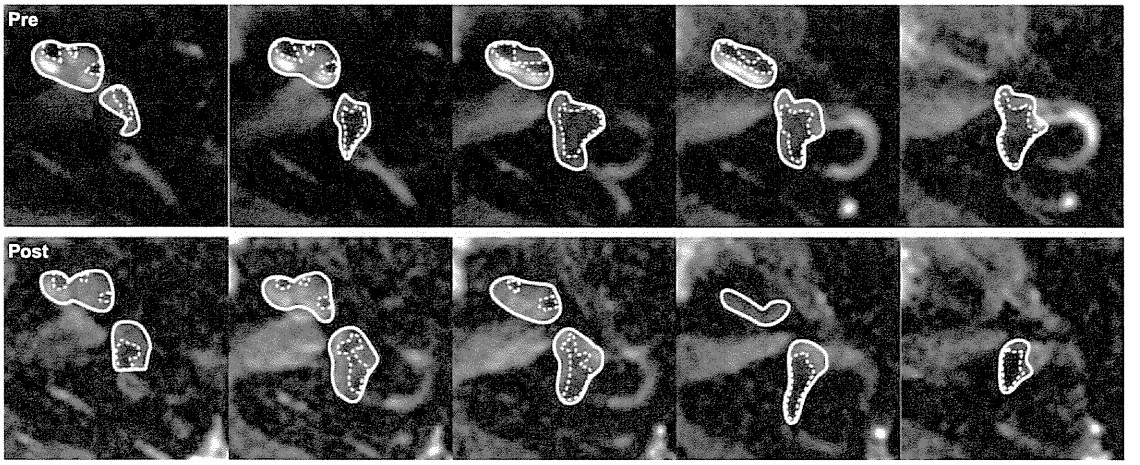

Figure 4. A case of hydrops that was reduced but still existed in both the cochlea and the vestibule (case P35). The endolymphatic space (dotted traces) was noticed even after surgery, although the proportions in the cochlea and the vestibule (solid traces) were reduced from 18.3% to 8.2% and from 51.8% to 35.4%, respectively.

of patient observation. A review from the temporal bone collection at the Massachusetts Eye and Ear Infirmary reported that hydrops could be detected in all 28 cases with classical symptoms of MD in at least 1 ear [15]. Does hydrops persist once it has formed? The present study using MRI could show cases of hydrops reduced in a comparison before and 6 months after surgery, which indicated that hydrops was a reversible change in at least some cases.

Sac surgery for MD has controversial efficacy based on the results of a placebo-control study [10]. A temporal bone study of cases after sac surgery showed that the sac shunt was incomplete in many cases and that hydrops persisted in all cases (15/15), even though the vertigo was well controlled [16]. We have modified the surgery with steroid instillation into the opened sac, and reported good results in vertigo control and hearing [11]. In the present study, two cases showed hearing improvement. In these two cases, endolymphatic hydrops was reduced and became negative. Sac surgery with steroid instillation may have the potential to reduce hydrops, although we do not have enough data regarding how hydrops varies with time over the entire life of the patient undergoing surgery, sham-surgery, or other treatment. On the other hand, even in the cases where hydrops was not modified after surgery, vertigo spells were significantly suppressed, which indicates that the effects of sac surgery are not limited to hydrops reduction. The mechanism of vertigo attack is not completely understood, and at least not explained by the state of endolymphatic hydrops alone.

As another treatment option for MD, intratympanic gentamicin therapy is widely used, which was originally based on the concept that lowering the vestibular function of the affected ear suppresses the variation in function, leading to vertigo suppression. A recent modification using low-dose gentamicin is supposed to act on the hydrops, but not destroy the inner ear function. However, intratympanic low-dose gentamicin treatment was reported not to reduce the extent of hydrops on MRI images in even successful cases [17], in contrast with our results after performing sac surgery. It may be possible that sac surgery influences more directly the endolymphatic flow. We use high-dose steroid applied into the opened endolymphatic sac, which may be another possibility to explain the hydrops reduction. On the other hand, vertigo control could be achieved even without the hydrops reduction, which also happened in our study as mentioned above.

Inner ear examination by MRI still has potential for further development. The quality of the inner ear images depends on the device and imaging technique, and is now far less than that of histologic sections. Criteria for endolymphatic hydrops depend on the image quality, and have not been unified yet among research groups [13,17]. Our criteria were still not quantitative. Particularly in the cochlear hydrops evaluation, the area of the cochlear duct (endolymphatic space) in other than hydrops (enlarged) cases was small and difficult to measure quantitatively. Further development of hardware and software and accumulation of control data will be necessary to deal with more precise comparisons.

In conclusion, we showed that after sac drainage surgery with steroid instillation, three cases of hydrops were reduced and the symptoms went

into remission. Therefore, it can be said that endolymphatic hydrops is reversible, at least in some cases, and that sac surgery may have the potential to ameliorate hydrops. However, vertigo suppression after sac surgery did not always result in a reduction in hydrops. As for the potential for surgery to affect hydrops, a large number of cases with or without surgery should be accumulated and further comparisons are necessary.

Acknowledgments

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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ORIGINAL ARTICLE

Psychological condition in patients with intractable Meniere's disease

MASASHI FURUKAWA[1,2], TADASHI KITAHARA[1], ARATA HORII[1], ATSUHIKO UNO[1], TAKAO IMAI[1], YUMI OHTA[1], TETSUO MORIHANA[1], HIDENORI INOHARA[1], YASUO MISHIRO[2] & MASAFUMI SAKAGAMI[2]

[1]*Department of Otolaryngology-Head and Neck Surgery, Osaka University School of Medicine, Osaka and* [2]*Department of Otolaryngology, Hyogo Medical Collage, Hyogo, Japan*

Abstract

Conclusions: Physicians should consider additional treatment strategies for Meniere's disease patients with a long history of disease and hearing loss in the secondary affected ear and also provide psychological support regarding future progressive bilateral hearing loss. *Objectives:* To treat intractable Meniere's disease patients effectively, we need to understand the psychological condition of each patient. We examined the state of neurosis and depression in patients and correlated this with demographic and background information. *Methods:* Between 1998 and 2009, we enrolled 207 patients with intractable Meniere's disease in this prospective study. We used the Cornell Medical Index and the Self-rating Depression Scale to evaluate their psychological condition. We also obtained demographic and background information relating to sex, age, duration of disease, vertigo frequency, hearing level in bilateral sides, and plasma vasopressin level. *Results:* Neurosis and depression was diagnosed in 40.1% and 60.4%, respectively, of patients with intractable Meniere's disease. Our results showed that surgical treatment significantly improved vertigo and hearing ability in patients with no psychological symptoms compared with those exhibiting psychological symptoms. Patients with a longer duration and worse hearing level in the secondary affected ear had a significantly higher incidence of mental illness than those with a shorter duration and better level of hearing.

Keywords: *Neurosis, depression, duration of disease, bilateral hearing loss, multivariate regression analysis*

Introduction

Meniere's disease is a common inner ear disease with an incidence of 15–50 people per population of 100 000 people. It is characterized by recurrent attacks of episodic vertigo, fluctuating sensorineural hearing loss, and tinnitus [1]. Some patients with Meniere's disease are unable to participate in activities of daily life and to interact with their social environment, such as work and schooling. This is because of frequent attacks of vertigo, often with progressive profound hearing loss and unremitting tinnitus, despite treatment with various types of medication. This type of Meniere's disease is called intractable Meniere's disease. The otopathology in Meniere's temporal bones was revealed in 1938 to be inner ear hydrops [2,3]. Therefore, in such intractable cases, inner ear drainage, i.e. endolymphatic sac decompression surgery, is the first recommended surgical option [1].

Meniere's disease remains a mysterious psychological disease, where some patients are completely cured of vertigo attacks after psychotherapy and/or cognitive therapy, even though they have not responded to various kinds of medication [4,5]. Clinical studies suggest that a stressful lifestyle and a stress-modulating hormone, vasopressin, correlate with inner ear fluid homeostatic disorder [6,7] and subsequent inner ear hydrops [8]. An additional factor is that mental problems in Meniere's patients may hinder good communication between patients and physicians. Mental health care is considered to

Correspondence: Tadashi Kitahara MD PhD, Department of Otolaryngology-Head and Neck Surgery, Osaka University School of Medicine, 2-2 Yamada-oka, Suita, Osaka 565-0871, Japan. Tel: +81 6 6879 3951. Fax: +81 6 6879 3959. E-mail: tkitahara@ent.med.osaka-u.ac.jp

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play an important role in good therapeutic compliance [9], resulting in effective medical and surgical results.

To treat patients with intractable Meniere's disease effectively even by way of surgery, we need to understand the psychological condition of each patient. We first examined the state of neurosis and depression in patients with intractable Meniere's disease using the Cornell Medical Index (CMI) and the Self-rating Depression Scale (SDS) before the treatment. We then examined the correlation between the mental state and each patient's background.

Material and methods

The present study was approved by the Ethics Committee of Osaka University Hospital (certificate no. 0421) and registered by ClinicalTrials.gov of the US Food and Drug Administration (certificate no. NCT00500474).

Patients

Patients were eligible for enrolment if they had received a clinical diagnosis of intractable Meniere's disease according to the American Academy of Head and Neck Surgery (AAO-HNS) criteria (1995) [10]. These criteria can be briefly described as follows. 1) Repeated attacks of vertigo: a definitive spell is spontaneous vertigo lasting at least 20 min. A mixed type of spontaneous nystagmus is observed during attacks. 2) Fluctuating cochlear symptoms: a hearing test usually reveals a marked fluctuation of the threshold in the low and middle tone range. Where necessary, we carried out a glycerol test or electrocochleogram to detect endolymphatic hydrops [11]. 3) Exclusion of other causes: to exclude other disorders, a thorough history was taken and neurological, neurotological, and MRI examinations were carried out. Intractable Meniere's disease was diagnosed in cases where various forms of medical and psychological management had failed over a period of least 3–6 months [1]. Medical management included diuretics, betahistine, diphenidol, dimenhydrinate, and diazepam, which are thought to be effective in treating persistent symptoms in Meniere's disease [12].

Enrolment and assignment

Over a period of 12 years, between April 1998 and March 2009, 220 patients with intractable Meniere's disease were enrolled in this prospective study at Osaka University Hospital. Of the 220 patients, 207 completed the CMI/SDS tests once before surgery. They also provided background information, which asked about sex, age, duration of disease, vertigo frequency (number of times per month), hearing level (in decibels, dB) in the initially affected ear and in the secondary affected ear, better hearing ear, worse hearing ear between bilateral ears, and plasma vasopressin level. The patients then underwent inner ear drainage, i.e. endolymphatic sac decompression surgery (performed by the corresponding author, T.K.), and were followed up regularly for 2 years. The surgical procedures were performed according to endolymphatic sac drainage with steroid instillation surgery [13].

Evaluation of CMI and SDS

In this study, patients in stages III and IV on the CMI were classified as having neurosis [14]. The CMI comprises 195 questions, which require an answer of 'yes' or 'no.' Each 'yes' response indicates that the subject claims the presence, currently or in some instances previously, of a stated symptom or disorder. The questionnaire consists of eight sections (A–H) which deal, respectively, with the eyes and ears, the respiratory system, the cardiovascular system, the digestive tract, the musculoskeletal system, the skin, the nervous system, and the genitourinary system. There are four sections (I–L) which deal with fatigability, the frequency of illness, miscellaneous diseases, and habits; and six sections (M–R) that deal with mood and feeling patterns.

In this study, patients with an SDS score of more than 40 were classified as having depression [15]. The SDS consists of 10 positively worded items and 10 negatively worded items, which enquire about symptoms of depression. The SDS scores were used to define four categories relating to the severity of depression: within normal range or no significant psychopathology (>40 points); presence of minimal to mild depression (40–47 points); moderate to marked depression (48–55 points); presence of severe to extreme depression (≥ 56 points). The SDS has been translated into Japanese and studies of the validity of the Japanese version have been published [16].

Evaluation of surgical results

A definitive vertigo spell lasting more than 20 min was regarded as a Meniere's vertigo attack according to the 1995 AAO-HNS criteria [10]. The frequency of vertigo was calculated based on the number of vertigo attacks during the 6 months before surgery ('before'). The frequency of vertigo attacks after treatment was calculated as the number of attacks during the

6 months before the end of the follow-up period; for example, at the second follow-up year, frequency of vertigo was calculated based on the number of vertigo attacks during the 6 months between 18 and 24 months after surgery ('after'). 'Complete' control of vertigo at the second follow-up year indicated no vertigo attacks during that period. The value 0< after/before ≤0.8 was regarded as 'better,' 1.2 ≤after/before as 'worse,' and the other values (0.8< after/before <1.2) as 'no change.'

Hearing function was measured by a pure tone audiometer and was evaluated based on the four-tone average formulated by (a + b + c + d)/4 (a, b, c, and d are hearing levels at 0.25, 0.5, 1, and 2 kHz, respectively) according to the modified 1995 AAO-HNS criteria [10]. The worst hearing level 6 months before surgery was adopted as the hearing level before treatment ('before'). The worst hearing level at follow-up was calculated as the worst hearing level during the 6 months before the end of the follow-up period; for example, the worst hearing level during the 6 month period between 18 and 24 months after surgery was adopted as the hearing level at the second follow-up year ('after'). Differences in hearing levels that were higher than 10 dB before and after treatment were regarded as 'better,' differences lower than 10 dB as 'worse,' and the other values in between 'better' and 'worse,' as 'no change.'

In total, the group classified as 'success' was defined as 'complete' control of vertigo and 'better' hearing during the 18–24 months after surgery. The group 'non-success' was defined as being opposite to the group 'success' 18–24 months after surgery (i.e. vertigo was not completely controlled and hearing was not improved).

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 14.0 (Chicago, IL, USA). The chi squared test was used to compare the ratio of the number of patients with psychological disturbance between the 'success' and 'non-success' groups (Figure 1). Univariate regression analysis was used to identify statistically significant demographic variables (Tables I and II). Furthermore, multivariate regression analysis was used to determine which factor was the most significant contributor to psychological state (Tables III and IV). The level of statistical significance (p value) was set at <0.05 for the chi-squared test and multivariate regression analysis. Values for the univariate analyses that were <0.2 were considered to be tending towards significance.

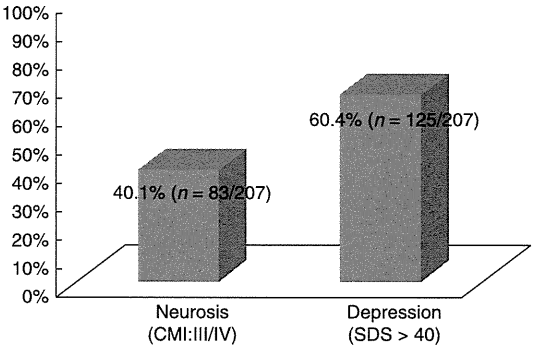

Figure 1. Neurosis and depression in patients with intractable Meniere's disease. Eighty-three cases (40.1%) were diagnosed as having neurosis according to the Cornell Medical Index (CMI) (stage III, IV). Based on the Self-rating Depression Scale (SDS) (>40), 125 cases (60.4%) were diagnosed as having depression.

Results

In the 207 patients with intractable Meniere's disease, 83 cases (40.1%) were diagnosed as having neurosis according to the CMI (stage III, IV) (Figure 1A). Based on the SDS (>40), 125 cases (60.4%) were diagnosed as having depression (Figure 1B). The neurosis/depression numbers were as follows: (–/–) = 56, (+/–) = 26, (–/+) = 68, (+/+) = 57.

Based on the definitions of 'success' and 'non-success' in the present study, 100 of the 207 cases were classified as belonging to the 'success' group. In this group, endolymphatic sac decompression surgery suppressed vertigo attacks completely and improved hearing by more than 10 dB. The remaining 107 cases fell into the 'non-success' group. Results from a chi-squared analysis indicated that decompression

Table I. Univariate logistic regression analysis for the Cornell Medical Index (CMI).

Characteristic	p value	Odds ratio (95% CI)
Sex (M/F)	0.183	1.463 (0.835–2.562)
Age (years)	0.884	0.985 (0.799–1.214)
Duration (months)	**0.0003**	**1.122 (1.054–1.194)**
Vf	0.985	1.000 (0.974–1.026)
Ini-HL (dB)	0.589	0.955 (0.809–1.128)
Sec-HL (dB)	**0.0001**	**1.031 (1.016–1.047)**
Wor-HL (dB)	0.554	1.049 (0.895–1.230)
Bet-HL (dB)	**0.0001**	**1.035 (1.017–1.054)**
pAVP (pg/ml)	0.803	1.012 (0.921–1.112)

Using univariate analysis for all nine items, p values for duration, Sec-HL and Bet-HL were <0.2. Duration, duration of disease; Vf, vertigo frequency per month; Ini-HL, hearing level in the initially affected ear; Sec-HL, hearing level in the secondary affected ear; Bet-HL, hearing level in the better hearing ear; Wor-HL, hearing level in the worse hearing ear; pAVP, plasma vasopressin level.

Table II. Univariate logistic regression analysis for the Self-rating Depression Scale (SDS).

Characteristic	*p* value	Odds ratio (95% CI)
Sex (M/F)	0.463	1.243 (0.695–2.222)
Age (years)	0.101	1.203 (0.965–1.500)
Duration (months)	**0.016**	**1.087 (1.015–1.163)**
Vf	0.869	0.998 (0.971–1.025)
Ini-HL (dB)	0.157	1.136 (0.952–1.356)
Sec-HL (dB)	**0.003**	**1029 (1.010–1.049)**
Wor-HL (dB)	**0.034**	**0.204 (1.014–1.431)**
Bet-HL (dB)	**0.003**	**0.032 (1.011–1.054)**
pAVP (pg/ml)	0.113	1.099 (0.978–1.236)

Using univariate analysis for all nine items, *p* values for duration, Sec-HL, Bet-HL, and Wor-HL were <0.2. See Table I for explanations of abbreviations.

surgery significantly improved vertigo and hearing results in the Meniere's patients who had no psychological symptoms (no neurosis or depression) compared with those patients who had some psychological symptoms (neurosis and/or depression) ('success' in no neurosis: 68/124 = 54.8%, $\chi^2 = 4.65$, $p = 0.031 < 0.05$ (Figure 2A); 'success' in no depression: 48/82 = 58.5%, $\chi^2 = 5.03$, $p = 0.025 < 0.05$ (Figure 2B)). Between-group analyses for patients with and without psychological symptoms showed no significant differences in surgical results of vertigo suppression only or hearing preservation only (data not shown).

Univariate regression analyses in CMI revealed that duration of disease, hearing level in the secondary affected ear, and hearing level in the better hearing ear had a tendency to influence patients' psychological condition of neurosis ($p < 0.2$) (Table I). The same analysis in SDS revealed that duration, secondary hearing level, better hearing level, and worse hearing level tended to influence their psychological condition of depression ($p < 0.2$) (Table II). Furthermore, multivariate regression analyses in both the CMI and SDS indicated that only duration of disease and hearing level in the secondary affected ear significantly affected their psychological conditions of neurosis and depression, respectively ($p < 0.05$) (Tables III and IV).

Table III. Multivariate logistic regression analysis for the Cornell Medical Index (CMI).

Characteristic	*p* value	Odds ratio (95% CI)
Duration (months)	0.025	1.942 (1.088–3.464)
Sec-HL (dB)	0.034	1.659 (0.935–2.943)

Using multivariate analysis for duration, Sec-HL, andBbet-HL, psychological condition of neurosis was influenced significantly only by duration and Sec-HL ($p < 0.05$). See Table I for explanations of abbreviations.

Table IV. Multivariate logistic regression analysis for Self-rating Depression Scale (SDS).

Characteristic	*p* value	Odds ratio (95% CI)
Duration (months)	0.045	1.842 (1.014–3.346)
Sec-HL (dB)	0.048	1.779 (0.981–3.227)

Using multivariate analysis for duration, Sec-HL, Bet-HL, and Wor-HL, the psychological condition of depression was influenced significantly only by duration and Sec-HL ($p < 0.05$). See Table I for explanations of abbreviations.

Discussion

In the 207 patients with intractable Meniere's disease, 40.1% were diagnosed as having neurosis according to the CMI. Based on the SDS, 60.4% of these

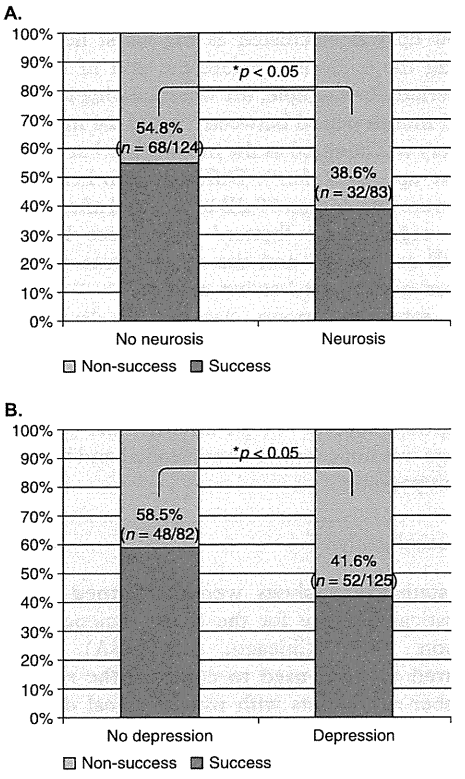

Figure 2. Correlation between surgical results and psychological condition of patients with intractable Meniere's disease. Endolymphatic sac decompression surgery suppressed vertigo attacks completely and improved hearing by more than 10 dB in 100 of 207 cases. This was defined as the 'success' group. Chi-squared analysis indicated that decompression surgery significantly improved results in Meniere's patients with no psychological symptoms ((A) no neurosis; (B) no depression) compared with those with psychological symptoms ((A) neurosis; (B) depression). (A) Neurosis: $\chi^2 = 4.65$, $p = 0.031 < 0.05$; (B) depression: $\chi^2 = 5.03$, $p = 0.025 < 0.05$.

patients were found to have depression. Compared with previous papers concerned with mental illness in non-advanced Meniere's disease [17,18], the ratios of psychological disturbances were relatively higher in this study. This may be explained by the fact that all the cases in this study were intractable candidates for surgery, i.e. belonging to the advanced stage.

As reported previously [13], endolymphatic sac decompression surgery suppressed vertigo attacks completely and improved hearing by more than 10 dB in 48.3% of cases. This was defined as the 'success' group. The other 51.7% of cases were classified as belonging to the 'non-success' group. Our results indicated that the decompression surgery significantly improved vertigo and hearing ability in Meniere's patients with no psychological disturbance compared with those who showed evidence of mental distress. Possible reasons for this are discussed as follows. Patients with mental distress have a tendency to be more susceptible to other types of stress [6,7], and they may also have a chronically elevated plasma stress hormone [8], which may be detrimental for inner ear function even after surgery. Patients with mental distress may struggle to communicate adequately with physicians and may not have good therapeutic compliance [9]; both of which are essential for the treatment of Meniere's disease even after surgery. It is suggested that attention should be given to patients' psychological condition even after surgery, as this may contribute to better surgical results.

Here, we have two important points, which neuro-otologists should not misunderstand. One is that decompression surgery can be effectual for even intractable Meniere's patients with mental disturbances. Based on our surgical results that looked at vertigo suppression and hearing preservation as separate categories, in the present study, decompression surgery was found to be effective regardless of patients' psychological condition (data not shown). The other is that even adequate psychotherapy cannot eliminate surgical treatment for intractable Meniere's disease. In our preliminary data, surgical treatment results in patients with intractable Meniere's with mental illness could be better than non-surgical medical treatment results in patients with intractable Meniere's without psychological disease (unpublished data).

Univariate regression analyses in CMI revealed that patients' duration of disease, hearing level in the secondary affected ear, and hearing level in the better hearing ear had a tendency to influence their psychological condition of neurosis. The same analysis in SDS revealed that duration, secondary hearing level, better hearing level, and worse hearing level, had a tendency to influence their psychological condition of depression. In addition, multivariate regression analysis in both CMI and SDS showed that only duration of disease and hearing level in the secondary affected ear significantly affected their psychological conditions of neurosis and depression, respectively. A possible reason for this may be that a long duration of disease gradually causes inner ear lesions that are irreversible and profound, resulting in mental distress [19]. Bilateral progressive hearing loss makes patients anxious about social communications in the future [18]. Patients who have had a long duration of disease as well as symptoms in the secondary affected ear may have more psychological disturbances than those with other neuro-otologic diseases [17], and could be more susceptible to stress in their daily life [6,7]. This can result in a vicious spiral of intractable diseases. It is suggested that awareness of patients' duration of disease and symptoms in the secondary affected ear could prevent the development of mental illness in patients with intractable Meniere's disease. As regards surgical results, multivariate regression analysis is also required to make it clear if mental illness has a direct influence on the prognosis after surgery. However, we previously reported no significant relationship between surgical results and duration of disease/hearing level at surgery [20].

In light of the data from this prospective study, there are two points that we should keep in mind when we treat patients with Meniere's disease. First, we should consider various treatment strategies ranging from steroid administration to decompression surgery, before Meniere's patients with a long duration of disease and some symptoms in the secondary affected ear develop mental illness [19]. Second, we should offer psychological support for patients who are anxious about receiving prognosis of bilateral hearing loss. We can do this by (a) providing adequate information about the possibility of progressive bilateral hearing loss in the future, and (b) suggest ways in which communication with other people who are in similar situations or who have hearing aids and cochlear implants can be improved [18].

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ORIGINAL ARTICLE

Long-term effects of the Meniett device in Japanese patients with Meniere's disease and delayed endolymphatic hydrops reported by the Middle Ear Pressure Treatment Research Group of Japan

HIDEO SHOJAKU[1], YUKIO WATANABE[1], HIROYUKI MINETA[2], MITSUHIRO AOKI[3], MASAHITO TSUBOTA[4], KAZUMICHI WATANABE[5], FUMIYUKI GOTO[6] & KOICHIRO SHIGENO[7]

Departments of Otolaryngology, [1]University of Toyama, Toyama, [2]Hamamatsu University School of Medicine, Hamamatsu, [3]University of Gifu, Gifu, [4]Joetsu General Hospital, Joestu, [5]Saiseikai Niigata Daini Hospital, Niigata, [6]Hino Municipal Hospital, Hino and [7]Shigeno Clinic, Nagasaki, Japan

Abstract

Conclusion: The Meniett device is a minimally invasive and safe treatment that may be used to provide longer-term reduction of vestibular symptoms in patients with delayed endolymphatic hydrops (DEH) as well as those with Meniere's disease (MD). *Objective:* The effects of the Meniett device were evaluated in patients with a diagnosis of definite MD or DEH according to the 1995 AAO-HNS criteria. *Methods:* Twenty-nine ears of 28 patients with MD and 5 ears of 5 patients with DEH (ipsilateral type 4, contralateral type 1) were treated with the Meniett device by the Middle Ear Pressure Treatment Research Group of Japan. All of the patients had failed to respond to medical treatment including diuretics before the pressure treatment. *Results:* Sixteen (57%) patients with MD and all five (100%) patients with DEH remained entirely free from vertigo spells; nine (32%) patients with MD responded with a significant decrease in the frequency of vertigo spells. In regard to hearing, 25 ears (74%: MD, $n = 21$; ipsilateral DEH, $n = 4$) had stable hearing levels; only 4 ears (12%: MD, $n = 3$; contralateral DEH, $n = 1$) showed a significant hearing improvement. No complications were attributable to the Meniett device.

Keywords: *Pressure treatment, vertigo, vestibular symptoms*

Introduction

The Meniett device is a low-pressure, portable delivery system used to treat patients with Meniere's disease (MD) who suffer from recurrent episodic vertigo that is not controlled by conservative therapy. To date, in non-Japanese populations, longer-term follow-up studies [1–9] have demonstrated the long-term efficacy of the Meniett device on intractable vertigo in patients with MD. However, the results of hearing outcomes after Meniett therapy are contradictory and not conclusive. There has been no long-term follow-up study to evaluate the effect of Meniett devices on both vertigo and hearing in Japanese patients with intractable MD.

Delayed endolymphatic hydrops (DEH) is one form of secondary endolymphatic hydrops. The clinical entity of DEH was first defined by Schuknecht in 1978 [10]. It is characterized by the development of symptoms consistent with endolymphatic hydrops either ipsilateral or contralateral to an ear with a profound hearing loss. In the ipsilateral type of DEH, when recurrent episodic vertigo is not controlled by conservative therapy, labyrinthectomy and

Correspondence: Hideo Shojaku MD, Department of Otolaryngology, University of Toyama, 2630 Sugitani, Toyama 930-0194, Japan. Tel: +81 764 34 7368. Fax: +81 764 34 5038. E-mail: hshojaku@med.u-toyama.ac.jp

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vestibular neurectomy on the deaf ear can be considered as a cure [11]. However, such surgical treatments are not available for recurrent episodic vertigo in contralateral DEH. In 2003, short-term effects on DEH following use of the Meniett device were first reported in Japanese patients [12]. So far, there have not been any long-term follow-up studies to evaluate the effect of this device in patients with either ipsilateral or contralateral types of intractable DEH [13].

The Meniett device has not been cleared by the Ministry of Health, Labour and Welfare of Japan; therefore, ear, nose, and throat (ENT) specialists have been required to import the devices themselves at the time of use in Japan. Under these circumstances we commenced an independent investigation in October 2001 of the short- and long-term effects of Meniett devices after approval from the institutional review board of the University of Toyama. To investigate the efficacy and safety of the Meniett device in Japanese patients with MD and DEH, the Middle Ear Pressure Treatment Research Group of Japan was convened in July 2005, and investigation of the Meniett device was started subsequently in several other institutions. The aim of our multicenter study was to investigate the long-term effects of Meniett devices in Japanese patients with medically intractable MD and DEH by use of outcome criteria devised by the Committee on Hearing and Equilibrium of the American Academy of Otolaryngology, Head and Neck Surgery in 1995 (1995 AAO-HNS criteria) [14].

Material and methods

Patients

This study comprised 28 patients with a diagnosis of definite MD, and 5 patients with DEH from 3 university hospitals, 3 general hospitals, and 1 private clinic, and whose ENT surgeons were members of the Middle Ear Pressure Treatment Research Group of Japan (Table I). MD patients were aged between 32 and 81 years (mean 57 years), and DEH patients were aged between 24 and 45 years (mean 35 years). In the MD group, 23 patients were unilateral, and 5 patients were bilateral sufferers. In the DEH group, four patients had the ipsilateral type and one patient had the contralateral type. The diagnosis was based on the history of the disease, neuro-otologic examinations, and audiometric measurements including pure-tone thresholds. The diagnostic criteria for MD defined in 1976 by the Meniere's Disease Research Committee of Japan and supported by the Ministry of Health, Labour and Welfare of Japan [15] were used. The diagnosis of definite MD was based on the coexistence of recurrent episodic vertigo (definitive spells) and fluctuating cochlear symptoms including hearing loss, tinnitus, and aural pressure. The diagnostic criteria for DEH proposed by the committee of the Japan Society for Equilibrium Research in 1987 [16] were used. The diagnosis of DEH was based on the presence of a precedent profound hearing loss (defined as a pure-tone average (PTA) of > 90 dB over the 500, 1000, and 2000 Hz frequencies) followed subsequently by the onset of recurrent episodic vertigo (ipsilateral type) and of fluctuating hearing loss in the hearing ear with or without recurrent episodic vertigo (contralateral type). As in MD, recurrent episodic vertigo in DEH occurs in definitive spells. This study was approved by the ethics committee of the University of Toyama. Informed consent was obtained from each patient in accordance with the Declaration of Helsinki.

Table I. Characteristics of MD and DEH cases.

Characteristics	MD	DEH
No. of cases	28	5
Age (years), mean ± SD (range)	57.2 ± 16.0 (32–81)	35.88 ± 10.4 (24–45)
Female (%)	62.5	40
Affected side, one/both	23/5*	5/0
Affected ear, right/left	10/13	4/1
MD stage		
Stage 1 (≤25 dB)	1	
Stage 2 (26–40 dB)	6*	
Stage 3 (41–70 dB)	13*	
Stage 4 (>70 dB)	9	
DEH		
Ipsilateral		4
Contralateral		1

MD, Meniere's disease; DEH, delayed endolymphatic hydrops. *In one of five patients with bilateral MD who used the Meniett device bilaterally, right and left ears were classified into stage 2 and 3, respectively.

Treatment and follow-up

All patients included in this study had previously received conservative treatment including diuretics. A ventilation tube was inserted in all patients, and a new evaluation was made about 4 weeks later, with pressure treatment commenced if the patients still presented with active vestibular symptoms.

The pressure pulses were delivered to the ear canal from an air pressure generator via a close-fitting cuff. Patients received training in how to apply pressure pulses and how to use the pressure device at home.

Three exposures were applied during the day. The patients were usually given the pressure treatment for at least 3 months (mean duration 12.8 months, SD 10.7 months). In bilateral MD patients, one of five patients used the Meniett device bilaterally, while the four remaining patients used it unilaterally. The frequency of attacks was reported during a period of 6 months before and 18–24 months after the start of treatment. We calculated numerical values and categorized each patient into one of six classes (A–F) according to the AAO-HNS guidelines published in 1995 [14].

Hearing was assessed utilizing PTA threshold at the frequencies of 500, 1000, and 2000 Hz before and after initiation of the Meniett device; 3000 Hz thresholds are rarely performed in Japan. PTA was evaluated according to the following equation: PTA = (hearing threshold of 500 Hz + 2 × (hearing threshold of 1000 Hz) + hearing threshold of 2000 Hz)/4. According to the 1995 AAO-HNS guidelines, the worst preoperative PTA for 6 months before treatment was compared with the worst postoperative PTA between 18 and 24 months after treatment. As per the guidelines, we considered a change of 10 dB or more as clinically significant. We also categorized each patient into one of four stages (stages 1–4) based on the 1995 AAO-HNS staging system [14].

The frequency of attacks, numerical values, vertigo improvement class, averaged PTA, and hearing change before and after treatment were analyzed. In regard to hearing assessment, 34 ears of 33 patients with MD or DEH treated by the Meniett device were evaluated. Only one of five patients with bilateral MD used the Meniett device bilaterally. For statistical analysis, the Wilcoxon matched-pair test and Mann-Whitney U test were performed with StatView for Windows (version 4.5, Abacus Concepts, Berkeley, CA, USA).

Results

Sixteen of 28 patients with MD and all 5 patients with DEH experienced freedom from definitive spells (class A response); 9 patients with MD responded with a significant decrease in the frequency of definitive spells (class B response); 2 patients with MD experienced limited control of definitive spells (class C response); and 1 patient with MD did not respond to pressure treatment (class D response) (Table II). Statistically, the average frequency of vertigo after treatment had significantly reduced in both MD and DEH (Table III). Regarding hearing ability, in 34 ears of 33 patients with MD or DEH treated by the Meniett device, 4 ears (unilateral MD, $n = 2$; bilateral MD, $n = 1$; contralateral DEH, $n = 1$) showed a significant hearing improvement of more than 10 dB; 25 ears (unilateral MD, $n = 17$; bilateral MD, $n = 4$; ipsilateral DEH, $n = 4$) had stable hearing levels; and 5 ears (unilateral MD, $n = 4$; bilateral MD, $n = 1$) showed significant hearing deterioration of more than 10 dB (Table IV). The hearing of one ear in the patient with unilateral MD in stage 1 was unchanged. In stage 2, the hearing of four ears (unilateral MD, $n = 2$; bilateral MD, $n = 2$) was unchanged, and in one ear of the patient with unilateral MD, hearing had deteriorated. In stage 3, the hearing of three ears (unilateral MD, $n = 2$; bilateral MD, $n = 1$) was improved; in six ears (unilateral MD, $n = 4$; bilateral MD, $n = 2$), it was unchanged; and in four ears (unilateral MD, $n = 3$; bilateral MD, $n = 1$), hearing was deteriorated. In stage 4, the hearing of 10 ears in patients with unilateral MD was unchanged. Of those with a class A response, 2 ears (unilateral MD, $n = 1$; bilateral MD, $n = 1$) were recorded with improved hearing; 13 ears (unilateral MD, $n = 10$; bilateral MD, $n = 3$) had unchanged hearing; and in 2 ears (unilateral MD,

Table II. Numerical values and vertigo improvement class of MD and DEH.

		MD		DEH	
Numerical value	Class	Unilateral	Bilateral	Ipsilateral	Contralateral
0	A	11 (48%)	5 (100%)	4 (100%)	1 (100%)
1–40	B	9 (39%)	0	0	0
41–80	C	2 (9%)	0	0	0
80–120	D	1 (4%)	0	0	0
>120	E	0	0	0	0
Secondary treatment initiated due to disability from vertigo	F	0	0	0	0
Total		23 (100%)	5 (100%)	4 (100%)	4 (100%)

MD, Meniere's disease; DEH, delayed endolymphatic hydrops.

Table III. Incidences of vertigo per month before and after treatment.

Parameter	MD (n = 28)	DEH (n = 5)
Before treatment*	2.6 (2.0) 0.2–8.3	1.7 (0.9) 0.2–2.2
After treatment*	0.4 (0.8) 0–3.3	0
p value†	<0.0001	0.043

MD, Meniere's disease; DEH, delayed endolymphatic hydrops.
*Averaged incidences of vertigo per month (SD) range of incidences of vertigo per month
†Wilcoxon signed rank test.

Table IV. Hearing changes with MD and DEH.

Hearing status	MD		DEH	
	Unilateral	Bilateral	Ipsilateral	Contralateral
Improved	2 (9%)	1 (17%)	0	1 (100%)
Unchanged	17 (74%)	4 (66%)*	4 (100%)	0
Deteriorated	4 (17%)	1 (17%)*	0	0
Total	23 (100%)	6 (100%)*	4 (100%)	1 (100%)

*In one of five patients with bilateral MD who used the Meniett device bilaterally, hearing outcome of right and left ears was classified into unchanged and deteriorated hearing, respectively.

n = 1; bilateral MD, n = 1), hearing ability had worsened. Among the nonclass A responses, the numbers of ears with unchanged or deteriorated hearing were seven (unilateral MD, n = 7) and two (unilateral MD, n = 2), respectively. There was no change in the average PTA before and after treatment in spite of the differences in the three stages (Table V) and two classes (Table VI). No complications were attributable to the Meniett device. In four ears of four patients, persistent perforation after tube insertion remained at the end of the pressure treatment. However, the patients refused tympanoplasty.

Discussion

To date, there have been four 2-year follow-up studies evaluating the effect of Meniett devices on definitive spells of MD following the class difference as defined in the 1995 AAO-HNS criteria (Table VII). Densert and Sass [1] showed that 19 of 37 Swedish patients who used the Meniett device experienced freedom from episodes of vertigo (class A response), and 15 patients reported a significant decrease in the frequency of vertigo (class B response). Gates et al. [4] reported that 26 of 58 US patients showed a class A response, and 13 patients showed a class B response. Barbara et al. [5] described that 25 of 36 Italian patients reported a class A response, and 11 showed a negative outcome. In the study by Huang et al. [8], 10 of 18 Chinese patients showed a class A response, and 8 showed a class B response. In the present study, 16 of 28 Japanese patients with MD showed a class A response, and 9 showed a class B response (Table II). The proportions of classes A and classes A and B in these studies ranged from 45% to 69% and from 69% to 100%, respectively. These findings suggest that, notwithstanding racial differences, Meniett devices may provide longer-term freedom or a reduction in definitive spells in the majority of patients with intractable MD according to the AAO-HNS criteria.

There are two longer-term studies evaluating the statistical effect of Meniett devices on the frequency of vertigo in patients with MD. In a 2-year follow-up, Densert and Sass [1] reported that the frequency of vertigo per month after treatment was significantly lower than before treatment, in spite of the difference in the stage. Dornhoffer and King in the USA [7] showed that the number of vertigo spells during the 6 months preceding the fourth anniversary post treatment was significantly lower than before treatment. In the present study, the incidence of vertigo per month

Table V. Hearing changes and levels before and after treatment of MD.

Hearing status	MD		
	Stages 1 and 2 (n = 6)*	Stage 3 (n = 13)*	Stage 4 (n = 10)
Improved	0	3 (23%)	0
Unchanged	5 (83%)	6 (46%)	10 (100%)
Deteriorated	1 (17%)	4 (31%)	0
Before treatment†	34 (5) 25–40	56 (10) 41–69	83 (13) 73–115
After treatment†	34 (18) 18–67	60 (23) 15–109	82 (14) 68–113
Wilcoxon's signed rank test	NS	NS	NS

*In one of five patients with bilateral MD who used the Meniett device bilaterally, right and left ears were classified into stage 2 and 3, respectively.
†Averaged hearing level (SD) range of hearing level (dB).

Table VI. Hearing change and levels before and after treatment of MD.

Hearing status	Class A (n = 17)*	Nonclass A (n = 12)
Improved	2 (12%)	1 (8%)
Unchanged	13 (76%)	8 (67%)
Deteriorated	2 (12%)	3 (25%)
Before treatment†	56 (16) 32–81	66 (26) 25–115
After treatment†	57 (21) 15–80	70 (31) 18–113
Wilcoxon's signed rank test	NS	NS

*In one of five patients with bilateral MD who used the Meniett device bilaterally, the numerical value was 0 (class A).
†Averaged hearing level (SD) range of hearing level (dB).

after treatment was significantly lower than before treatment in the Japanese patients with MD. Our results support those of previous studies and suggest on the basis of the statistical analysis that the Meniett device may reduce the frequency of vertigo over the longer term in patients with intractable MD.

It is clear that the Meniett device can reduce vertiginous symptoms and maintain an improvement in patients with medically intractable MD. Recently, the proportion of elderly Japanese patients with MD was quoted as 27% [17], and this could increase in the future due to the rapid aging of the population. Because vestibular compensation becomes more difficult with advancing age [18], destructive intervention is more likely to cause disequilibrium after elderly patients are treated [19]. Therefore, from a practical point of view, a Meniett device should be considered first of all as an intermediate step before surgical or chemical intervention, especially in the management of elderly MD patients [1].

There are three longer-term studies evaluating the Meniett device on hearing outcomes in patients with MD according to the 1995 AAO-HNS criteria (Table VIII). In an average 18-month follow-up, Rajan et al. [2] in Australia reported that the hearing had improved in 3 of 17 ears and remained unchanged in 14 ears. Huang et al. [8] noted that the hearing in 9 of 17 ears had improved, and it had not changed in 8 ears during a 2-year follow-up. Dornhoffer and King [7] showed that the hearing in two of six ears was unchanged, whereas after an average of 3 years of treatment, hearing had deteriorated in four ears. In the present study, 3 of 29 ears were recorded with improved hearing, 21 ears had unchanged hearing, and 5 ears showed worse hearing. The number of ears with improved, unchanged, and deteriorated hearing in these studies is thus summarized as 15 (22%), 45 (65%), and 9 (13%), respectively. These findings suggest that Meniett devices may induce insignificant changes to hearing in the majority of ears treated in patients with MD according to the AAO-HNS criteria.

In 1989, Stahle et al. [20] reported the long-term results of the natural course of Meniere's disease in a series of 161 patients followed for at least 9–12 years. After 5–10 years of the disease, the hearing loss stopped at a hearing threshold of 50–60 dB. After 20 years, 82% of their subjects still exhibited a mean hearing loss of 50 dB. With such poor levels of hearing, further deterioration is less likely, and therefore, this possibly contributes to the lack of significant changes in hearing after treatment. Similarly, where there are good levels of hearing, further improvement is hard to observe, and therefore, possibly also contributes to the lack of significant changes in hearing after treatment. Indeed, all patients with improved hearing were classified into stage 3 as in the study by Densert and Sass [1]. The Meniett device may have an advantage in the early stages of MD, before irreversible damage occurs to the inner ear sensory systems [1]. Before deciding whether this device can be offered as a reasonable treatment modality for hearing preservation, hearing results must be shown consistently to be equal to or better than results in patients undergoing other treatment, and both longer

Table VII. Vertigo improvement class according to AAO-HNS criteria in 2-year follow-up studies of MD.

	Vertigo improvement class							
Study	A	B	C	D	E	F	NonA	Total
Densert & Sass [1]	19 (51%)	15 (41%)	0	0	0	3 (8%)		37 (100%)
Gates et al. [4]	26 (45%)	13 (32%)	4 (7%)	0	1 (2%)	14 (24%)		58 (100%)
Barbara et al. [5]	25 (69%)						11 (31%)*	36 (100%)
Huang et al. [8]	10 (56%)	8 (44%)	0	0	0	0		18 (100%)
Present study	16 (57%)	9 (32%)	2 (7%)	1 (4%)	0	0		28 (100%)
Total	96	45	6	1	1	17	11	177

*Negative response.

Table VIII. Hearing outcomes according to AAO-HNS criteria in longer-term follow-up studies of MD.

	Hearing status			
Study	Improved	Unchanged	Deteriorated	Total
Rajan et al. [2]	3 (18%)	14 (82%)		17 (100%)
Dornhoffer & King [7]		2 (34%)	4 (66%)	6 (100%)
Huang et al. [8]	9 (53%)	8 (47%)		17 (100%)
Present study	3 (11%)	21 (71%)	5 (18%)	29 (100%)
Total	15 (22%)	45 (65%)	9 (13%)	69 (100%)

follow-up periods and larger numbers of patients must be examined.

In ipsilateral DEH, when recurrent episodic vertigo is not controlled by conservative therapy, labyrinthectomy and vestibular neurectomy on the deaf ear can be considered as a curative treatment [11]. However, such surgical treatments are not available for recurrent episodic vertigo in contralateral DEH due to endolymphatic hydrops occurring in only hearing ears. In the present study, four patients with ipsilateral DEH and one patient with contralateral DEH showed class A responses. In addition, the incidence of vertigo per month after treatment was significantly lower than before treatment in Japanese patients with DEH, suggesting that this device may be associated with longer-term freedom from, or reduction in, definitive spells in patients with both types of DEH. As in cases of MD, the Meniett device should be considered for elderly patients before surgery or chemical intervention because of the inefficient vestibular compensation under DEH. In contralateral DEH, this device may be worthwhile for use as an intermediate treatment between medical and surgical management in patients with endolymphatic hydrops in their only hearing ear [21]. The number of subjects in the present study was too low; therefore, further studies are necessary to elucidate the benefit of this safe, minimally invasive therapeutic device for the management of DEH.

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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ORIGINAL ARTICLE

Intermittent pressure therapy of intractable Meniere's disease and delayed endolymphatic hydrops using the transtympanic membrane massage device: a preliminary report

YUKIO WATANABE, HIDEO SHOJAKU, MAKIKO JUNICHO, MASATSUGU ASAI, MICHIRO FUJISAKA, HIROMASA TAKAKURA, MASAHITO TSUBOTA & SATSUKI YASUMURA

Department of Otolaryngology, University of Toyama, Toyama, Japan

Abstract

Conclusion. Middle ear pressure treatment by the tympanic membrane massage (TMM) device as well as the Meniett device is effective and provides minimally invasive options for intractable vertigo in patients with Meniere's disease (MD) and delayed endolymphatic hydrops (DEH). *Objective:* The effects of the TMM device were evaluated according to the criteria of the Japan Society for Equilibrium Research (1995) in patients with MD and DEH and compared to those in patients treated with the Meniett device. *Methods:* Twelve ears of 10 patients (MD 8; DEH 2) were treated with the TMM device, while 16 ears of 15 patients (MD 11; DEH 4) were treated with the Meniett device. All the patients had failed to respond to medical treatment including diuretics before each pressure treatment, and were followed up for more than 12 months after treatment. Tympanotomy is necessary before treatment for the Meniett device, not but for the TMM device. *Results:* With both devices, the frequency of vertigo after treatment was significantly lower than before treatment ($p < 0.05$). The time course of vestibular symptoms with the TMM device was not significantly different from that with the Meniett device ($p > 0.05$). No complications were directly attributable to treatment with the TMM device.

Keywords: *Intractable vertigo, tympanic massage device, Meniett device, middle ear pressure treatment*

Introduction

The Meniett device is an intermittent pressure treatment device used for patients with Meniere's disease (MD) suffering from recurrent episodic vertigo that is not controlled by conservative therapy [1]. Longer-term follow-up studies [2–5] and double-blind studies [6] have demonstrated the efficacy of the Meniett device on intractable vertigo in patients with MD. Recently, a Japanese study showed the longer-term effects of the Meniett device in patients with delayed endolymphatic hydrops (DEH) as well as MD [7]. This device is safe, minimally invasive, and therefore worthwhile for use as an intermediate treatment between medical and surgical management in patients with endolymphatic hydrops, occurring in the only hearing ear. However, in Japan, medical practitioners have been required to import the devices themselves to provide this middle ear pressure treatment because Meniett devices have not been cleared by the Ministry of Health, Labour and Welfare of Japan.

The tympanic membrane massage (TMM) device is an intermittent pressure treatment device initially used in western European countries in the late 19th century for patients with otitis media with effusion (OME) and without a tympanotomy [8]. In Japan, the TMM device has been cleared for use in patients with OME by the Ministry of Health, Labour and Welfare of Japan, and currently medical practitioners can buy

Correspondence: Hideo Shojaku MD, Department of Otolaryngology, University of Toyama, 2630 Sugitani, Toyama-city 930-0194, Japan. Tel: +81 764 34 7368. Fax: +81 764 34 5038. E-mail: hshojaku@med.u-toyama.ac.jp

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this pressure pulse generator device (Tympanic Massage Unit) from a domestic supplier (Kawanishi Medical Manufacturing Corp., Tokyo, Japan) (Figure 1). Although TMM devices are electronically controlled middle ear pressure treatment devices, and are similar to Meniett devices, it is not clear whether the TMM device is as effective on intractable MD and DEH as Meniett devices. Therefore, we commenced a study to investigate the effect of the TMM device on intractable vertigo in patients with MD and DEH. In this study, based on a 12 month follow-up program, we present the efficacy and safety of TMM devices compared to Meniett devices in the treatment of intractable vertigo in patients with MD and DEH by use of treatment outcome criteria devised by the Japan Society for Equilibrium Research in 1995 (1995 JSER criteria) [9]. Patient data from the Meniett device treatment have been partially reported previously [7].

Material and methods

Patients

The ethics committee of the University of Toyama approved clinical application of the Meniett device in patients with intractable endolymphatic hydrops, such as MD and DEH, in 2001. Six years later, it approved clinical application of the TMM device in patients with intractable endolymphatic hydrops. Until 2006, when patients failed to respond to medical treatment, they had been asked to use the Meniett device prior to surgical or destructive management. Thirteen patients used the Meniett device. Since 2007, patients have been asked to select either the Meniett or TMM devices. In that time, 2 patients used the Meniett device, while 10 patients selected the TMM device. The present study comprised 25 patients with a diagnosis of endolymphatic hydrops (definite MD, $n = 19$; DEH, $n = 6$) from the University Hospital of the University of Toyama from 2001 to 2010 (Table I). In the MD group, 15 patients were unilateral and 4 patients were bilateral sufferers. In the DEH group, five patients had unilateral DEH (ipsilateral type, two patients; contralateral type, three patients) and one patient had the bilateral type. In 12 ears of 10 patients (MD, 9 ears of 8 patients; DEH, 3 ears of 2 patients), the TMM device was used for the pressure treatment (defined as the TM group). In one patient with bilateral MD and one patient with bilateral DEH, pressure treatment with the TMM device was performed bilaterally. In 16 ears of 15 patients (MD, 12 ears of 11 patients; DEH, 4 ears of 4 patients), the Meniett device was used (defined as the ME group). In one patient with bilateral MD, pressure treatment with the Meniett device was performed bilaterally. The patients in the TM group were aged between 36 and 82 years (mean (M) ± standard deviation (SD), 61.8 ± 13.3 years), while those in the ME group were aged between 24 and 75 years (M ± SD, 51.8 ± 17.6 years) ($p > 0.05$). Before each pressure treatment, informed consent was obtained from each patient in accordance with the Declaration of Helsinki.

Diagnostic criteria

Diagnosis was based on the history of the disease, neuro-otologic examinations, and audiometric measurements including pure-tone thresholds. The diagnostic criteria for MD defined in 1976 by the

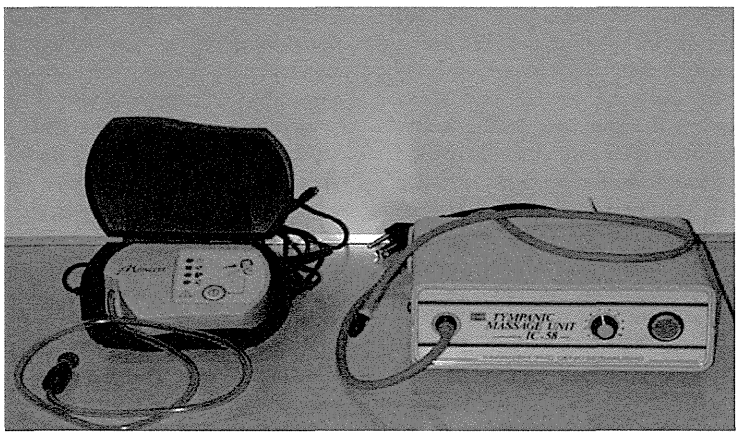

Figure 1. Transtympanic membrane massage (TMM) device. External appearance of the Meniett device (left) and TMM device (right), manufactured by Kawanishi Medical Manufacturing Corp., Tokyo, Japan. The TMM device is 2 kg in weight, 20 × 17 × 8 cm in size.

Table I. Characteristics of the patients in the TM group (TMM device) and ME group (Meniett device).

Characteristics	TM group	ME group	*p* value
No. of cases	10	15	
Age (years), mean ± SD (range)	61.8 ± 13.3 (36–38)	51.8 ± 17.6 (24–27)	0.141
Female (%)	40.0	46.7	
Disease duration (months), mean ± SD (range)	65.4 ± 47.8 (0.5–204)	51.8 ± 17.6 (6–132)	0.459
Treatment duration (months), mean ± SD (range)	4.4 ± 3.9 (1.3–12)	6.0 ± 3.9 (0.25–12)	0.792
MD			
Unilateral	7	8	
Bilateral	1*†	3‡	
Stage 1	0	0	
Stage 2	2†	3	
Stage 3	5†	6‡	
Stage 4	1	3‡	
DEH			
Ipsilateral	1	1	
Contralateral	0	3	
Bilateral	1*	0	

MD, Meniere's disease; DEH, delayed endolymphatic hydrops.
*One patient with bilateral MD and one patient with bilateral DEH used the TMM device bilaterally.
†In one patient with bilateral MD who used the TMM device bilaterally, right and left ears were classified into stage 2 and 3, respectively.
‡In one patient with bilateral MD who used the Meniett device bilaterally, right and left ears were classified into stage 3 and 4, respectively.

Meniere's Disease Research Committee of Japan and supported by the Ministry of Health, Labour and Welfare of Japan [10] were used. The diagnosis of definite MD was based on the coexistence of recurrent episodic vertigo (definitive spells) and fluctuating cochlear symptoms including hearing loss, tinnitus, and aural pressure. The diagnostic criteria for DEH proposed by the committee of the JSER in 1987 [11] were used. The diagnosis of DEH was based on the presence of preceding profound hearing loss (defined as a pure-tone average of >90 dB over the 500, 1000, and 2000 Hz frequencies) followed subsequently by the onset of recurrent episodic vertigo (ipsilateral type) and of fluctuating hearing loss in the better hearing ear, with or without recurrent episodic vertigo (contralateral type). Patients with a previous instance of bilateral profound hearing loss followed by the onset of recurrent episodic vertigo were diagnosed with the bilateral type of DEH. As in MD, recurrent episodic vertigo in DEH occurs in definitive spells.

TMM device (Figure 1)

The TMM device is an electronically controlled, low-pressure pulse generator that delivers pressure oscillating with a frequency of about 7 Hz. The intensity of the peak pressure can be controlled within ±20 cmH_2O by the power control, i.e. the output conditioning dial, on the front panel. The mean peak amplitude of the pressure pulse is set to be almost equal (about 12 cmH_2O) to that in the Meniett device. The positive-negative pressure pulses are delivered to the ear canal through a rubber tube with a close-fitting plastic ear cuff covered by rubber. The pressure applications are always delivered continuously for 3 min.

The TMM device delivers air pressure to the ear canal similarly to the Meniett device. Both devices produce an intermittent low-pressure pulse within 20 cmH_2O. In the Meniett device, the peak positive middle ear pressure is 12 cmH_2O [2]. In the TMM device, based on Figure 5 in the study by Nishihara et al. [12], the peak positive middle ear pressure is estimated to be 9 cmH_2O, while the peak negative middle ear pressure is estimated to be –5 cmH_2O. In both devices, it is thought that the middle ear pressure does not exceed the opening pressure of the eustachian tube [13]. The frequency of the pressure oscillation is 6 Hz (Meniett device) or 7 Hz (TMM device). The pressure of the TMM device is biphasic (positive-negative pressure), while that of the Meniett device is monophasic (only positive pressure).

In Japan, the TMM device has been used for many years in patients with OME prior to tympanotomy. The

original TMM devices were imported from Western Europe about 100 years ago, and by 1929, mechanically controlled TMM devices made in Japan were already on sale, alongside the Delstanche type of TMM device. In 1970, electronically controlled TMM devices were initially cleared for use in patients with OME by the Ministry of Health, Labour and Welfare of Japan. Although many patients with OME have been treated with this device throughout Japan, alternative applications of positive-negative pressure have not been shown to cause vertigo in patients with an intact tympanic membrane. Therefore, it is claimed that the negative pressure provided by TMM devices does not have harmful effects on the inner ear.

Treatment and follow-up

All patients included in this study had previously received conservative treatment including diuretics. In the ME group, before pressure treatment with the Meniett device, all patients were fitted with a tympanostomy tube, and an evaluation was made 4 weeks after their first visit. Pressure treatment commenced if the patients still presented with active vestibular symptoms. In the TM group, it was possible to start the pressure treatment without insertion of tympanostomy tubes.

Patients received training in how to apply pressure pulses and how to use the pressure device at home. Two or three pressure treatments were applied each day, with the course of pressure treatment lasting for at least 3 months. The mean duration ±SD was 10.2 ± 6.8 months in the TM group, while for the ME group it was 9.2 ± 10.3 months ($p > 0.05$). The frequency of attacks of definitive spells was reported over a period of 6 months before treatment and 12 months after. Because the effect of the Meniett device on vertigo (definitive spells) occurred within the first 3 months after treatment [3–5], the efficacy of the pressure treatment in both groups was evaluated in each half of the 12 month period after treatment. The 12 months were divided into two 6 month periods. The first 6 month period (from 1 month to 6 months after treatment) was defined as the 1–6 month period. The second 6 month period (from 7 to 12 months after treatment) was defined as the 7–12 month period. According to the JSER guidelines [10], we calculated two types of numerical values (NVs) with the following formula: NV = average number of definitive spells per month in either the 1–6 month period or the 7–12 month period after treatment/ average number of definitive spells per month in the 6 month period before treatment. In addition, remissions were defined as 6 consecutive months with no definitive spells [3].

Hearing was assessed utilizing a pure-tone average threshold (PTA) at frequencies of 500, 1000, and 2000 Hz before and after initiating treatment with the TMM or Meniett devices; 3000 Hz thresholds are rarely performed in Japan. PTA was evaluated according to the following equation: PTA = (hearing threshold of 500 Hz + 2 × (hearing threshold of 1000 Hz) + hearing threshold of 2000 Hz)/4. According to the 1994 JSER guidelines, the worst preoperative PTA for 6 months before treatment was compared to the worst postoperative PTA 1–6 months and 7–12 months after treatment. As per the guidelines, we considered a change of 10 dB or more as clinically significant. We also categorized each patient into one of four stages (stages 1–4) based on the 1995 American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) staging system [14].

Statistical analysis was conducted using the JMP 9.0.0 package for Microsoft Windows (SAS Institute Inc., Cary, NC, USA) to assess the clinical efficacy of the two pressure treatments. Between-group comparisons of age, disease duration, and pressure treatment duration were performed with the Mann-Whitney U test. The between-group comparison of vertigo and hearing outcomes according to the JSER guidelines was performed with the chi squared test. The between-group comparison of frequency of definitive spells and hearing level before and after treatment was performed by repeated measures ANOVA. The between-group comparison with respect to the time until remission occurred was performed with the Kaplan–Meier method and log-rank test. Comparisons were two-sided, with a significance level of 5%.

Results

Table II shows the vertigo outcomes in the post-treatment period in the TM and ME groups. In the TM group during the 1–6 month period after treatment, 3 of 10 patients (MD, $n = 2$; DEH, $n = 1$) experienced freedom from definitive spells (NV = 0; i.e. complete control); 5 patients (MD, $n = 4$; DEH, $n = 1$) responded with a significant decrease in the frequency of definitive spells (NV = 1–40; i.e. substantial control); 1 MD patient experienced limited control of definitive spells (NV = 41–80; limited control); and 1 MD patient did not respond to pressure treatment (NV = 81–120; insignificant control). In the 7–12 month period after treatment, 7 of 10 MD patients (MD, $n = 5$; DEH, $n = 2$) experienced complete control of definitive spells and the 3 remaining MD patients responded with substantial control of definitive spells. In the case of the ME group, during the 1–6 month period after treatment, 4 of 15 patients

Table II. Changes in vertigo outcomes in the post-treatment period in the TM group (TMM device) and ME group (Meniett device).

	TM group		ME group	
Numerical value	1–6 months	7–12 months	1–6 months	7–12 months
0	3 (30%)	7 (70%)	4 (27%)	9 (60%)
1–40	5 (50%)	3 (30%)	8 (53%)	6 (40%)
41–80	1 (10%)	0	2 (13%)	0
80–120	1 (10%)	0	1 (7%)	0
≥120	0	0	0	0
Total	10 (100%)	10 (100%)	15 (100%)	15 (100%)

Chi squared test: TM group vs ME group 1–6 months after treatment, $p > 0.05$; 7–12 months after treatment, $p > 0.05$.

(MD, $n = 3$; DEH, $n = 1$) experienced freedom from definitive spells; 8 patients (MD, $n = 7$; DEH, $n = 1$) responded with substantial control of definitive spells; 2 patients (MD, $n = 1$; DEH, $n = 1$) experienced limited control of definitive spells; and 1 patient did not respond to the pressure treatment. In the 7–12 month period after treatment, 9 of 15 patients (MD, $n = 7$; DEH, $n = 2$) experienced complete control of definitive spells and the remaining 6 patients (MD, $n = 4$; DEH, $n = 2$) responded with substantial control of definitive spells. The distribution of the NV according to the five grade evaluation system (complete control; substantial control; limited control; and insignificant control; poorer of definitive spells) in the TM group was not statistically different from the ME group in both the 1–6 month and 7–12 month periods after treatment ($p > 0.05$).

In the TM group, the mean frequency of definitive spells in the 6 months before treatment was 18.5 ± 15.8, while in the 1–6 month period after treatment it was 4.2 ± 5.8. The mean frequency of definitive spells in the 7–12 month period after treatment was 0.7 ± 1.6. In the ME group, the mean frequency of definitive spells in the 6 months before treatment was 15.1 ± 13.5, while in the 1–6 month period after treatment it was 3.1 ± 3.4. The mean frequency of definitive spells in the 7–12 month period after treatment was 1.4 ± 2.4. Figure 2 indicates that the frequency of definitive spells after treatment had a significant reduction in both groups ($p < 0.01$), but the time course of reduction of definitive spells in the TM group was not significantly different from the ME group ($p > 0.05$).

Of the 25 patients with active definitive spells at the start date of treatment, 17 achieved remission during the 12 month follow-up. Eight patients achieved remission of definitive spells in 45.3 ± 60.6 days in the TM group, while nine patients achieved remission of definitive spells in 23.1 ± 30.0 days in the ME group ($p > 0.05$) (Figure 3). In addition, 60% of the patients achieved remission of vertigo within the first 3 months following treatment in both groups. Kaplan–Meier estimates show that there was no significant difference in the time course of achieving remission between the two groups ($p > 0.05$).

Table III shows hearing outcomes in the post-treatment period in the TM and ME groups. In the TM group, in 12 ears of 10 patients with MD or DEH, all 12 ears (MD, $n = 9$; DEH, $n = 3$) showed stable hearing levels in the 1–6 month period after treatment. In the 7–12 month period after treatment, 11 ears (MD, $n = 8$; DEH, $n = 3$) had stable hearing levels, while only one MD patient showed significant hearing deterioration of more than 10 dB. As for the ME group, in 16 ears of 15 patients with MD or DEH, hearing in 2 ears (MD, $n = 2$) was improved, in 12 ears (MD, $n = 9$; DEH, $n = 3$) it was unchanged, and in 2 ears (MD, $n = 1$; DEH, $n = 1$) hearing had deteriorated during the 1–6 month period after treatment.

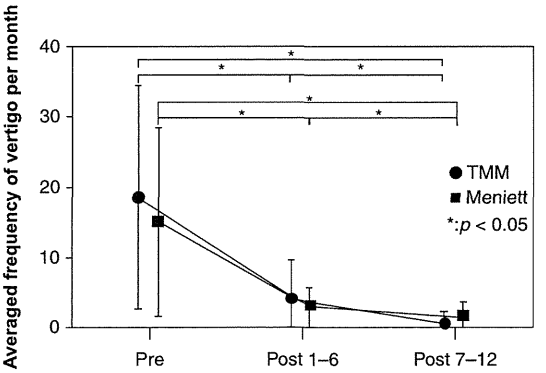

Figure 2. Change in averaged frequency of definitive spells per month. The black circle indicates the TM group (TMM device), while the black square indicates the ME group (Meniett device). The frequency of definitive spells after treatment was significantly reduced in both groups ($p < 0.01$). However, the time course of the frequency of definitive spells was not significantly different between the two groups ($p > 0.05$).