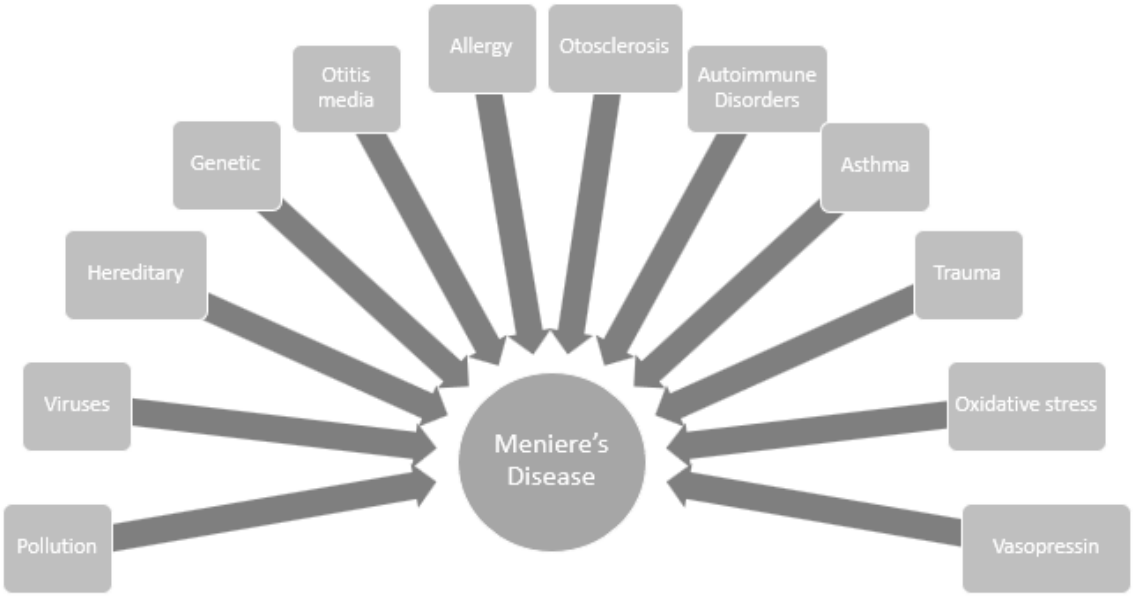

Figure 2: Various aetiologies of Meniere's disease.

EPIDEMIOLOGY

MD has a prevalence of 34.5 to 513 per 100,000 persons, and the incidence ranges from 5.2 to 118.8 per 100,000 persons in different countries (Figure 1).[10–18]

MD can affect unilaterally (one ear) or bilaterally (both ears) , but unilateral MD is more common than bilateral MD. Up to 45 per cent of patients with unilateral MD will develop bilateral MD over time.[4]

The majority of research indicates a modest female predominance of up to 1.89 fold that of males, but the age of onset appears to be identical.[10,23] The prevalence increases with age and peaks at between 60-69 years, and it is uncommon among persons under the age of 20 [10 24]. Prevalence of MD differs according to ethnicity; Caucasians are affected at a much higher rate than African, Asian and Hispanics.[23]

AETIOLOGY

There are various aetiologies of MD (Figure 2). Histologic and temporal bone studies have found abnormalities in the inner ear like:- endolymphatic hydrops, membranous labyrinth rupture, fistulae in the membranous labyrinth, the collapse of the membranous labyrinth, obstruction of longitudinal flow, vestibular fibrosis, sensory lesions, and neural lesions.[25] MD is a complex ailment that should not be treated as a single disease since the aetiology of each subgroup of MD patients is likely to be distinct.[4]

MD is accompanied by an excess of endolymph in the scala media. There is ample evidence for this relationship, and majority of the authors concur that EH causes MD. It has been suggested that endolymphatic malabsorption may lead to the development of EH. Such a process is slow and may take years to develop and, the precipitating event may have occurred years before, delaying manifestation.[26]

Temporal bone and imaging tests have revealed that EH occurs in practically all patients with MD.[6] While some authors have noted that EH is only a marker for MD, the evidence for a causal link is overwhelming. Currently, most specialists consider that EH is required but not sufficient for the development of MD.

Animal models shed light on the association between EH and MD. Many surgical, chemically induced, and genetic models have been developed to induce the EH.[27]

EH is most likely complex in its pathogenesis in MD. Various aetiologies have been hypothesised to have a contribution in the development of MD. A few of the specific causes involved in the EH are described below.

Alexithymia

In a recent study, 58% of MD patients were identified as alexithymic. Probably, alexithymia contributes significantly to the etiopathogenesis of the disease by its influence on homeostatic mechanisms, particularly the inner ear. Alexithymic features are associated with poor immunological response. Alexithymics' neuroendocrine and immunological responses appear similar to those of people suffering from prolonged stress, although anguish goes unrecognised emotionally. Additionally, several experts have discovered that alexithymia may be a risk factor for various medical and psychological diseases. The alexithymic personality feature may act as a risk factor for developing hydrops by affecting the neuroendocrine system. Alexithymic MD patients appeared to feel increased stress and a worse quality of life in psychological health and social connections areas and may adopt preferable less advanced cooping tactics such as humour, active coping, and acceptance, planning including behavioural disengagement.[28]

Asthma

It was recently demonstrated that MD was associated with past asthma history in allergic and nonallergic asthma patients. Prior asthma history was connected with a 1.30-fold increased risk of Meniere's disease. Both allergic and nonallergic asthma patients significantly increased the risk of developing Meniere's disease than the control group.[29]

Pollution

A study has shown that there might be a link between the development of MD and air pollution containing air contaminants such as SO2, NO2, CO and PM10. However, the mechanism is unclear.[30]

Viruses

Arenberg et al. hypothesised that MD is caused by a virus. In their view, a virus enters the inner ear via the round window membrane, then the virus assaults and destroys several inner ear parts. Variation in the virus's load or the host's immunological response is suggested to account for the varying degrees of symptom presentation. Unilateral illness is presumably caused by virus introduction via a middle ear leak, while the bilateral disease is likely caused by virus hematogenous dissemination. The disease's first signs are perhaps the most serious due to the virus's direct influence or its inflammatory immune and microvascular effects on the inner ear. Additional attacks occur due to injury to the stria vascularis, dark cells, and endolymphatic sac and duct.[31]

Arnold and Niedermeyer, in 1997, had shown the presence of antibodies of herpes simplex virus in the patients suffering from MD.[32] Vrabec in 2003 had found the antibodies herpes simplex in the vestibular ganglion of the patients.[33] According to Yazawa et al. investigating endolymphatic sacs, 70 per cent of patients had antibodies of varicella-zoster virus, 40% had antibodies of Epstein-Barr virus (EBV), and 10% had antibodies of cytomegalovirus (CMV).[34]

Genetic cause

MD may have a rare monogenic inheritance in restricted families and polygenic heritability in most familial and sporadic cases.[35] The majority of the MD cases are sporadic in nature. Familial MD (FMD) affects around 5 – 19% of MD cases [3,36,37], with some authors suggesting FMD could be up to 35%.[38] The inheritance of FMD is of autosomal dominant type with incomplete penetrance with some monozygotic twins showing autosomal recessive inheritance [38], and there is a modest propensity for cases to be transmitted maternally.[36]

There is no clinical difference in SMD and FMD [38], except the age of onset of FMD is earlier and experience much longer vertigo episodes as compared to the sporadic cases.[21 39] Studies have reported that 34% of MD patients have a family history of hearing loss, recurrent vertigo, or both.[38]

The genetics of MD is complicated. Several genes and their allelic variants are linked to the development of MD. Several studies have been conducted on various genes to determine their association with the risk of developing MD. The genes involved in MD are given in Table 2.

Table 2: Genes involved in Meniere's disease.

Genes involved in familial MD	
Gene	**Reference**
OTOG	40
DTNA & FAM136A	41
PRKCB	42
SEMA3D & DPT	43
HMX2 & TMEM55B	44
PIK3C2G	45
MYO7A	46
Genes involved in sporadic MD	
Gene	**Reference**
NTN4	47
GJB2, USH1G, SLC26A4, ESRRB, CLDN14 & MARVELD2	48
PTPN22, NFKB1, CXCL10, TLR2, MTHFR, SLC44A2, NOS3, NOTCH2	49
Gene allelic variants involved in sporadic autoimmune MD	
Gene allelic variants	**Reference**
HLA-Cw*04	50
HLA-Cw*04, HLA-Cw*16 & HLA-Cw*012	51
HLA-DRB1*1101	52
MICA*A.4	53
TLR10 rs11096955	54
PTPN22 rs2476601	55
NFKB rs3774937 and rs4648011	56
HLA-Cw07	57
MIF-173 G/C	58
HRH4 rs77485247	59
HSPA1A	60
IL1A	61
Genes involved in the regulation of endolymph	
Gene	**Reference**
KNCE1 and KNCE3	62
ADD1	63
SLC26A4, SLC4A1, SLC9A2, SLC12A3, SLC34A2	64
Other genes involved in Meniere's disease-like symptoms	
Gene	**Reference**
TBX1	65

Otitis media

It has been suggested that chronic otitis media can play a role in developing EH. A study examining temporal bone of 560 cases discovered 75 temporal bones, both otitis media and hydrops. The probable hypothesis for this is that chronic infection products, particularly enzymes, likely permeate through the round window membrane, creating severe labyrinthitis, which firstly damages the basal turn. The toxicity of the chemical perilymph may be transported to endolymph, perhaps impairing stria vascularis function and resulting in modification of the blood endolymph barrier, resulting in endolymphatic hydrops.[66]

Allergy

Derebery in the year 1966 had proved that 30% of those suffering from MD had a food allergy and came up with three hypotheses: i) Mediators released from food may act on the endolymphatic sac; hence endolymphatic sac could be the target organ of the mediators released by the food; ii). Precipitation of inflammation due to deposition of immune complex, thus resulting in the incapability of the sac to filter; iii). A viral infection may cause decompensation of the endolymphatic sac, thus resulting in endolymphatic hydrops.[67]

Otosclerosis

Numerous case reports in the literature demonstrate that the clinical and histological characteristics of sensorineural deafness are associated with otosclerosis. Occasionally, patients with otosclerosis will also suffer from vertigo with or without sensorineural deafness.

The mechanisms that cause sensorineural deafness in otosclerosis might also affect the vestibular labyrinth, producing vertigo[68]. Vestibular symptoms, sensorineural hearing loss, aural pressure, bilateral hearing loss, episodes of vertigo, visual aura, tinnitus, fullness in the ear have all been reported in patients with otosclerosis. Otosclerosis can engulf the vestibular aqueduct, resulting in the endolymphatic duct and sac dysfunction. Additionally, otosclerotic bone may enter the endosteum, altering the chemical composition of perilymph and endolymph and impairing radial and longitudinal flow of endolymph.[68 26]

Trauma

Meniere's disease associated with acoustic (e.g., Sudden noise) or physical trauma (blow to the head or car accident) is referred to as post-traumatic Meniere's disease (PTMD). PTMD has histopathologic similarities with idiopathic Meniere's disease such as head impacts, temporal bone

fractures, prior ear surgery such as stapedectomy, or acoustic trauma are all examples of traumatic insults that might result in PTMD. The patient experiences tinnitus, fluctuating sensorineural hearing loss, aural fullness and recurrent vertigo.[69]

PTMD was previously unknown to otorhinolaryngologists. Although PTMD appears to be an uncommon clinical condition, clinical and histopathologic research indicates that it is a critical clinical condition.[69]

Trauma may result in dysfunctional endolymph-producing or endolymph-absorbing cells. Impulse damage to the membranous labyrinth can also cause displacement of the epithelia of sensory organs and other cellular elements like the otoconia of the saccule or the utricle. The resulting cellular debris that float could disrupt the absorption of endolymph through the duct of endolymphatic fluid in various ways, whether chemically or mechanically, and cause endolymphatic hydrops.

Finally, damage to the endolymphatic duct or sac resulting from a traumatic insult may obstruct the endolymphatic drainage system. On the other side, a perilymphatic fistula might imbalance the pressures of the perilymphatic and endolymphatic systems. If perilymph leakage persists, the pressure of perilymphatic decreases, causing endolymphatic hydrops.[69]

Autoimmune disorders

Numerous investigations have demonstrated the existence of inflammatory cells in the inner ear, suggesting the inner ear's immune function.[70] Yoo et al. were the first to discover elevated anti-collagen II antibodies in MD patients.[71] The circulating antigens or immunological complexes can enter the periphery of the endolymphatic sac and fenestrated blood capillaries, causing mast cell degranulation resulting in immune complex-mediated damage in the inner ear. [27 72] Hence, various animal models are developed for inducing the EH by exposing the inner ear to the antigens like lipopolysaccharide (LPS). LPS applied to the scala media can induce a significant immunological response in the inner ear. In guinea pigs, immunological stimulation of the cochlea with LPS results in the development of EH.[27] Numerous investigations have reported a link between MD and various autoimmune diseases (AD) such as autoimmune hypothyroidism, psoriasis, rheumatoid arthritis, autoimmune thyroiditis, Systemic lupus erythematosus (SLE) and other autoimmune disorders, and these autoimmune diseases are more prevalent in FMD as compared to SMD cases.[73 74 75 39]

Studies have reported that MD patients have increased cytokine levels such as TNF- α, NFkB, IL-6, and CCL18 in 10 to 20% of cases.[76 77 78] Immunostaining techniques have shown the presence of antibodies in vestibular ganglion and endolymphatic sac.[79]

Increased IgE levels are connected with an increased risk of developing MD in patients with SNHL.[80] A recent study discovered the first locus at 6p21.33 in bilateral MD using immunological genotyping arrays. It was observed, using signalling analysis, that TWEAK/Fn14, which regulates inflammation in many autoimmune diseases, may cause an inflammatory response in MD through nuclear factor-kb.[81]

Oxidative stress

Oxidative stress also has a specific role in forming endolymphatic hydrops and damage cells and apoptosis, leading to sensorineural deafness in the later stages of MD. Reactive oxygen species (ROS), when regulated, have an important impact on cell signalling; however, an abundance of ROS are toxic. Under stressful conditions, cells produce molecules having pro-apoptotic, antioxidant, anti-apoptotic activities.[82] Calabrese et al. reported that MD patients had increased systemic oxidative stress with elevated protein carbonyl, GSSG and 4-hydroxynonenal levels.[83]

Vasopressin

Aquaporins have an essential role in controlling the osmotic pressure of cells. To date, 13 isoforms of aquaporin have been discovered. An imbalance of the aquaporin-vasopressin system in the inner ear is responsible for the pathogenesis of MD.[84] Vasopressin regulates aquaporin 2 expression in the collecting duct through the type-2 vasopressin receptor. Certain hormones, including vasopressin, aldosterone, and natriuretic peptide, are involved in the inner ear's homeostatic mechanisms. MD patients show an increased vasopressin concentration in the blood, thus causing endolymphatic hydrops.[85] Therefore, vasopressin has a critical function in sustaining the homeostasis of the endolymph. Aquaporin 3, 4 and 5 are also found in the inner ear, along with Aquaporin 2. Nishio et al. reported a link between the risk of MD and Aquaporin 4 and 5 polymorphism.[86]

DIAGNOSIS

A thorough medical history and information of clinical symptoms with auditory and vestibular function testing are required to diagnose MD.[87] MD is diagnosed by the presence of episodic vertigo, SNHL, tinnitus or aural pressure in the afflicted ear. Since MD is not a single disease, there is no biological marker for its diagnosis. Comorbidities can be confirmed or ruled out with a battery of further diagnostic procedures.[4] In 2015, the Barany Society developed diagnostic criteria that classified MD into two categories:- Probable MD and Definite MD.[19] Diagnostic criteria by Barany society are summarised in tabular data in Table 3.

Further, a differential diagnosis of MD is to be done. Attacks of MD last longer than those of benign paroxysmal positional vertigo (BPPV).[88,89] Vestibular migraines can mimic MD, but patients with vestibular migraines generally have a history of migraines. Several viral infections can mimic MD.[88,90] There are several audiological and vestibular tests for diagnosing MD.

Table 3 Diagnostic criteria of MD [19]

Definite	Probable
Two or more spontaneous episodic vertigo that lasts twenty minutes to twelve hours.	Two or more episodic vertigo or dizziness that lasts twenty minutes to twelve hours.
Audiometrically documented low- to medium frequency sensorineural hearing loss in one ear, defining the affected ear on at least one occasion before, during or after one of the episodes of vertigo.	Fluctuation of aural symptoms
Fluctuations of aural symptoms such as (tinnitus, hearing, fullness).	
Not accounting for any other vestibular disease.	Not accounting for any other vestibular disease.

Audiological tests

Pure Tone Audiometry (PTA)

PTA is an important test used to diagnose and monitor the patient during therapy. This test is necessary to distinguish between Probable MD and Definite MD according to the diagnostic criteria formulated by the Barany Society.[19] It is used to establish the severity and kind of hearing impairment. The tones are delivered to the patient using circumaural headphones, insert phones, and bone oscillators to estimate air- and bone-conduction thresholds across a frequency range of 250 to 8000 Hz. The observed thresholds are shown using standardised symbols on an audiogram. The audiogram pattern indicates the kind of hearing loss, which may be conductive, sensorineural, or mixed. All individuals with sensorineural hearing loss are further subjected to additional glycerol test based on the PTA findings.[91]

Glycerol dehydration test

Glycerol dehydration test is combinedly used with audiometry. It is highly sensitive in diagnosing MD. A baseline audiogram is first recorded; after that patient is administered orally with hundred grams of ninety-five per cent glycerol. A second audiogram is then recorded after 3 hours. The test is positive if there is an improvement of ten decibels or more at two or more than two frequencies, usually around 250-2000Hz or more than 12% improvement in speech discrimination.[92] About 60% of MD patients are positive for the glycerol test; thus, this test is a good criterion for selecting MD patients who are more likely to respond to osmotic diuretic drugs.[91]

Speech Audiometry

Speech audiometry is used to assess a patient's capacity to recognise speech stimuli, validate the results of pure tone audiometry, and exclude the possibility of nonorganic hearing loss or retro-cochlear pathology.

The speech audiometry test includes three parameters: - speech detection threshold (SDT), speech recognition threshold (SRT), and word recognition score (WRS).

Otoacoustic Emissions (OAEs)

Otoacoustic emissions (OAEs) are low-frequency cochlear-generated sounds recorded using a microphone placed in the ear. Cochlea generates these sounds in response to the auditory stimulus. This test provides information about the functioning of the outer hair cells (OHC). OAEs have been extensively studied in the evaluation of MD patients. OAEs are present in ears with mild hearing loss but are missing with pure tone thresholds greater than 60 dB HL.[91] Sakashita et al. have demonstrated the clinical utility of OAEs, especially distortion product OAEs (DPOAEs), in diagnosing MD and DPOAE was found to be more sensitive than PTA in glycerol test.[93]

Tests for vestibule functioning.

The criteria for measuring MD have been enhanced with new laboratory procedures. The caloric vestibular test (CVT) and the video head impulse test (vHIT) are two of the most frequently used tests for evaluating vestibular function.

Video Head-Impulse Test

vHIT records the eye movements (saccades) of the patients using videooculography (video camera placed on the spectacle frame) during the head impulses applied in the horizontal plane in both directions. The velocity of the head impulses is increased from 50°/second to 250°/ second.

The camera records the images of the eye positions, and it can be analysed using a pupil detection technique by LabVIEW software, and eye velocities are obtained. It can record both covert and overt saccades.[94]

Caloric Vestibular Test

The CVT is routinely used to assess the functioning of the vestibule because of its ability to examine both horizontal semicircular canals separately, and it has the most significant probability of detecting and localising a peripheral lesion.[95] In CVT, the patient is made to lie horizontally with the face and torso facing up, and the head is leaned forward 30 degrees. Coldwater (30 degrees Celsius) is irrigated into one ear using a syringe for 20 seconds using 20 mL water. The same is repeated using warm water (44 degrees Celsius). Eye movements in the

horizontal directions (nystagmus) are noted using direct-current electro-oculography (EOG), and the formula by Jongkees is used to quantify peripheral vestibular function.[96]

CVT analyses just the horizontal semicircular canals, whereas the vHIT examines each semicircular canal independently. Enlarged membranous ducts caused by the EH generate alterations in the CVT, whereas the exact mechanism does not play a role during the angular accelerations generated in the vHIT test. There can be alterations in the CVT results, but vHIT results are normal. In the case of patients with Refixation Saccades (RS), the CVT results are normal, but the vHIT were found to be abnormal. Therefore both CVT and vHIT should be used together because the results from both the tests are complementary, and no test is superior to the other.[97]

Vestibular Evoked Myogenic Potentials (VEMPs)

Vestibular Evoked Myogenic Potentials (VEMPs) test helps assess the functioning of the utricle and the saccule by measuring the myogenic potentials produced by the sternocleidomastoid (SCM) muscle and orbital muscle in response to the acoustic stimuli of high intensity. Nowadays, VEMPs are primarily utilised to assess otolith function.[98] Historically, the vestibular function was evaluated using the caloric test, but it did not adequately represent the function of the saccule and the utricle. VEMP can evaluate the inner ear activity excluding the cochlea and the semicircular canal by introducing loud sounds in the ear and stimulating the contracted sternocleidomastoid muscle. VEMP is produced via a disynaptic route that originates in the saccule, and then it continues via vestibular afferent fibres to the vestibular nuclei, then it synapses with sternomastoid nuclei. Thus, this test helps clinicians by expanding the test battery to investigate other saccular diseases. VEMP is recorded at the sternocleidomastoid muscle by stimulating one ear by a short tone-burst of about 95 dB. The SCM muscle is activated by raising the patients head in a supine position.[99]

Electrocochleography (ECochG)

Electrocochleography is a valuable diagnostic tool for Meniere's disease. ECochG monitors summating and action potentials. Summating and action potentials are the electric potentials produced by the cochlea in response to auditory stimuli. The summating potential is increased as compared to the action potential in MD. The summating potentials are increased due to the changes in the structure of the basilar membrane arising from the enlarged scala media compartment. The electrode measures the evoked electric potentials, amplified due to the intrinsically weak signal. The electrodes can be placed either transtympanically or extratympanically. The signals obtained from transtympanic electrodes are expected to be six to seven times greater than those recorded from extratympanic locations; because when electrodes are placed transtympanically, they are closer to the cochlea, which is the signal generator. Hence transtympanic electrocochleography (t-ECochG) is more favoured than extratympanic electrocochleography. However, this technique is invasive because the electrode has to be placed through the tympanic membrane using phenol to anaesthetise the tympanic membrane. Possible complications include perforation of the tympanic membrane, hearing loss, discomfort, haemorrhage, infection, ear canal damage, otitis externa and otitis media.

The evoked responses were difficult to produce since the optimum location was the promontorium, which was not feasible to regularly place the electrodes near the round window in office-based settings. The response quality was poor with the tympanic membrane surface electrodes. Hence electrocochleography's popularity has waned over time. [100] Traditional ECochG methods could not evaluate low-frequency hearing loss in the initial stages of MD because they are restricted for usage at frequencies higher than 1 kHz. Therefore, a new ECochG method was developed by Lichtenhan et al. called ANOW (Auditory Nerve Overlapped Waveform), which was proved to be more sensitive than traditional ECochG for evaluating the cochlea.[101]

Imaging

Endolymphatic hydrops (EH) may be examined in patients using magnetic resonance imaging (MRI). Nakashima et al. proposed a three-stage grading system based on the histology of dilated endolymphatic spaces, with different assessments for the vestibule and cochlea, but not for the utricle or saccule.[102] However, 3D reconstructions of the membranous labyrinth from temporal bone sections indicate that alterations in saccular morphology are more susceptible to EH than changes in utricle morphology. This grading method revealed inconsistencies in the incidence and grade of EH in individuals with (MD). Therefore, in a study, the inversion of the saccule to utricle area ratio (SURI) was compared to the semi-quantitative technique of grading often employed to diagnose MD by using 3-T MRI scanner for imaging. Hence, SURI should be regarded as the most specific imaging diagnostic criteria for MD.[103]

MRI with gadolinium administered intravenously (IV) has also been proposed. After the injection of gadolinium, a 4-hours delay is required. Both ears may be evaluated, although systemic toxicity is a risk due to gadolinium's large dosage.[104] A three-dimensional inversion-recovery sequence with a real reconstruction (3D-real IR) sequence was utilised for the visualisation of endolymphatic hydrops (EH) in Meniere's disease following intravenous gadolinium injection.[105] When the endolymphatic duct extends beyond 33%, it can be considered endolymphatic hydrops[104], but visualising the endolymphatic hydrops is not necessary to define MD, and it should not be utilised in place of the diagnostic criteria for determining MD.[98]

TREATMENT AND MANAGEMENT APPROACHES

To date, there exists no cure for Meniere disease; only various treatment options are available that could give the patients some relief from the multiple symptoms (Figure 3).

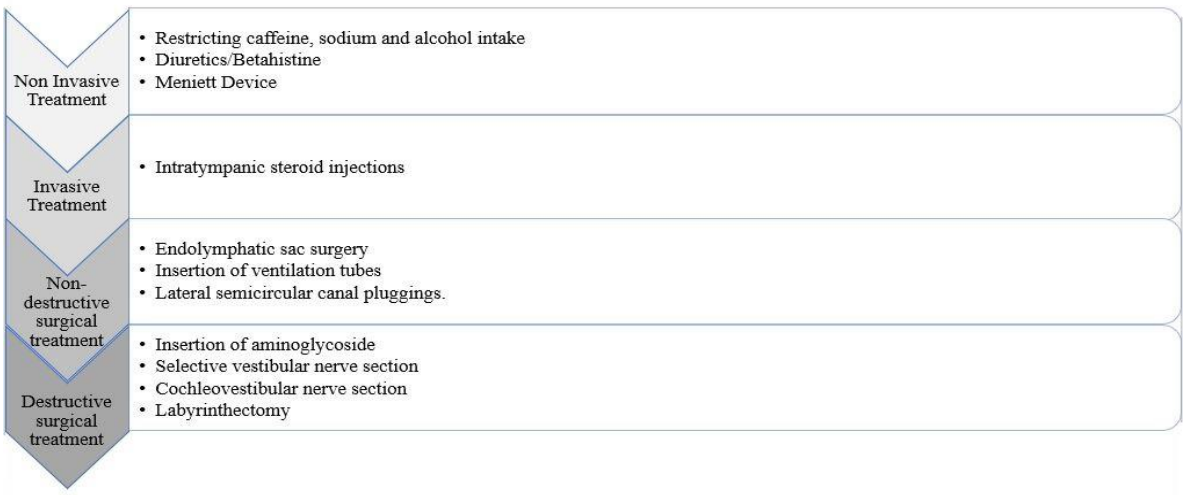

Figure 3 Treatment of Meniere's disease

First step: Medical treatment

The first and foremost recommended care given to patients is advising them for reducing the caffeine, sodium (< 1500 mg/day)[106] and alcohol intake in their diet[107]. Diuretics are considered the most widely used first-line treatment of MD.[108] An improvement in the frequency of vertigo episodes have been reported by use of hydrochlorothiazide, acetazolamide, chlorthalidone, hydrochlorothiazide-triamterene, and nimodipine.[109]

There is insufficient evidence on the beneficial effect of the administration of betahistine on vertigo and tinnitus from a Cochrane review. Many studies have shown a beneficial effect on reducing vertigo, while some trials have shown no difference between the placebo and the treatment group.[110] Compared with the placebo group, a recent nine-month trial on the efficacy of the long-term administration of betahistine (2x24 mg and 3x48mg daily) showed no difference in the incidence of vertigo attacks between the three groups. However, the treatment was well tolerated.[111]

Meniett system is yet another minimally invasive and safe method for treating vertigo symptoms.[112] [113] Through an earbud worn in the outer ear, the Meniett generator produces micropressure (0.6s at 6 Hz)[114], controlled by the software. The pulses pass through the ventilator placed in the tympanic membrane and reach the middle ear further; they reach the inner through the oval and round window, impacting the semicircular canals and the cochlea fluid system. The pulses replace the excessive endolymph and restore the normal ear pressure.[113]

Second step: Intratympanic Steroid injections

It comprises intratympanic corticosteroid injections (dexamethasone or prednisolone), and they are regarded as the second-line treatment. After the treatment by lifestyle modifications like salt, coffee and alcohol restriction and use of diuretics and vasodilators fail intratympanic dexamethasone injection is recommended. Inner ear perfusion by intratympanic dexamethasone injection (4mg/ml, 0.5-0.8ml, five consecutive daily intratympanic injections) improves vertigo by repeating this therapy every 12 months for unilateral MD. A topical anaesthetic is recommended because of discomfort produced during the injection. This therapy should be initiated before any other surgical treatment because it is the least invasive and practical.[106] Patients suffering from concomitant obstructive sleep apnea syndrome (OSAS) can be benefitted from continuous positive airway pressure therapy (CPAP).[115]

Third step: Non-Destructive Surgical treatment

The surgery for MD is usually reserved for patients who failed to respond to medical treatment. However, there has been a decline in surgical treatments in two decades because of the rising popularity of intratympanic steroids and the use of the Meniett device.[116]

The non-destructive surgery includes- Endolymphatic sac surgery (ELSS), insertion of ventilation tubes and lateral semicircular canal pluggings.

Endolymphatic sac surgery: - drains the excess endolymph.

Insertion of ventilation tubes: - reduces middle ear pressure fluctuations and the severity of symptoms caused by middle ear pressure issues.

Lateral semicircular canal pluggings:- It has the objective of ablating endolymphatic movement within the blocked canal.[117]

Endolymphatic sac surgery is the most favoured and most accepted surgical treatment recommended for MD treatment.[108]

In a Cochrane review, Endolymphatic sac surgery (ELSS) is the sole surgical procedure that has been investigated in two randomised controlled trials.

Both studies did not report any positive effects of surgery compared to placebo surgery or grommet insert.[117]

However, in a more recent systematic review, it has been concluded that there remains a gap in studies of high quality that confirm the fact that an endolymphatic sac surgery could provide substantial and effective relief from symptoms for patients who have Meniere's Disease.[118]

Fourth step: Destructive surgical treatment

Destructive surgical treatment includes: - Insertion of aminoglycoside, selective vestibular nerve section, cochleovestibular nerve section and labyrinthectomy. Intratympanic gentamicin injections control vertigo in 87% of cases of patients. Injections are administered not more than once per week. Use of local anaesthetic is recommended. To reduce the burning sensation felt by the patients, gentamicin intravenous preparation (40mg/ml) is usually buffered with 8.4% sodium bicarbonate to give a final concentration of 26.7mg. Generally, 0.4 to 1 ml is sufficient, and the injections are repeated every 1 to 3 weeks.

However, this therapy has disadvantages such as hearing loss (21%) and reoccurrence of vertigo (29%).[119] In contrast to intratympanic gentamicin, a growing trend and evidence support the use of intratympanic corticosteroids, which aid with vertigo management while also preserving hearing and vestibular function.[114]

The last resort for treatment of MD includes labyrinthectomy and vestibular neurectomy. Literature reports show that these surgical treatments are very effective and have positive results in controlling vertigo.[120],[121] Yet some authors suggest using cochlear implantation rather than labyrinthectomy to rehabilitate hearing; the process is quite common in Australia and USA than in Europe or Japan.[108] Although both surgical labyrinthectomy and vestibular nerve section have documented cure rates of more than 95% for vertigo in MD, labyrinthectomy leads to complete hearing/vestibular loss and vestibular nerve section involves a craniotomy, both of which are significant causes of morbidity.[117]

CONCLUSION

Meniere's disease is an inner ear ailment characterised by episodes of vertigo, tinnitus, hearing loss, and auditory pressure. Meniere's disease continues to affect hundreds of thousands of individuals each year. This chronic disease has afflicted patients of various ethnic and racial origins. MD is diagnosed based on the patient's clinical history. True, we still do not have a cure for this condition, as we have for many other disorders in medicine. However, significant advances in treating this condition have been achieved throughout the ages, particularly in the last decade, and various safe and effective medicinal and surgical therapies are now available to assist patients in coping with the disorder's repercussions. Non-pharmacological therapy (dietary and lifestyle adjustments), pharmacological treatment (betahistine, diuretics, gentamicin, and corticosteroids), and surgical management are all options if non-pharmacological and pharmacological therapy fails.

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Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.