Original Article

Characteristics of the Cochlear Symptoms and Functions in Meniere's Disease

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Abstract

Background: Meniere's disease is a unique, progressive disease of the inner ear. The complex manifestation presents diagnostic challenges. The cochlear symptoms often present before vertigo and tend to be ignored. This study aimed to analyze the characteristics of cochlear symptoms and functions associated with Meniere's disease to investigate the regularity of the development of this disorder.

Methods: One-hundred fifteen patients who were diagnosed with definite unilateral Meniere's disease at the Hearing and Vestibular Clinic of the Department of Otorhinolaryngology of Beijing Tongren Hospital from August 2013 to November 2015 were recruited in this retrospective study. Initial symptoms, duration from initial symptoms to the diagnosis, hearing thresholds, audiogram patterns, and caloric test results were collected and analyzed for each patient. Data were analyzed using SPSS 13.0 statistical software by Spearman's correlation, Kruskal–Wallis *H* test, Chi-square test, and Fisher's exact test.

Results: The average hearing threshold of these patients was 45.24 ± 18.40 dB HL. A majority of the patients (55.65%) were in Stage 3. The initial presentation of the disorder in 58 cases (50.43%) comprised only cochlear symptoms without vertigo. A weak, positive correlation was found between the degree of hearing loss and duration of the disease from initial symptoms to the diagnosis ($r_s = 0.288$, $P = 0.002$). Upward-sloping, inverted "V," downward-sloping, and flat pattern were the main audiometric patterns observed with a distinctive distribution between stages ($P < 0.001$). Based on the configurations of audiograms, the audiometric patterns had a weak correlation to the duration ($r_s = 0.269$, $P = 0.004$), and there was a tendency of duration to rising from upward-sloping, inverted "V", downward-sloping to flat pattern. ($H = 10.024$, $P = 0.018$). Frequencies of tinnitus in 56 patients (64.4%) were at the lowest points of the audiograms, i.e., the frequencies of the poorest hearing threshold. The patients at an advanced stage (Stage 3 [56] and Stage 4 [73]) exhibited a significantly higher abnormality of canal paresis than those at the earlier stages (Stage 1 [23] and Stage 2 [42]) ($\chi^2 = 5.973$, $P = 0.015$).

Conclusions: Patients with definite Meniere's disease always have a moderate to severe sensorineural hearing loss before diagnosis. Cochlear symptoms are the most common initial presentation. With the progression of the duration, the hearing impairment becomes more severe and the distribution of the audiometric pattern is distinctive between stages.

Key words: Caloric Test; Hearing Loss; Meniere's disease; Tinnitus; Vertigo

Introduction

Meniere's disease is a unique, progressive disease of the inner ear, with unclear pathophysiology to be an enigma. It is known that episodic vertigo, fluctuating sensorineural hearing loss, tinnitus, and/or aural fullness are the four typical clinical symptoms of this disease. However, the clinical features that the patient presents are always quite atypical, especially in an early stage. In general, cochlear symptoms and vestibular symptoms always presented separately, and cochlear symptoms were constantly

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considered to be the most common initial presentation of Meniere's disease as stated in a previous study.[1,2] When not all symptoms are present, the atypical symptoms tend to be confused with other diseases, and the complex manifestation presents diagnostic challenges to the clinicians in actual practice. Thus, the disease duration from initial presentation to the confirmed diagnosis may be from months to years.[2] To date, the diagnosis of Meniere's disease still relies on clinical symptoms, physical examinations, and laboratory data while other causes of vertigo and deafness need to be excluded.[3] Although many diagnostic techniques have been widely used and studied by clinicians for Meniere's disease,[4] such as distortion product otoacoustic emission,[5] glycerol test,[6] electrocochleography,[7,8] cochlear hydrops analysis masking procedure,[9] their diagnostic values are still controversial. In the criteria, sensorineural hearing loss is the required symptom necessary for the diagnosis of Meniere's disease, and pure-tone audiometry is still the only required test for suspected and confirmed patients. Typically, patient hearing fluctuates throughout progression of the disease but may recover after each attack in the early stages. However, Meniere's disease is a disabling disease of the inner ear that is associated with a severe hearing loss and even a disturbance of the vestibule[10] in advanced stages. Thus, in this study, we analyzed the characteristics of cochlear symptoms and functions associated with Meniere's disease to investigate the regularity of the development of this disorder.

Methods

Subjects

A retrospective study was performed identifying patients at the Hearing and Vestibular Clinic of the Department of Otorhinolaryngology of Beijing Tongren Hospital from August 2013 to November 2015, whose pure-tone audiometric results were consistent with Meniere's disease. One-hundred fifteen patients with definite unilateral Meniere's disease were recruited for the study with a mean age of 47.9 ± 11.6 years (ranging from 17 to 70 years). Sixty-two patients were men and 53 patients were women, with a male:female ratio of 1.17:1. Due to the retrospective nature of the study, informed consent was waived, but the study was approved by the Ethics Committee of our hospital.

Inclusion criteria

Patients were diagnosed with definite Meniere's disease according to the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) Committee on Hearing and Equilibrium criteria for Meniere's disease (1995).[3] They met the diagnostic scale of at least two episodic vertiginous spells lasting 20 min or longer, a documented hearing loss in the affected ear at least once throughout progression of the disease, and subjective complaints of tinnitus or aural fullness. Other possible causes, such as acoustic neuroma or auditory neuropathy spectrum disorder, were excluded either with magnetic resonance imaging or with auditory brainstem response testing.

Exclusion criteria

Patients with disorder of the middle ear, previous head trauma, administration of intratympanic gentamicin injections, or those who have accepted cochlear implantation surgery were excluded from the study.

Material

All outpatient medical records were collected for the analysis. These records included patients' reported symptoms, demographic data, audiometric reports, and duration (in months) from the initial symptoms onset to the time when they were diagnosed at our clinic.

All patients were evaluated for pure-tone audiometry with a GSI 61 audiometer in a soundproof booth with background noise lower than 18 dB A. The audiometric thresholds by air and bone conduction were determined for the frequencies of 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz. The value of the average four-tone threshold was obtained at the frequencies of 0.5, 1, 2, and 3 kHz, as recommended by the criteria of AAO-HNS. Staging of this disease is based on the four-tone average of the audiogram of the affected side.[3] The average thresholds for Stage 1 to Stage 4 were ≤25 dB HL, 26–40 dB HL, 41–70 dB HL, and >70 dB HL, respectively. Then, the pure-tone audiometric pattern was determined and observed. The audiograms were classified according to the shape, and the four patterns[10,11] of audiometric curves which are considered as follows: (1) audiometry that presented mainly low-frequency hearing loss refers to an upward-sloping pattern, (2) mainly high-frequency hearing loss refers to a downward-sloping pattern, (3) both a low and high-frequency loss with preservation of hearing in the mid-frequencies refers to an inverted "V" pattern, and (4) an all-frequency hearing loss with variability within a range of 20 dB refers to a flat pattern. The audiometric patterns of different stages were analyzed.

Tinnitus pitch matching was performed using the same pure-tone audiometer for both frequency and loudness of the tinnitus. Low- and speech-frequency tinnitus refers to a range of 0.125–2 kHz, and high-frequency tinnitus corresponds to a range of 3–8 kHz.

Videonystagmography (Synapsys, Ulmer, France) was performed with eye movement recording. By convention, caloric tests used binaural, bithermal, closed loop air irrigations of 40-s durations with warm (50°C) and cold (24°C) temperatures separately. Slow component velocity data were collected and recorded in the following sequence: left cool (LC), right cool (RC), left warm (LW), and right warm (RW). Canal paresis (CP) was calculated according to the formula: $\frac{|(LC+LW)-(RC+RW)|}{LC+LW+RC+RW}\times 100\%$.[12] A CP value of <15% was considered to be within normal limits which was obtained from our Vestibular Laboratory whereas a CP value of greater than 15% was considered abnormally elevated.

Statistical analysis

Data were entered into MS Excel and were analyzed with SPSS 13.0 (SPSS Inc. Chicago, IL, USA) statistical software. The Kolmogorov–Smirnov test was used to test the parameter distribution. Mean and standard deviation were calculated to most factors. Skewed data were presented as medians and the range, and the Spearman's nonparametric correlation was used to analyze the relationship. The Kruskal–Wallis *H* test was used to compare the overall difference within groups. In addition, the Chi-square test and Fisher's exact test were used for comparing group ratios.

Results

A total of 115 patients met the AAO-HNS (1995) criteria for definite unilateral Meniere's disease, of whom 62 patients were left ear involved and 53 patients were right ear involved.

Hearing loss

Of all the patients, the average hearing threshold at frequencies of 0.5, 1, 2, and 3 kHz was 45.24 ± 18.40 dB HL. A majority of the patients (64/115, 55.65%) were in Stage 3. A number of 24 (20.87%) patients were in Stage 2, 18 (15.65%) patients in Stage 1, and 9 (7.82%) patients in Stage 4. The composition of the audiogram patterns is different among different stages by Fisher's exact test ($P < 0.001$) [Table 1].

Tinnitus

All of the patients experienced tinnitus in the affected ears. The initial presentation of the disorder in 58 (50.43%) patients included only cochlear symptoms such as tinnitus, hearing loss, or both, without vertigo. Another 39 (33.91%) patients had both cochlear and vestibular symptoms. Only 18 (15.65%) patients had isolated vertigo without cochlear symptoms.

Eighty-seven (75.65%) patients received the tinnitus pitch matching while at the clinic whereas 28 (24.35%) patients' tinnitus was not present at that time. Distribution of the frequencies of the tinnitus is 38 (43.68%) patients for 125–250 Hz, 21 (24.14%) patients for 500–2000 Hz, and 28 (32.18%) patients for 3–8 kHz. The frequency of the tinnitus in 56 (64.4%) patients was at the lowest points of the pure-tone curves.

Duration from the initial symptoms to diagnosis

Of all the patients, the median duration from the initial symptoms to the diagnosis was 36 months (ranging from 0 to 240 months). The median durations for stages 1–4 were 20.5, 27, 36, and 60 months, respectively. Figure 1 shows Spearman's correlation between disease duration and pure-tone average ($r_s = 0.288$, $P = 0.002$). Patients with an upward-sloping audiogram had the shortest duration from the initial symptoms to the diagnosis while patients with a flat audiogram tended to have the longest duration from the initial symptoms to the diagnosis. There was a tendency of duration to progress from upward-sloping, inverted "V," downward-sloping to a flat pattern ($H = 10.024$, $P = 0.018$). The audiogram patterns correlated to the disease duration ($r_s = 0.269$, $P = 0.004$).

Caloric tests

The percentage of abnormal CP of all patients was 68.70%. The patients of relatively advanced stage (Stage 3 [56] and Stage 4 [73]) exhibited a significantly higher percentage of abnormality of CP than those of the early stages (Stage 1 [23] and Stage 2 [42]) ($\chi^2 = 5.973$, $P = 0.015$).

Discussion

Meniere's disease is a condition which is mainly diagnosed from a detailed history and examination. However, it is difficult to diagnose due to the absence of typical presentations, especially in the early stages.

In our series of 115 patients with definite Meniere's disease, 64 (55.7%) patients had a moderate to severe hearing loss, whose average hearing thresholds at the frequencies of 0.5–3 kHz displayed a predominance of Stage 3 (four-tone

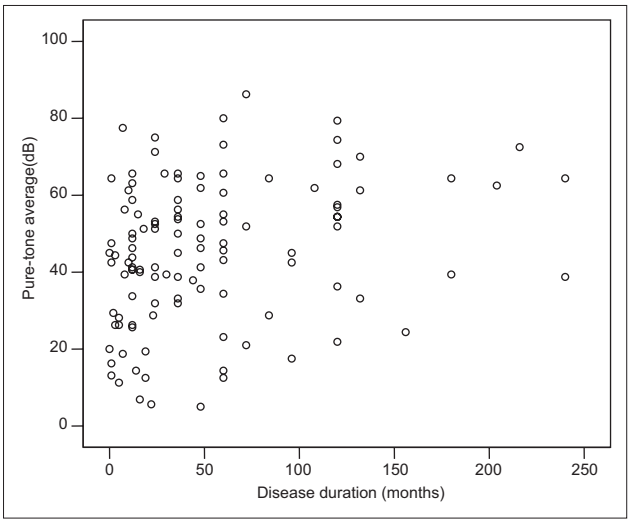

Figure 1: The scatter plot shows Spearman's correlation between disease duration and pure-tone average ($r_s = 0.288$, $P = 0.002$) ($n = 115$).

Table 1: Pure-tone audiogram patterns of different stages (*n* (%))

Stage	Number of patients	Upward-sloping	Inverted "V"	Downward-sloping	Flat
Stage 1 (≤25 dB)	18	15 (83.3)	3 (16.7)	0	0
Stage 2 (26-40 dB)	24	11 (45.8)	11 (45.8)	1 (4.2)	1 (4.2)
Stage 3 (41-70 dB)	64	13 (20.3)	16 (25)	5 (7.8)	30 (46.9)
Stage 4 (>71 dB)	9	1 (11.1)	0	0	8 (88.9)
Total	115	40 (34.8)	30 (26.1)	6 (5.2)	39 (33.9)

average at 41–70 dB HL). There were markedly fewer patients in Stage 1 (four-tone average ≤25 dB HL) and Stage 2 (four-tone average at 26–40 dB HL) than in Stage 3. Meanwhile, the number of patients in Stage 4 was the smallest among the four stages. That means more than half of these patients may acquire an irreversible hearing impairment if not promptly diagnosed and controlled. One potential cause of this phenomenon was that the diagnosis was often missed due to lack of typical signs in the early stages, especially when there were only cochlear symptoms without vertigo. Simple cochlear symptoms were always difficult to distinguish from other causes which could also lead to sensorineural hearing loss and tinnitus. Another suspected reason may be the characteristic of fluctuating hearing loss. Hearing loss can almost be recovered in the early stage, which can result in patients with true Meniere's disease being overlooked by the clinicians. Besides, a group of the patients were collected from a tertiary referral clinic because their Meniere's disease was difficult either to diagnose or to manage, which is also the probable reason for the delayed diagnosis. Thus, the patient selection may also have an effect on the results presented above. Overall, patients with Meniere's disease almost always receive a somewhat delayed diagnosis. Early diagnosis is important to prevent patients from acquiring a hearing disability.

Although Meniere's disease was discovered more than 100 years ago, clinicians and scientists worldwide are still searching for parameters as indicators for diagnosis and evaluation. To date, pure-tone audiometry is still the only identified and recommended measurement in diagnostic criteria according to both AAO-HNS[3] and Barany Society.[13] As a useful measurement which can reflect the degree and feature of hearing loss and cochlear function, pure-tone audiometry is used most extensively and is easy to obtain as an established technique.

The audiograms of the patients with Meniere's disease have special features which may provide useful information for diagnosis and evaluation of the disease. Most of the patients with Meniere's disease, in general, typically presented pure-tone audiometric results with an isolated low-frequency hearing loss (upward-sloping pattern) at the time of initial presentation, as shown in Stage 1 (83.3%) in this study. In Stage 2, nearly half of the patients demonstrated an upward-sloping pure-tone pattern, and the other half of the patients had an inverted "V" audiogram. The flat pure-tone curve became the main pattern of patients in Stage 3 with the proportion of patients with upward-sloping and inverted "V" audiograms decreasing in this stage. The maximum percentage of the flat pattern curve was reached at Stage 4. In a previous study, the configuration of the audiograms of patients with Meniere's disease showed a great variance;[14] however, the hearing loss was always considered to be low-frequency dominated[15] and the hearing threshold shifted to approximately 50–52 dB and became stabilized after several years of onset.[15,16] The fact that only six patients showed a downward-sloping curve in the present series may be the result of other simultaneous etiologies of sensorineural hearing loss, such as presbycusis or noise exposure.[17] It is worth noting that a new diagnostic criteria for Meniere's disease came out in 2015.[13] In the new criteria, the evaluation of hearing threshold at 3 kHz was removed. Nonetheless, we consider the evaluation of the hearing threshold at 3 kHz to be valuable clinically in patients of Meniere's disease, especially for distinguishing the audiogram pattern.

Tinnitus is another necessary symptom for diagnosis of Meniere's disease as one of the common initial symptoms. Tinnitus can lead to patient's anxiety, sleeping disorders, depression, as well as difficulties in listening tasks.[18] In this study, tinnitus was experienced by all the patients. In spite of the fact that tinnitus disappeared after the attack in a minority of the patients while at the clinic, most of the tinnitus continued to exist at all time. More than two-thirds of the tinnitus demonstrated to be low and speech frequencies. When compared, the tinnitus frequency and the frequency of the lowest point on the pure-tone audiograms revealed that nearly two-thirds of the patients had a good concordance between the two. Vernon *et al*.[19] have suggested that the tinnitus pitch of Meniere's disease can range from a loud roar to a soft ringing among which low-frequency is the most common type. 125, 250, and 500 Hz were the most common tinnitus frequencies in Meniere's disease and were consistent with the characteristics of the low-frequency hearing loss. Results from the current study were consistent with this previous study. In patients with other types of sensorineural hearing loss, the pitch of the tinnitus was often in the high-frequency range. A recent report demonstrated a correlation between the tinnitus pitch and the same range of the maximum hearing loss shown in the audiogram but not the edge frequency.[20]

Initially, not all patients present all of the common symptoms. In our results, half of the patients presented only the cochlear symptoms as the initial presentation. These patients cannot obtain the diagnosis for a period due to the absence of vertigo or due to atypical symptoms. In this study, the disease durations, the intervals from the initial symptoms onset to the diagnosis, were collected. Meanwhile, since the staging applied to the case of definite Meniere's disease is based on the four-tone average of hearing, stage information can reflect the level of hearing loss in a patient. Any correlation between hearing loss and disease duration from the initial symptom was attempted to be determined. It was found that the resulting correlation of $r_s = 0.288$ was statistically significant (Spearman's rho, $P = 0.002$), but there was no clear relationship between disease duration and average hearing thresholds in individual cases as shown in Figure 1. As a result, there may be a weak relationship between disease duration and average hearing loss as presented. In addition, the duration corresponding to the four audiometric patterns presented a difference between stages. There was a tendency of duration to rising from upward-sloping, inverted "V", downward-sloping to flat pattern. Patients with the

upward-sloping audiograms had the shortest duration while patients with the flat audiograms tended to have the longest duration. Havia *et al*.[21] reported the relationship between the pure-tone average and the disease duration (days, weeks, months, and years). It clearly showed the longer duration of the disease, the more profound the hearing loss. Our observation in this study is similar to what they observed although the association is not as strong. On the one hand, fluctuating hearing loss may be a prominent component of the presentation, particularly in the early stage. The hearing manifestation and duration reported by the patients have great variation upon the recognition of the disease. On the other hand, not all patients may progress through the series of stages in sequence. Hence, increasing the sample size in a future study is needed. Nevertheless, our results of the concordance with the pure-tone pattern and duration are different from the previous study of Mateijsen *et al*.[22] who suggested that the audiometric configuration did not depend on disease duration. Unfortunately, our observation may not be directly compared with their results because bilateral-affected patients were included in their study. The classification of audiogram patterns in the present study is not unique. We consulted the previous reports for four easily identifiable patterns.[10,11] Although it belongs to a somewhat subjective manner, the audiometric patterns can provide valuable information at the first sight of the audiogram reports. In addition, from the pathophysiological point of view, different from the vascular findings[23] in the cochlea in patients with presbycusis, the cause of Meniere's disease is recognized as the hydrolabyrinth with evidence.[24] The degree of endolymphatic hydrops in Meniere's disease has its regulated changes during progression. Endolymphatic hydrops always grow from the cupola of the cochlea and cause the abnormality of the low-frequency pure-tone threshold at first. The impairment of the cochlea increases in response to the development of endolymphatic hydrops. Therefore, changes of the audiometric pattern which are typical of the development of Meniere's disease may reveal the degree of endolymphatic hydrops. Moreover, as generally considered, the effect of hearing impairment due to the disease duration is greater than the effect of aging.[11] Hearing fluctuation is another characteristic of Meniere's disease although it is not necessary for the disease. Audiometric follow-up at various time points can provide important evidence.[25] The present study did not involve longitudinal follow-up data. Further studies will be needed to examine the nature of the hearing fluctuation in patients with Meniere's diseases.

There is no evidence to insist that vestibular functions will directly correlate with audiometric changes,[26] and the use of vestibular testing in evaluation of the disease remains controversial. Previous literature reported a common vestibular test abnormality in up to 66%–74.7% of the patients.[27,28] This observation is similar to what we observed. Furthermore, the variance of CP at different stages was also noticed in our study. The abnormality of caloric tests occurs much more often in patients with severe hearing loss than in patients with mild hearing loss in our study. There was a trend of increased CP from early stage to advanced stage. Despite this, more than half of the patients in early stage already had the abnormality of the vestibule; meanwhile, another half had normal caloric test results. In addition, some of the patients in advanced stage also had normal caloric test results. We suspect that vestibular compensation may play a role in the course of the disease. Based on pathological studies, the mechanism for caloric paresis may be related to ampullary distortion with accumulation of endolymph.[29] With further evolution of the disease process, the vestibular function changes gradually. That is, the vestibular function may have a close but not a parallel relationship with cochlear impairment.[30] Therefore, the mild, atypical vertigo and the compensated CP are possible symptoms that could be ignored by a clinician, especially in early stage.

In conclusion, patients with definite Meniere's disease always have a moderate to severe sensorineural hearing loss before diagnosis. Cochlear symptoms are the most common initial presentation. The hearing impairment has a relationship with disease duration. With the extension of the duration, the hearing impairment becomes more severe and the distribution of the audiometric pattern is distinctive between stages. With the hearing loss, more patients will present a vestibular abnormality such as CP.

Therefore, we suggest paying more attention to the characteristics of cochlear symptoms and functions in patients with Meniere's disease which may provide information and ideas for clinical practice. Focusing on the early presentation and carrying out a complete follow-up procedure may be the key points for protecting the patients with Meniere's disease from acquiring a hearing disability altogether.

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Conflicts of interest

There are no conflicts of interest.

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