

ORIGINAL ARTICLE

Vestibular-evoked myogenic potential in response to bone-conducted sound in patients with otosclerosis

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Abstract

Conclusion: Saccular dysfunction is a major cause of balance problems in patients with otosclerosis. Vestibular-evoked myogenic potential in response to bone-conducted sound (BC-VEMP) testing is useful for diagnosis of these patients. **Objectives:** The purpose of this study was to elucidate the origin of balance problems in patients with otosclerosis using BC-VEMP. **Methods:** Subjects comprised 25 patients with unoperated otosclerosis (9 men and 16 women). They were divided into two groups depending on type of balance problems. Results of cochleo-vestibular functions including pure-tone audiometry, caloric testing, and BC-VEMP testing were compared between the two groups. **Results:** Ten patients had complained of dizziness and/or vertigo (disequilibrium group), and the other 15 patients had not (Non-disequilibrium group). Nine patients showed abnormal results on BC-VEMP testing in the disequilibrium group, while one patient had abnormal results in the non-disequilibrium group ($p < 0.001$).

Keywords: Balance problems, saccular dysfunction, endolymphatic hydrops, direct invasion of otosclerotic focus

Introduction

Patients with otosclerosis complain of hearing loss or tinnitus at the early stage of the disease, and the symptoms worsen progressively. A sclerotic lesion commonly appears on the anterior part of the oval window and spreads to the annular ligament of the stapes, and consequently the stiffness produces conductive hearing loss. It is known that approximately 20–37% of patients have accompanying dizziness or vertigo [1,2], but the pathogenesis of balance problems remains unclear.

Conventional vestibular-evoked myogenic potential (VEMP) was first reported by Colebatch and Halmagyi in 1992 [3] and has been established as an examination of otolith function. VEMP is a useful tool to diagnose balance problems due to otolith

dysfunction, which have not been well studied. As conventional VEMP is stimulated by air-conducted sound, it cannot be recorded for patients with conductive hearing loss [4]. Sheykhholes et al. revealed that VEMP response to bone-conducted sound (BC-VEMP) was recordable for patients with conductive hearing loss [5]. Welgampola et al. described that affected ears with inner ear dysfunction showed abnormal results on BC-VEMP [6]. Miyamoto et al. reported that results of BC-VEMP are not significantly different from those of conventional VEMP [7]. Seo et al. reported that results of BC-VEMP were abnormal in 54% of patients with chronic otitis media who complained of disequilibrium [8]. Thus BC-VEMP can detect vestibular dysfunction in patients with conductive hearing loss.

Table I. Summary of patients.

| Case no. | Age (years) | Sex | Side | Duration | AC | | BC | | Caloric CP% | BC-VEMP | | V or D | Balance problems | | |
|----------|-------------|-----|------|----------|-------|-------|-------|------|-------------|---------|-------|----------------|------------------|------------|-------------|
| | | | | | Right | Left | Right | Left | | Right | Left | | Duration | Recurrence | Trigger |
| 1 | 56 | F | B | 15 | 62.5 | 43.1 | 28.8 | 24.4 | 3.4 | 0.00* | 0.69 | D | Seconds | Recurrent | Positional |
| 2 | 45 | F | L | 6 | 9.4 | 65.6 | NM | 18.1 | 18.9 | 1.62 | 0.00* | - | | | |
| 3 | 62 | F | B | 19 | 56.9 | 67.5 | 31.3 | 35.0 | 3.8 | 0.97 | 1.14 | - | | | |
| 4 | 36 | F | L | 2 | 25.6 | 38.8 | 23.1 | 23.1 | 44.3* | 1.06 | 0.00* | D | Seconds | Recurrent | - |
| 5 | 37 | F | R | 8 | 60.0 | 31.9 | 29.4 | 24.4 | -13.8 | 1.93 | 1.06 | - | | | |
| 6 | 66 | F | L | 6 | 23.1 | 38.8 | 20.0 | 29.4 | 16.3 | 0.92 | 0.00* | - | | | |
| 7 | 49 | F | B | 9 | 65.0 | 49.4 | 44.4 | 34.4 | 8.8 | 0.00* | 1.86 | D | Seconds | Recurrent | Up-and-down |
| 8 | 44 | F | B | 34 | 105.0 | 103.8 | 67.5 | 66.3 | 17.0 | 1.30 | 1.05 | V | Minutes | Once | Up-and-down |
| 9 | 60 | M | L | 2 | 19.4 | 70.6 | 6.3 | 48.1 | -18.2 | 0.82 | 0.00* | D | Days | Once | - |
| 10 | 70 | M | B | 6 | 45.0 | 44.4 | 26.9 | 23.8 | 21.2 | 0.32 | 0.57 | - | | | |
| 11 | 61 | F | R | 15 | 96.3 | 48.8 | 52.5 | 42.5 | -3.1 | 0.53 | 0.64 | - | | | |
| 12 | 38 | F | B | 2 | 45.6 | 27.5 | 23.1 | 21.9 | -9.8 | 1.41 | 0.77 | - | | | |
| 13 | 51 | M | B | 18 | 68.1 | 44.4 | 28.1 | 20.6 | 10.1 | 1.05 | 1.50 | - | | | |
| 14 | 42 | F | B | 5 | 25.0 | 54.4 | 10.0 | 13.8 | -12.7 | 0.00* | 0.00* | D | Minutes | Recurrent | Positional |
| 15 | 79 | M | L | 5 | 35.6 | 65.6 | 31.3 | 46.9 | 4.2 | 0.63 | 0.67 | - | | | |
| 16 | 52 | M | B | 3 | 42.5 | 22.5 | 18.1 | 16.3 | 35.0* | 0.88 | 0.00* | D | Hours | Recurrent | - |
| 17 | 56 | M | R | 2 | 43.1 | 15.6 | 20.6 | 11.3 | 16.7 | 0.87 | 0.64 | - | | | |
| 18 | 39 | F | B | 5 | 51.9 | 45.6 | 37.5 | 26.3 | -3.4 | 0.70 | 0.00* | V | Minutes | Twice | Up-and-down |
| 19 | 60 | M | R | 1 | 46.3 | 30.0 | 40.0 | 26.9 | 0.0 | 0.73 | 0.89 | - | | | |
| 20 | 29 | F | B | 10 | 35.0 | 49.4 | 16.9 | 22.5 | 25.0* | 0.83 | 0.74 | - | | | |
| 21 | 62 | F | B | 5 | 80.6 | 53.1 | 36.3 | 26.9 | -6.7* | 0.00* | 0.00* | D [†] | Hours | Once | - |
| 22 | 52 | F | L | 4 | 22.5 | 46.9 | 16.3 | 29.4 | 0.0 | 0.85 | 0.90 | - | | | |
| 23 | 55 | F | L | 7 | 13.8 | 42.5 | 12.5 | 31.9 | -4.8 | 0.57 | 0.00* | V + D | Minutes | Recurrent | Up-and-down |
| 24 | 35 | M | B | 5 | 51.9 | 56.9 | 28.8 | 23.8 | 2.3 | 1.88 | 2.03 | - | | | |
| 25 | 78 | M | B | 15 | 92.5 | 76.3 | 43.1 | 37.5 | 6.7 | 0.60 | 0.68 | - | | | |

AC, air-conducted thresholds; B, bilateral; BC, bone-conducted thresholds; CP, canal paresis; D, dizziness; Duration, mean duration of disease; NM, not measured; V, vertigo.

*Abnormal results.

[†]Past history of benign paroxysmal positional vertigo (BPPV).

We consider that BC-VEMP reveals the origin of the balance problem in patients with otosclerosis. The purpose of this study was to elucidate the origin of balance problems in patients with otosclerosis using BC-VEMP.

Material and methods

Subjects comprised 25 consecutive patients (9 men and 16 women) who were diagnosed with non-operated otosclerosis and underwent cochleo-vestibular examinations at Hyogo College of Medicine between June 2009 and November 2011 (Table I). The diagnostic criteria for otosclerosis were based on progressive conductive or mixed-type hearing loss, changes in the

stapedial reflex, and presence of Carhart notch on audiogram. The mean age was 52.6 years (range, 29–79 years). Eleven patients had unilateral involvement and 14 had bilateral involvement. Subjects were divided into two groups according to the incidence of balance problems after onset of hearing disturbance due to otosclerosis: the disequilibrium group (D group), subjects complaining of balance problems; and the non-disequilibrium group (ND group), subjects without balance problems.

Cochleo-vestibular function was evaluated by pure-tone audiometry, caloric testing, and BC-VEMP testing. Detailed symptoms of balance problems, i.e. repetition, duration, and inducing factor of symptoms were obtained in interviews. Balance problems

were qualified as symptoms after incidence of otosclerosis. Results of cochleo-vestibular function testing and detailed symptoms were compared in the two groups.

Audiometry

Cochlear functions were evaluated with air-conducted thresholds and bone-conducted thresholds in each ear. Both thresholds were obtained from averaged hearing thresholds at the frequencies of 500, 1000, 2000, and 3000 Hz.

Caloric testing

Mono-thermal caloric testing was performed by stimulation with air at 15°C for 50 s, and evoked nystagmus was recorded using an FNG1004 electro nystagmograph (First Co., Tokyo, Japan). The stimulating condition was based on the recommendation by the Japan Society for Equilibrium Research [9]. Abnormal results were defined when canal paresis (CP) was >25% or maximum slow-phase velocity was <10°/s in both ears.

BC-VEMP testing

Detailed measurement of BC-VEMP testing was performed according to our previous report [8]. To summarize, bone-conducted stimuli were delivered with a BR41 bone vibrator (Rion Co., Tokyo, Japan) placed on the ipsilateral mastoid process of the stimulated ear. Tone burst sound stimuli of 60 dB nHL (127 dB force level) and 250 Hz (duration, 8 ms; rise/fall time, 1 ms) were delivered. The myogenic responses were amplified by bandpass (50 Hz to 3 kHz) filtered with the Neuropack μ (Nihon Kohden Co., Tokyo, Japan), and imported to a personal computer via analog-digital converter. After normalization with the root mean square value of background electromyogram during 20 ms before stimuli, the responses to 100 stimuli were averaged. The subjects remained in a supine position and were instructed to turn their head to the opposite side for constant and strong contraction of the sternocleidomastoid muscle during recording.

Results of BC-VEMP were evaluated by the existence of p13-n23 biphasic wave. When the biphasic wave was not detected, we considered the result to be abnormal.

Statistical analysis

Mann-Whitney U test was used for the analysis of numerical value categorized by the interval scale between two groups. Fisher's exact probability test

was used for analysis of the relationship between the details of symptoms and the results of BC-VEMP by 2×2 tables.

Results

The D group was composed of 10 patients and the ND group was composed of 15 subjects. There were no significant differences between the D group and ND group as regards mean age, sex ratio, mean duration of disease, and unilateral or bilateral involvement (Table II).

The mean air-conducted thresholds in affected ears in the D group and ND group were 56.3 ± 23.3 and 55.6 ± 17.3 dB, respectively (mean \pm SD). There were no significant differences between the two groups. Mean bone-conducted thresholds in affected ears of the D group and ND group were 32.6 ± 16.5 and 29.5 ± 9.5 dB, respectively. No significant difference was observed between the two groups. Therefore cochlear function did not relate to the existence of balance symptoms in patients with otosclerosis.

For caloric testing, 3 of 10 (30%) patients showed abnormal results in D group, and 1 of 15 (7%) patients in the ND group. No significant difference was found between these groups.

In BC-VEMP testing, 9 of 10 (90%) patients in the D group and 2 of 15 (13%) patients in the ND group showed abnormal results. A significant difference was found between the groups ($p < 0.001$). Abnormal results were found on the lesion side in all patients with abnormal results on BC-VEMP. In six of nine patients in the D group, caloric testing did not show abnormal results but BC-VEMP did (Table III). Therefore, balance problems in otosclerosis were related to abnormal results of BC-VEMP.

Two patients complained of vertigo, seven complained of dizziness, and one patient had both vertigo and dizziness in the D group. Balance problems were reported in six patients. The symptoms lasted for seconds in three patients, minutes in three patients, hours in three patients and days in one patient. The symptoms were evoked in six patients. Two patients

Table II. Details of disequilibrium (D) group and non-disequilibrium (ND) group.

| Characteristic | D group ($n = 10$) | ND group ($n = 15$) | p value |
|-----------------------------|-------------------------|--------------------------|-----------|
| Age (years) | 48.9 ± 9.0 | 54.3 ± 15.5 | 0.319 |
| Male:female | 2:8 | 7:8 | 0.176 |
| Duration of disease (years) | 8.9 ± 9.7 | 7.8 ± 5.9 | 0.329 |
| Unilateral:bilateral | 3:7 | 8:7 | 0.231 |

Table III. Comparison of results of auditory and vestibular examination between disequilibrium (D) group and non-disequilibrium (ND) group.

| Examination | D group | ND group | <i>p</i> value |
|-----------------|-------------|-------------|----------------|
| Audiometry | | | |
| AC (dB) | 56.3 ± 23.3 | 55.6 ± 17.3 | 0.25 |
| BC (dB) | 32.6 ± 16.5 | 29.5 ± 9.5 | 0.482 |
| Caloric testing | | | |
| Normal | 7 | 14 | |
| Abnormal | 3 | 1 | 0.119 |
| BC-VEMP | | | |
| Normal | 1 | 13 | |
| Abnormal | 9 | 2 | < 0.001 |

AC, mean air-conducted thresholds in affected ears; BC, mean bone-conducted thresholds in affected ears.

complained of positional dizziness and four patients of disequilibrium during up-and-down movement. The relationship between detailed balance symptoms and results of BC-VEMP in the D group are shown in Table IV.

Discussion

Results of BC-VEMP for patients with otosclerosis were previously reported in two papers. Singbartl et al. [10] reported 3 patients complaining of dizziness out of 23 patients with otosclerosis, and all 3 patients showed normal BC-VEMP. On the other hand, Yang and Young [11] reported 5 patients complaining of vertigo out of 15 patients with otosclerosis, and 2 of 5 (40%) patients indicated absence of BC-VEMP. The details of balance problems were not described in either of the latter studies. In the present study, detailed balance symptoms were obtained by interview, and were compared to results of BC-VEMP. We showed that 10 of 25 patients complained of balance problems and 9 of them (90%) showed abnormal BC-VEMP, thus balance problems were related to the results of BC-VEMP.

What pathophysiological mechanisms can cause saccular dysfunction in patients with otosclerosis? We propose two mechanisms. The first is endolymphatic hydrops. Many reports have described the relationship between endolymphatic hydrops and otosclerosis. Paparella and Chasin [12] reported otosclerosis patients with typical signs and symptoms of Meniere’s disease. Shea et al. [13] revealed endolymphatic hydrops in five patients with otosclerosis using electrocochleography. Human temporal bone studies revealed the coexistence of endolymphatic hydrops in patients with otosclerotic focus [14–16]. The otosclerotic focus extending over the endolymphatic duct or sac and malabsorption of fluid

may cause endolymphatic hydrops [15]. In our series, no patients complained of typical symptoms of Meniere’s disease, i.e. fluctuating hearing loss, tinnitus, and recurrent vertigo. Seo et al. [17] reported that patients with cochleosaccular hydrops revealed by VEMP did not complain of any recurrent vertigo but of recurrent short-lasting disequilibrium. Three patients in our series suffered from recurrent disequilibrium lasting for a short duration (cases 1, 4, and 7). The symptoms may have originated from saccular hydrops.

The other possibility is direct invasion of the otosclerotic focus to the saccular macula or saccular afferent. Igarashi et al. [18] reported that otosclerotic invasion had grown close to the utricular and lateral ampullary nerves by temporal bone study. The distance from the central areas of the stapedial footplate to the saccule (1.7–2.1 mm) was shorter than that to the utricle (1.9–2.4 mm). Furthermore, the distances in the patients with otosclerosis were shorter than those in normal subjects [19], indicating that the otosclerotic lesion may directly invade the saccule. What kind of disequilibrium occurs with isolated saccular dysfunction? Seo et al. studied the symptoms of patients with normal vestibular function except for VEMP. They concluded that dizziness with a sensation of falling lasting for a few seconds was related to abnormal VEMP results [20]. The symptoms are interestingly similar to the above-mentioned symptoms of saccular hydrops. Also, disequilibrium

Table IV. Relationship between detailed symptoms and results of BC-VEMP.

| Symptoms | Results of BC-VEMP | |
|-----------------------|--------------------|----------|
| | Normal | Abnormal |
| Vertigo or dizziness | | |
| Vertigo | 1 | 1 |
| Dizziness | 0 | 7 |
| Vertigo and dizziness | 0 | 1 |
| Repetition | | |
| Yes | 0 | 7 |
| No | 1 | 2 |
| Duration | | |
| Seconds | 0 | 3 |
| Minutes | 1 | 3 |
| Hours | 0 | 2 |
| Days | 0 | 1 |
| Trigger | | |
| Positional | 0 | 2 |
| Up-and-down | 1 | 3 |
| None | 0 | 4 |

was evoked on an elevator in one of their patients [20]. The up-and-down movement may stimulate the sacculus because the polarization vectors of the saccular macula are placed on the sagittal plane [21]. Thus, the dizziness evoked by up-and-down head movement may be caused by saccular dysfunction. In the present study, four patients suffering from vertigo or dizziness evoked by up-and-down head movement (cases 7, 8, 18, and 23) might have had saccular dysfunction.

We speculated that the balance problem associated with otosclerosis is caused by saccular dysfunction due to otosclerotic involvement. Therefore, hearing loss may result from cochlear invasion in patients with balance problems. However, there was no significant difference between the D group and ND group in air-conducted and bone-conducted thresholds of hearing in our study. Singbartl et al. [10] also found no correlation between the extent of hearing loss and VEMP induction. Elonka and Applebaum [22] suggested that cochlear endosteal involvement alone may not explain the hearing loss associated with otosclerosis in a temporal bone study. Therefore, we considered that the balance problem in patients with otosclerosis is not related to the extent of hearing loss.

Although the origin of balance problems in patients with otosclerosis is not caused by a single factor, 9 of 10 patients in the D group showed abnormal results on BC-VEMP testing. Six of them did not show abnormal results except for BC-VEMP. Therefore, in our patients, balance problems in otosclerosis were associated with abnormal results for BC-VEMP. In other words, saccular dysfunction is a major cause of balance problems in patients with otosclerosis. We conclude that BC-VEMP testing is useful for detection of the origin of balance problems in patients with otosclerosis.

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