The Laryngoscope
Lippincott Williams & Wilkins
© 2007 The American Laryngological,
Rhinological and Otological Society, Inc.

Treatment of Ménière's Disease by Low-Dosage Intratympanic Gentamicin Application: Effect on Otolith Function

Kai Helling, MD; Uwe Schönfeld, MSc; Andrew H. Clarke, PhD

Objectives: The intratympanic application of a low dosage of gentamicin is increasingly favored as treatment for Ménière's disease. While posttreatment observations have confirmed a long-term success of the therapy of vertigo attacks, clear differences in the posttreatment recovery interval can be observed. In addition to differences in central-vestibular compensation, the degree of peripheral vestibular damage, i.e., to the saccule, utricle, and semicircular canal ampullae, varies among patients. This study provides comprehensive pre- and posttreatment results from unilateral functional tests of the individual vestibular receptors and of the cochlea in patients with Ménière's disease.

Study Design: Prospective clinical study.

Methods: Nineteen patients with unilateral Ménière's disease were treated by intratympanic application of gentamicin by injection of 0.3 mL (12 mg) through the tympanic membrane under local anesthesia. Tests were performed immediately previous to treatment and subsequently in the periods 4 to 8 weeks and 12 to 16 weeks after treatment. Unilateral saccular function was tested by means of acoustic-click, vestibular-evoked myogenic potentials (VEMP), and unilateral utricular function by subjective visual vertical (SVV) during unilateral centrifugation. Bithermal caloric testing was performed to assess unilateral semicircular canal function.

Results: Prior to gentamicin treatment, the caloric response from the diseased ear was normal in 3 patients, below normal in 14 patients, and in 2 cases almost completely absent. VEMP responses could be recorded bilaterally in 13 patients; while in 6, no VEMPs could be measured from the diseased ear. Utricular function measured by SVV estimation was found to be normal in 11 patients and marginally abnormal in 2 patients. In six cases, the SVV was clearly underestimated during centrifugation of the diseased side. The posttreatment findings demonstrate that VEMPs were absent in all treated patients, and the caloric response was abnormally low in all but one case. In contrast, only 12 of 19 patients produced abnormal SVV responses.

Conclusion: The results demonstrate that incremental, intratympanic application of gentamicin effectively eliminates semicircular canal and saccular function. In contrast, utricular function appears to be maintained in 30 to 40% of cases.

Key Words: Utricle, saccule, vestibular evoked myogenic potentials, subjective visual vertical, unilateral centrifugation, gentamicin, Ménière's disease.

***Laryngoscope,* 117:2244–2250, 2007**

INTRODUCTION

Conventional pharmaceutical therapy of Ménière's disease is often ineffective in reducing or eliminating complaints. For many such patients, intratympanic instillation of gentamicin has proved considerably more successful. The application of a low dosage of gentamicin, typically 12 mg, is currently the favored treatment for the shutdown of labyrinth haircell function.[1] This low dosage is known to cause little damage to the cochlea, and posttreatment observations have confirmed the long-term success of the therapy approach.[1,2]

Nevertheless, despite identical therapy regimens, clear differences in the posttreatment recovery interval are observed. While in most cases the attacks resulting from Ménière's disease are completely eliminated, the early phase after treatment is characterized by those compensation processes resulting from the induced damage to the peripheral organ.

This initial dizziness, often described as a general feeling of insecurity and manifesting as postural instability, usually vanishes during vestibular training, presumably due to central compensatory processes. However, the period required for vestibular compensation and the quality of therapy success varies considerably among patients. It would appear that in addition to differences in individual central-vestibular processes, the varying degrees of peripheral damage due to the gentamicin treatment contribute to this variability.

From the Department of Otorhinolaryngology (K.H.), Johannes Gutenberg University Medical School, Mainz, Germany, and Charité, University Medicine Berlin (U.S., A.H.C.), Campus Benjamin Franklin, Germany.

Editor's Note: This Manuscript was accepted for publication June 19, 2007.

Send correspondence to K. Helling, MD, Department of Otorhinolaryngology, Johannes Gutenberg–University Medical School, Mainz, Langenbeckstr. 1, D-55101 Mainz, Germany. E-mail: kai.helling@ukmainz.de

DOI: 10.1097/MLG.0b013e3181453a3c

Copyright © The American Laryngological, Rhinological and Otological Society, Inc. Unauthorized reproduction of this article is prohibited

A further aspect is the observation in individual cases of an improvement in caloric response after application of gentamicin, indicating regeneration of hair cell function.[1,3] Despite this functional recovery, most patients remained free of attacks resulting from Ménière's disease. This is presumably due to a reduction in endolymphatic pressure, which would also explain the reports of distinct improvements in hearing.[1] Histologic examination revealed damage to those epithelial cells involved in the production of endolymph, particularly the dark cells in the ampullae of the semicircular canals (SCC).[4] All told, it emerged that gentamicin affects the epithelial cells of the maculae, the cristae, and the cochlea to varying degrees.[5]

Consequently, a number of studies have been performed with the aim of characterizing the damage to the vestibular labyrinth caused by intratympanic application of gentamicin.[6–13]

To date, however, no study has been performed that includes comprehensive pre- and posttreatment examination of the individual labyrinth functions (i.e., SCC, saccule, utricle) and of the cochlea.

To this end, unilateral testing of otolith function has become practicable in recent years. Measurement of vestibular-evoked myogenic potentials (VEMP) has become established as a unilateral test of saccular function.[8,9,13] More recently, unilateral functional testing of utricular function by measurement of the otolith-ocular response and the subjective visual vertical (SVV) during unilateral centrifugation has been proven effective.[14–16]

The aim of this study was to examine how intratympanic application of gentamicin as treatment for Ménière's disease influences the function of the individual macula organs and of the SCC. More specific knowledge of the effect of gentamicin on the individual epithelia is important for improvement of the therapy regimen and for the prescription of the appropriate compensation training program.

MATERIALS AND METHODS

Tested Patients

Nineteen patients (11 women and 8 men) with unilateral Ménière's disease were examined and treated in the outpatient clinic. All patients met the criteria for diagnosis of definite Ménière's disease according to the American Academy of Otolaryngology (AAO) guidelines.[17] All demonstrated recurrent vertigo attacks of more than 20 minutes, sensorineural hearing loss of the affected side, and additional symptoms such as tinnitus or aural fullness. In all cases, gentamicin treatment was not performed until the history lasted for more than 12 months and conservative therapy (betahistin, sulpirid, picrotoxin, ventilation tube, Meniett) failed. The treated patients had a mean age of 53.7 (25 – 75; ±12.5 SD) years.

All patients were treated by intratympanic instillation of gentamicin. Under local anesthesia, a single dose of 12 mg (0.3 mL) was applied. If attacks persisted for more than 4 weeks and the complete functional testing demonstrated no change of caloric tests, a second dose of 12 mg was injected (n = 2). In cases of reduced caloric responses, a second dose of 6 mg was applied (n = 5). The effect of the treatment for Ménière's disease was examined 4 to 8 weeks and again 12 to 16 weeks after therapy.

In cases where more than one dose was applied, time to testing refers to the interval from the final application. The treated patients were monitored in the outpatient clinic over a period of at least 12 months (maximum of 36 months).

Audiometric Testing

Patients' hearing was tested by determining the pure-tone thresholds in the frequency range of 0.5, 1, 2, and 3 kHz by air and bone conduction, and the average of the threshold values was calculated to stage Ménière's disease (AAO stages 1–4).[17]

Caloric Testing

Caloric testing was performed using a standardized sequence of 30-second irrigations with water (44°C right ear, 44°C left ear, 30°C left ear, 30°C right ear). Nystagmus activity was recorded throughout by electrooculography (EOG) and the slow phase velocity (SPV) calculated. The culmination SPVs from the four irrigations (extracted from the interval 30–60 seconds after stimulation) were used to determine the overall response intensity and left/right symmetry.

$$\frac{|\,SPV_{max}(44°C_{right})\,| \;+\; |\,SPV_{max}(30°C_{right})\,|}{|\,SPV_{max}(44°C_{left})\,| \;+\; |\,SPV_{max}(30°C_{left})\,|}$$

These were classified according to the nomogram described by Scherer.[18] Normal response intensity was defined as within the 10% to 90% normal range. Responses that lay between the normal range and the 3%, respectively 97% level, were classified as unilateral weakness. Responses that lay beyond this range were classified as unilateral loss of SCC function.

VEMP Testing

The saccular function was tested by measurement of the VEMP. Electromyography (EMG) activity was recorded from symmetrical sites on the upper half of each sternocleidomastoid (SCM), a reference electrode on the upper part of the sternum and a ground electrode on the forehead. During the measurements, the test subject was supine and was required to raise and hold his head to tension the SCM muscle. The acoustic stimuli (Click stimuli; 0.25ms; rarefaction; 5/s) were presented via a headphone. For averaging, the EMG signal was extracted over the interval from 20 milliseconds before stimulus to 100 milliseconds after stimulus and normalized to the EMG activity. A total of 150 EMG signal extracts were averaged. The maximum stimulus intensity used was 145 dB (SPL). The amplitude and symmetry of the patients' responses were compared to those of a normal control group (n = 32). Response was classified as normal if the side difference calculated by the asymmetry ratio of the normalized p13/n23 amplitude was $<30\%$.[13]

SVV Testing

The utricular function was tested by estimation of the subjective visual vertical (SVV) during unilateral centrifugation (UC). A dual-axis human rotator (Neurokinetics, Inc., Pittsburgh, PA) with lateral chair translation was employed for eccentric displacement profiles. Details of this equipment and stimulus technique were published previously.[15,16]

The visual cue for the SVV estimation was generated with a luminous line of 20 cm in length mounted in a black dome with a diameter of 60 cm, which was fixed approximately 40 cm in front of the seated subject with its center in line with the test subject's naso-occipital axis. This permitted free field-of-view, binocular viewing of the stimulus. The head was fixed by a helmet to set the head on axis. The test subject could rotate the motor driven luminous line by push button, and was required to align the line to the gravitational vertical. The SVV is defined here as the set angle, as measured with reference to the true vertical. Between settings, the line was switched off and rotated to a random

Copyright © The American Laryngological, Rhinological and Otological Society, Inc. Unauthorized reproduction of this article is prohibited

position under program control. Estimation and measurement of the SVV was performed in otherwise total darkness. SVV estimation was performed 3 to 5 times and the corresponding median values were calculated.

The UC stimulus profile consists of angular acceleration (3 degrees/s^2) around the earth-vertical z-axis up to an angular rate of 300 degrees/second. After at least 2 minutes of constant angular rate rotation for extinction of any perrotatory nystagmus, unilateral stimulation was generated by translating the subject chair radially by ± 3.5 cm from the vertical rotation axis. In this case, one labyrinth is positioned on axis (i.e., exposed to zero centrifugal force), while the eccentric labyrinth is exposed to a force equivalent to ωr^2 along the interaural axis. This corresponds to an effective tilt of the gravito-inertial vector at center of head of 5.5 degrees. At an angular rate of 300 degrees/second and a laterally displacement of 3.5 cm, the SVV values from the normal group ranged between 3.5 and 8.7 degrees (10% to 90%).[15]

Statistical Testing

The data for the test results are shown as box-and-whiskers plots (minimum and maximum, 10%–90% percentiles, 25%–75% quartiles, median). Statistical testing was performed with the Wilcoxon test for dependent samples (for paired differences). A significance level of $P < .05$ was employed.

RESULTS

Pretreatment Testing

The average duration of patients' complaints before treatment ranged between 12 and 336 months (median 44 months).

Sensorineural hearing loss (HL) was found in all cases in the diseased ear. Prior to treatment, the bone-conduction threshold lay between 9.4 and 60 dB HL (median 53.8 dB HL). In one patient, HL was so severe that the threshold could not be determined. According to the AAO classification for staging of definite and certain Ménière's disease, one patient was rated as stage 1, one as stage 2, 16 as stage 3, and one as stage 4.[17]

Caloric testing resulted in the slow phase velocity (SPV) distributions shown in Figure 1A. Intraindividual comparison confirmed the reduction ($P = .0001$) in function on the diseased ear. Immediately prior to gentamicin treatment, the SPV of the caloric nystagmus was below normal in 14 patients (74%), and in 2 cases (10%) barely detectable. In the remaining three patients (16%) the caloric response was normal (see Fig. 2A, left column).

Unilateral testing of saccular function demonstrated a significantly reduced response amplitude ($P = .003$) in the diseased ear (Fig. 1B). Good quality VEMPs could be recorded bilaterally in 13 patients (68%). In nine of these cases (47%), the responses were within the normal range. In the remaining four cases, reduced amplitudes and increased threshold levels were recorded on the diseased side, indicating a partial dysfunction of the saccule. In six of the treated patients (32%), no VEMP response could be measured from the diseased ear. In one case, a bilateral absence of response was determined (see Fig. 2B, left column).

Unilateral testing of utricular function produced median values from healthy and diseased ears within the normal range ($P = .26$) (Fig. 1C). However, the shift of the quartile range suggests a lower sensitivity of the utricle in the diseased ear.

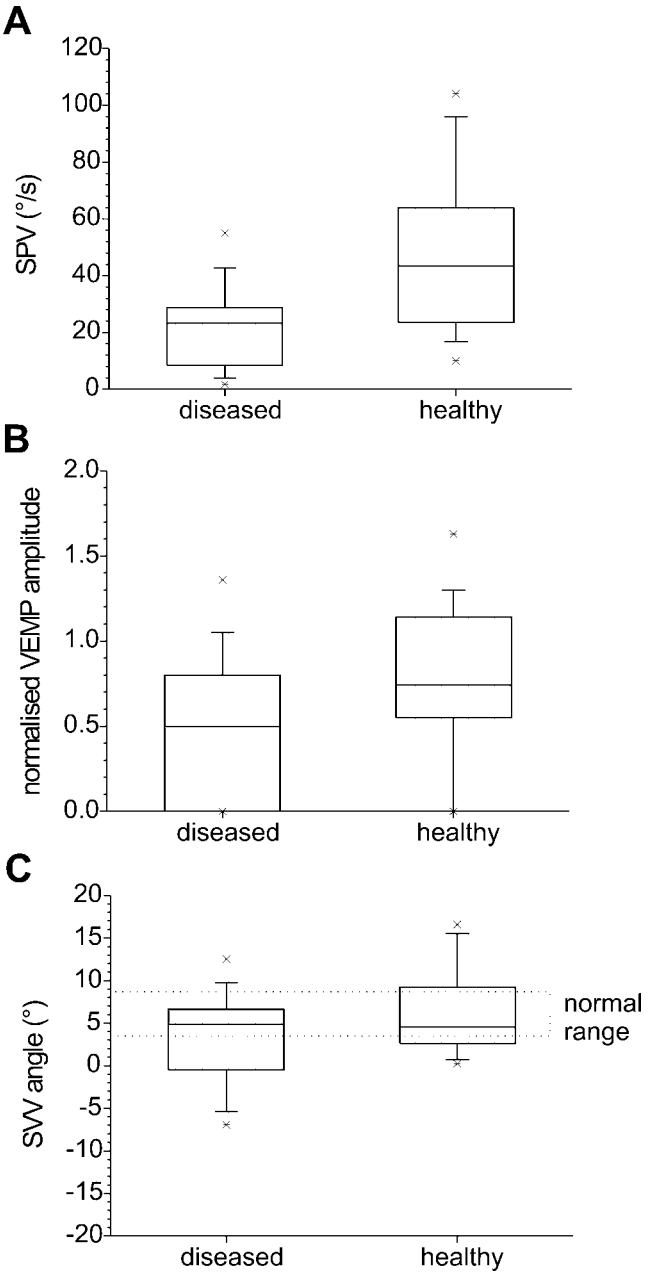

Fig. 1. Distribution of the pretreatment vestibular findings for healthy and diseased ears (Box and Whiskers plot: minimum, maximum, 10%–90% percentiles, 25%–75% quartiles, median); (A) slow phase velocity (SPV) values, calculated as the sum of the absolute response intensities during the culmination phases of the 44-degree and 30-degree irrigations; (B) normalized vestibular-evoked myogenic potentials (VEMP) amplitudes for a click stimulus of 145 dB (SPL); (C) subjective visual vertical angle, as estimated during unilateral centrifugation of the healthy and diseased ears.

In 10 patients (53%), normal SVV values were found during testing of both ears. In one case, the SVV was overestimated consistently during testing of both ears. Due to the lack of asymmetry, this case was regarded for present purposes as normal. In six further cases (32%),

Copyright © The American Laryngological, Rhinological and Otological Society, Inc. Unauthorized reproduction of this article is prohibited

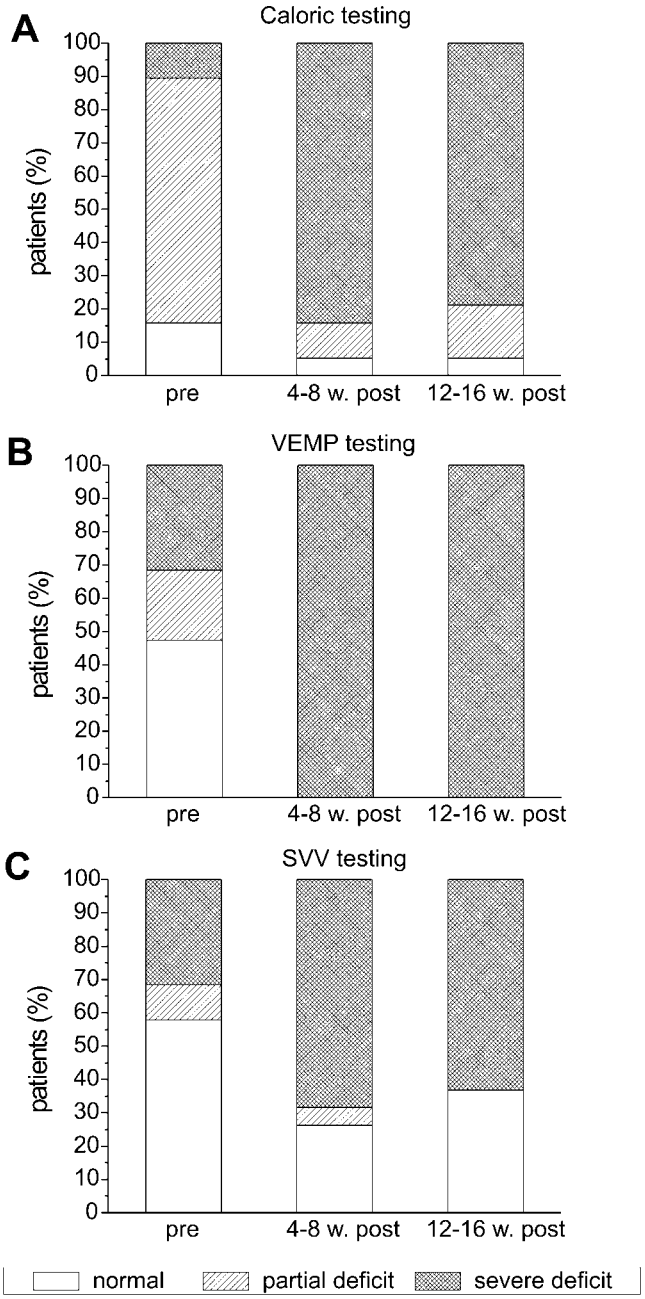

Fig. 2. Percentage distributions of normal and pathologic results during pre- and posttreatment testing: (A) caloric response, (B) vestibular-evoked myogenic potentials (VEMP) response, (C) subjective visual vertical estimation during unilateral centrifugation.

the SVV was clearly underestimated during centrifugation of the diseased side. In one patient, the SVV was consistently overestimated during stimulation to the diseased ear, this was regarded as pathological. In two patients (10%), a marginally abnormal response was found in the diseased ear (see Fig. 2C, left column).

Posttreatment Testing

In 13 of the 19 patients (68%), the single 12-mg dose resulted in complete cessation of dizziness attacks over the control period of 12 to 36 months. In five patients (26%), a second dose (see Table I) was required to eliminate the attacks. In one further patient, a third dosage was required.

All patients were free of Ménière's attacks after treatment apart from a moderate sensation of dizziness experienced over several days after an interval of 5 to 6 days subsequent to treatment.

Audiometric testing after treatment yielded a bone-conduction threshold of 51.8 dB HL (median), ranging from 6.8 to 71 dB HL. Comparing intraindividual pre- to posttreatment bone-conduction threshold, a median increase of 2.5 dB (range: −16.8 to +13.1 dB) was found. A noticeable difference was found between those patients with a single and those with repeated application of gentamicin (single dose: −0.3 dB median [−7.5 to +6.9 dB]; repeated-dose: 3.8 dB median [−16.8 to +13.1 dB]).

Caloric testing 4 to 8 weeks after gentamicin treatment failed to elicit responses from the treated ear in 16 patients (84%) (Fig. 2A, center column). Reduced responses were measure in two patients (10%), and in one case, the response remained within the normal range.

During testing 12 to 16 weeks after treatment, one patient appeared to have regained partial caloric response (Fig. 2A, right column).

VEMP responses were absent in all patients after treatment during both measurement periods, indicating that gentamicin application resulted in loss of saccular function. (Fig. 2B, center and right).

SVV test results, in contrast to the caloric and VEMP findings, indicated that a number of patients had retained normal responses (Fig. 2C). All told, 7 (37%) of the 19 patients were found to make normal SVV estimates after treatment. However, taken case by case, the situation is more complex. Of the 11 patients with normal pretreatment responses, only 3 (16%) tested normal after treatment. Of the remaining eight patients who tested pathologically previous to treatment, four cases proved normal by the second posttreatment period.

The additional statistical evaluation of the pre- to posttreatment SVV results is presented in Figure 3. The median values for both posttreatment periods lay outside the normal range, close to zero, i.e., indicating little or no response to the stimulus. While comparison of the first posttreatment period compared to the pretreatment values proved statistically significant ($P = .005$), a tendency to recover could be observed during the second posttreatment period ($P = .08$).

An overview of all patients is presented in Table I with a description of their pre- and posttreatment results and their subjective symptoms. Ten patients (age: minimum: 25 years; maximum: 69 years; mean: 50.1 years) were completely free of dizziness after treatment, whereby 50% (4, 9, 13–15) made normal SVV estimates and 50% (3, 5, 11, 12, 19) tested pathological. Seven complained of minor postural instability or nonsystematic dizziness (age: minimum: 40 years; maximum: 73 years; mean: 56.0 years) with five (6–8, 10, 16) showing abnormal, and two (17, 18) showing normal SVV responses. The two (1, 2) remaining patients (age: 53, 75 years) had severe postural instability, suffering both from Ménière attacks and postural instability previous to treatment. While the Ménière

Copyright © The American Laryngological, Rhinological and Otological Society, Inc. Unauthorized reproduction of this article is prohibited

TABLE I.
Summary of Patients Treated With Gentamicin Doses, Pre- and Posttreatment Results and Symptoms of Dizziness After Treatment.

				Pretherapeutic Test Results on Diseased Side			Post-Therapeutic Test Results on Diseased Side			Post-Therapeutic Dizziness	
Patient	Gentamicin Dose	Gender	Age (Years)	Caloric	VEMP	SVV	Caloric	VEMP	SVV	Quality	Intensity
1	12 mg	M	75	o	o	−	+	−	−	Postural instability	Severe
2	12 mg	M	53	o	+	−	−	−	−	Postural instability	Severe
3	12 mg + 6 mg	M	52	o	o	+	−	−	−	No dizziness	—
4	12 mg	F	41	o	+	o	−	−	+	No dizziness	—
5	12 mg + 6 mg	F	69	o	−	+	−	−	−	No dizziness	—
6	12 mg	M	65	o	+	+	−	−	−	Non-systematic	Low
7	12 mg	F	73	o	−	+		−	−	Non-systematic	Low
8	12 mg	F	40	−	o	−	−	−	−	Postural instability	Low
9	12 mg	F	53	+	−	+	−	−	+	No dizziness	—
10	12 mg + 6 mg	F	54	o	−	−	−	−	−	Non-systematic	Low
11	12 mg	M	55	o	o	+	−	−	−	No dizziness	—
12	12 mg + 12 mg	M	25	o	−	+	−	−	−	No dizziness	—
13	12 mg + 12 mg + 6 mg	M	54	o	+	+	o	−	+	No dizziness	—
14	12 mg	F	48	o	+	−	−	−	+	No dizziness	—
15	12 mg	F	63	o	+	−	−	−	+	No dizziness	—
16	12 mg	F	43	+	+	−	−	−	−	Non-systematic	Low
17	12 mg + 6 mg	M	57	o	+	o	o	−	+	Non-systematic	Low
18	12 mg	F	60	+	−	+	o	−	+	Non-systematic	Low
19	12 mg	F	41	−	+	+	−	−	−	No dizziness	—

VEMP = vestibular-evoked myogenic potentials; SVV = subjective visual vertical; + = normal; o = partial deficit; −= severe deficit.

attacks were eliminated, chronic postural instability persisted after treatment.

Finally, four patients (4, 14, 15, 17) were found to recover utricular function after treatment.

DISCUSSION

Previous reports describe the detrimental influence of Ménière's disease on peripheral vestibular function.

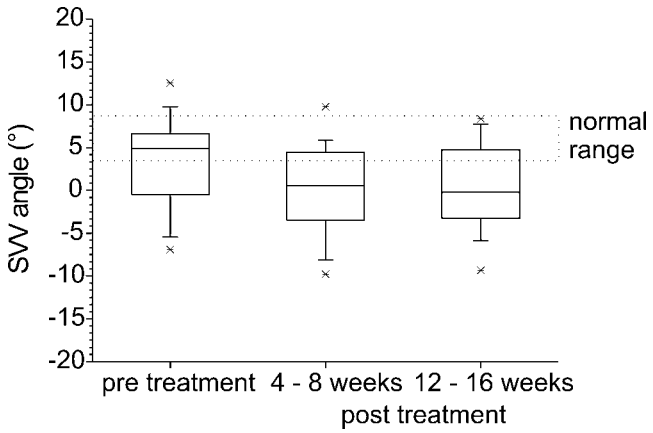

Fig. 3. Distribution of subjective visual vertical estimations during pre- and posttreatment testing (Box and Whiskers plot: minimum, maximum, 10%–90% percentiles, 25%–75% quartiles, median).

Deficits in semicircular canal function are reflected as reduced caloric and head-impulse response.[10,19] Unilateral testing of the saccular function in Ménière's disease by means of VEMP recording has been reported in a number of studies.[8,9,13] With respect to the utricular function, Odkvist et al. reported highly variable and sometimes even paradoxical responses in the estimation of subjective visual horizontal (SVH) during tests with head tilted to gravitoinertial vector.[6] Furthermore, these results did not correlate with the caloric asymmetry or with audiometric findings. Takai et al. also measured the SVH in their six patients after treatment with gentamicin and observed a slight improvement over the course of one year.[20]

The pre- and post-therapy test regime employed in the present study permits discrimination between the influence of Ménière's disease as such, and of the subsequent ototoxic effect of gentamicin.

Pretreatment Findings

As in previous studies, the pretreatment results clearly demonstrate that over the course of Ménière's disease, damage occurs—not only to the cochlear, but also to the vestibular apparatus. In general, patients were selected on the basis of the AAO guidelines.[17] Most of our patients could be classified as stage 3, and in accordance with previous reports, they also showed a high degree of caloric asymmetry.[4,7,12] In contrast to the semicircular

Copyright © The American Laryngological, Rhinological and Otological Society, Inc. Unauthorized reproduction of this article is prohibited

canal function, otolith function was preserved in a larger proportion of cases. A similar percentage (42%) of reduced or absent VEMPs as previously reported by Welgampola and Colebatch (35% to 54%) was found.[13] Unilateral testing of utricular function permitted comparison of the diseased ear with the healthy ear.[15] This provides considerable advantage over the technique employed, e.g., by Odkvist et al., whose paradigm involved simultaneous stimulation to both right and left labyrinths, and thus confounds the responses from healthy and diseased ears.[6] The more specific UC technique demonstrates clearly that utricular function is least affected by Ménière's disease.

Gentamicin Therapy

Treatment of unilateral Ménière's disease with low-dosage, interval application of gentamicin has been shown to be both economical and therapeutically successful.[1,11] Lange et al. reported elimination of dizziness attacks in 53% of their patients after a single dose, while application of a second dose in 8 or 15 days proved effective in 95% of the treated cases.[1] While Lange et al. also noted that hearing function was maintained in most patients, studies in which multiple applications in short intervals or continuous application were employed resulted in degradation in hearing function.[1,21] In the present study, post-treatment hearing loss was slightly greater among patients who had received repeated applications.

The present findings agree largely with those of Lange et al. and Carey, whereby the interval in the present study was 4 weeks (rather than 2 weeks).[1,19] In 68% of the treated patients, a single dose was sufficient to eliminate the dizziness attacks, while additional doses were required in the remaining 32%.

Posttreatment Findings

The caloric response was reduced in the diseased ear in almost all patients after treatment. In 84%, there was complete loss of function and in a further 10%, the response was substantially reduced. De Waele et al. documented a loss of caloric response in 76% of patients one month after treatment, increasing to 86% after six months and reducing again to 75% after one year.[8] Picciotti et al. found a total loss of caloric response in 50% of their treated patients, with a further 17% with reduced response.[12] Carey et al. examined semicircular canal function by means of the head-thrust test and found gain reductions of varying degree for all three canals.[19] Thus it can be concluded that successful therapy of the dizziness attacks does not necessarily require elimination of canal function.

Regardless of their initial condition, loss of VEMP response resulted in all treated patients. This agrees with other studies where VEMP responses were absent in a large proportion (92%–100%) of patients after application of gentamicin.[8,12,13] However, in patients who received repeated dosages, this loss of response was noted after the first application, and this demonstrates that the VEMP response cannot be considered as a reliable indicator for success of treatment.

In contrast to the semicircular canal and saccular tests, the SVV findings indicate that utricular function is affected to a lesser degree by gentamicin therapy. It remains unclear why the utricle should be less affected by gentamicin. It is conceivable that this is due to the kinetics pattern for gentamicin absorption in the inner ear.[22,23] This idea is supported by the findings of animal experiments where gentamicin affected the labyrinthine epithelia to varying degrees.[5]

Notable are the four patients in whom a recovery of utricular function was observed after treatment. It is conceivable that this recovery was to some degree due to reduced endolymphatic pressure resulting from damage to the vestibular supporting cells (dark cells) that regulate endolymph production. This may also explain the retention of semicircular canal function after successful therapy.[24]

Complaints Versus Test Results

No clear relation could be established between dizziness complaints and the test results. For example, of the seven patients with normal SVV results, five reported cessation of complaints, while two continued to suffer from minor unspecific dizziness. It was also noted that of the six patients who had received repeated instillations, only two reported some form of dizziness after treatment. In comparison, of the 13 patients who had received only a single dose, more than half (7) continued to have complaints of dizziness.

Finally, there appears to be a tendency for elderly patients to suffer from diffuse complaints of dizziness after treatment. This might be attributable to the reduced capacity for central vestibular compensation in older patients.

CONCLUSION

In summary, saccular function—as tested by VEMPs—was absent in all treated patients, and in all but one case, canal function—as tested by caloric tests—was abnormally low. On the other hand, only 12 of 19 patients produced abnormal SVV responses. This indicates that utricular function is least affected by the incremental application of gentamicin as employed in this study. Whether this resulted from different concentrations of gentamicin infiltrating to the various intralabyrinthine structures, i.e., leading to a reduced toxification of the hair cells on the utricular epithelium remains unclear.

BIBLIOGRAPHY

1. Lange G, Maurer J, Mann W. Long-term results after interval therapy with intratympanic gentamicin for Ménière's disease. *Laryngoscope* 2004;114:102–105.
2. Cohen-Kerem R, Kisilevsky V, Einarson TR, Kozer E, Koren G, Rutka JA. Intratympanic gentamicin for Ménière's disease: a meta-analysis. *Laryngoscope* 2004;114:2085–2091.
3. Cruz RM, Lambert PR, Rubel EW. Light microscopic evidence of hair cell regeneration after gentamicin toxicity in chick cochlea. *Arch Otolaryngol Head Neck Surg* 1987;113: 1058–1062.
4. Park JC, Cohen GM. Vestibular ototoxicity in the chick: effects of streptomycin on equilibrium and on ampullary dark cells. *Am J Otolaryngol* 1982;3:117–127.
5. Kimura RS, Iverson NA, Southard RE. Selective lesions of the vestibular labyrinth. *Ann Otol Rhinol Laryngol* 1988;97: 577–584.
6. Odkvist LM, Noaksson L, Olsson S, Ledin T. Subjective visual horizontal determination during otolith stimulation by eccentric rotation in conservatively treated Ménière's disease. *Int Tinnitus J* 1998;4:75–77.

Copyright © The American Laryngological, Rhinological and Otological Society, Inc. Unauthorized reproduction of this article is prohibited

7. de Waele C, Tran Ba Huy P, Diard JP, Freyss G, Vidal PP. Saccular dysfunction in Ménière's patients. A vestibular-evoked myogenic potential study. *Ann N Y Acad Sci* 1999; 871:392–397.
8. de Waele C, Meguenni R, Freyss G, Zamith F, Bellalimat N, Vidal PP, Tran Ba Huy P. Intratympanic gentamicin injections for Ménière disease: vestibular hair cell impairment and regeneration. *Neurology* 2002;59:1442–1444.
9. Rauch SD, Silveira MB, Zhou G, et al. Vestibular evoked myogenic potentials versus vestibular test battery in patients with Ménière's disease. *Otol Neurotol* 2004;25: 981–986.
10. Park HJ, Migliaccio AA, Della Santina CC, Minor LB, Carey JP. Search-coil head-thrust and caloric tests in Ménière's disease. *Acta Otolaryngol* 2005;125:852–857.
11. Perez N, Rama-Lopez J. Vestibular function at the end of intratympanic gentamicin treatment of patients with Ménière's disease. *J Vestib Res* 2005;15:49–58.
12. Picciotti PM, Fiorita A, Di Nardo W, Quaranta N, Paludetti G, Maurizi M. VEMPs and dynamic posturography after intratympanic gentamycin in Ménière's disease. *J Vestib Res* 2005;15:161–168.
13. Welgampola MS, Colebatch JG. Characteristics and clinical applications of vestibular-evoked myogenic potentials. *Neurology* 2005;64:1682–1688.
14. Wetzig J, Reiser M, Martin E, Bregenzer N, Baumgarten RJ. Unilateral centrifugation of the otoliths as a new method to determine bilateral asymmetries of the otolith apparatus in man. *Acta Astronautica* 1990;21:519–525.
15. Clarke AH, Schönfeld U, Hamann C, Scherer H. Measuring unilateral otolith function via the otolith-ocular response and the subjective visual vertical. *Acta Otolaryngol (Stockh)* 2001;545(Suppl):84–87.
16. Clarke AH, Schönfeld U, Helling K. Unilateral examination of utricle and saccule function. *J Vest Res* 2003;13: 215–225.
17. Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Ménière's disease. American Academy of Otolaryngology–Head Neck Surgery. *Otolarngol Head Neck Surg* 1995;113:181–185.
18. Scherer H. Provoked vestibular nystagmus and caloric reactions after sudden loss of vestibular function. *Adv Otorhinolaryngol* 1981;27:168–175.
19. Carey JP, Minor LB, Peng GC, Della Santina CC, Cremer PD, Haslwanter T. Changes in the three-dimensional angular vestibulo-ocular reflex following intratympanic gentamicin for Ménière's disease. *J Assoc Res Otolaryngol* 2002;3: 430–443.
20. Takai Y, Murofushi T, Ushio M, Iwasaki S. Recovery of subjective visual horizontal after unilateral vestibular deafferentation by intratympanic instillation of gentamicin. *J Vestib Res* 2006;16:69–73.
21. Chia SH, Gamst AC, Anderson JP, Harris JP. Intratympanic gentamicin therapy for Meniere's disease: a meta-analysis. *Otol Neurotol* 2004;25:544–552.
22. Aran JM, Chappert C, Dulon D, Erre JP, Aurousseau C. Uptake of amikacin by hair cells of the guinea pig cochlea and vestibule and ototoxicity: comparison with gentamicin. *Hear Res* 1995;82:179–183.
23. Hoffer M, Allen K, Kopke RD, Weisskopf P, Gottshall K, Wester D. Transtympanic versus sustained-release administration of gentamicin: kinetics, morphology, and function. *Laryngoscope* 2001;111:1343–1357.
24. Pender DJ. Gentamicin tympanoclysis: effects on the vestibular secretory cells. *Am J Otolaryngol* 1985;6:358–367.

Copyright © The American Laryngological, Rhinological and Otological Society, Inc. Unauthorized reproduction of this article is prohibited