Saccular Function in Otosclerosis Patients: Bone Conducted-Vestibular Evoked Myogenic Potential Analysis

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Received: 15 Nov. 2012; Accepted: 29 Apr. 2013

Abstract- Vestibular involvements have long been observed in otosclerotic patients. Among vestibular structures saccule has the closest anatomical proximity to the sclerotic foci, so it is the most prone vestibular structure to be affected during the otosclerosis process. The aim of this study was to investigate the saccular function in patients suffering from otosclerosis, by means of Vestibular Evoked Myogenic Potential (VEMP). The material consisted of 30 otosclerosis patients and 20 control subjects. All participants underwent audiometric and VEMP testing. Analysis of tests results revealed that the mean values of Air-Conducted Pure Tone Average (AC-PTA) and Bone-Conducted Pure Tone Average (BC-PTA) in patients were 45.28 ± 15.57 and 19.68 ± 10.91, respectively and calculated 4 frequencies Air Bone Gap (ABG) was 25.64 ± 9.95. The VEMP response was absent in 14 (28.57%) otosclerotic ears. A statistically significant increase in latency of the p13 was found in the affected ears (P=0.004), differences in n23 latency did not reach a statistically significant level (P=0.112). Disparities in amplitude of p13-n23 in between two study groups was statistically meaningful (P=0.009), indicating that the patients with otosclerosis had lower amplitudes. This study tends to suggest that due to the direct biotoxic effect of the materials released from the otosclerosis foci on saccular receptors, there might be a possibility of vestibular dysfunction in otosclerotic patients.

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Key words: Otosclerosis; Saccule; Bone Conducted-Vestibular; Myogenic

Introduction

Otosclerosis is an osseous dysplasia, limited to the human otic capsule. It is characterized by enzyme-mediated bone resorption and bone redeposition (1,2). The common site of the otosclerotic foci is the area just in front of the oval window, around the stapes footplate. However, bony invasion could also occur in other areas of the labyrinthine capsule, leading to sensorineural hearing loss and vestibular symptoms (1,3).

Clinically, otosclerosis affects both ears. Conductive hearing loss, particularly in low frequencies which may sometimes occur with sensorineural hearing loss is the most frequent functional deficit and may appear gradually. Other symptoms include tinnitus, vertigo, dizziness and loss of balance (2). The possibility of these conditions to occur depends on the location, size and histological features of the pathologically involved area (2).

Symptoms pertaining to vestibular disturbances have long been observed in otosclerotic patients; Approximately 3-35% of otosclerosis patients has been reported to have vestibular involvement (3,4). It seems that vestibular symptoms in patients with otosclerosis can be due to a variety of etiologies and though opinions vary among clinicians. Several histopathologic studies have shown otosclerotic involvement of the vestibular apparatus to be a cause of vestibular symptoms owing to invasion and degeneration of the vestibular nerve and reduction of Scarpa’s ganglion cell counts (5,6). Other reports postulate that disequilibrium might be caused by changes in the biochemical composition of the endolymph due to the release of toxic proteolytic enzymes into the inner ear by the active areas of
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Among vestibular structures, the saccule has the closest anatomical proximity to the sclerotic foci, on this ground the saccule is the most prone vestibular structure to be affected during otosclerosis process. There are poor research focus on the vestibular assessment in subjects with otosclerosis, in so doing, the present study was intended to carry out vestibular evoked myogenic potential (VEMP) in these patients.

VEMP has been described to be electromyographic (EMG) responses of sternocleidomastoid muscle (SCM) upon high-level stimulation of the saccule (7,8). That the VEMP is useful in early diagnosis of vestibular involvement during otosclerosis has been examined in just few studies and thus so far the plethora of research studies has only attested to the impact of otosclerosis on the waveform morphology, including presence or absence of waves (8-11). As the combination of various VEMP indices may seem to be a reasonable approach to improve the test’s overall efficiency, this is the first study in which latency and amplitude of VEMP were analyzed in otosclerotic patients, in order to more precise evaluation of the saccular pathway.

Since the stimulation threshold of the saccule is so high, the probability of detecting a VEMP via air-conducted stimuli is dependent on the integrity of sound transmission through the middle ear conductive mechanism to the inner ear. So, AC-VEMP might be absent in presence of even mild conductive component of hearing loss (12), thus, we have come to prefer applying bone-conducted VEMP (BC-VEMP) in our survey. This rout of stimulation by-passes the middle ear conductive apparatus and results in a direct stimulation of vestibular end organ.

Materials and Methods

Subjects

This study was carried out in the audiology clinic in Imam Khomeyni Hospital, Tehran University of Medical Sciences, between January 2011 and August 2012. A total number of 30 otosclerotic patients (16 females/ 14 males) and 20 healthy volunteers (12 females/ 8 males) were studied after obtaining informed consent and local ethics committee approval.

Patients all had a definitive diagnosis of otosclerosis through the contour of the medical history; audiogram; CT findings; family history; and exclusion of other possible causes of hearing loss. In patients group, 19 (63.33%) were bilaterally and 11 (36.67%) were unilaterally affected, overlay, 49 ears (23 right, 26 left) and in controls group 40 ears (20 right, 20 left) were included.

Study protocol

After an otoscopic examination, participants underwent audiometric testing using a Madsen Orbiter 922 diagnostic audiometer (Madsen Electronics, Denmark) at frequencies of 0.25, 0.5, 1.0, 2.0, 3.0, 4.0, and 8.0 kHz for air conduction (AC) and between 0.25 and 4.0 kHz for bone conduction (BC). Calculation of 4-frequency Pure Tone Averages (PTA) for both AC and BC were done at frequencies of 0.5, 1.0, 2.0 and 3.0 kHz and an air-bone gap (ABG) was obtained at these 4 frequencies.

All candidates underwent VEMP testing using a clinical device of EPIC-Plus (LABAT, Italy). The BC stimuli used to evoke the VEMP were delivered to the participants ear using clinical bone vibrator (B71, Radioger Corporation) placed on the mastoid process. The external auditory canals were plugged to minimize osseotympanic bone conduction. During the recording participants were in a sitting position with the head rotated away from the stimulated side in order to activate the ipsilateral SCM muscle. Muscle activation was monitored via a feedback method. The active electrode was placed over the middle portion of the ipsilateral SCM muscle body. The reference and ground electrodes were placed over the upper sternum and midline forehead, respectively. Tone bursts of 500 Hz with 8 ms duration were presented at a rate of 4.7/sec. The stimuli intensity was 70 dBnHL. The analysis window was 100 ms. Myogenic potentials were averaged and bandpass filtered (10-2000 Hz) over a series of 150 stimuli. The responses were recorded twice in both sides to confirm replication.

The measured parameters were the peak latency (in ms) of the two early waves p13 and n23, the peak to peak amplitude of the p13–n23 waves (in µv), and to determine the relation of the amplitudes of both sides in one patient, an asymmetry ratio (AR) was calculated using the following formula: AR=(AI-As)/(AI+As), where Al and As are the larger and smaller amplitudes, respectively, obtained from stimulating each ear.

Statistical analysis

SPSS software, version 11.5 (Chicago, IL, USA), was used for statistical evaluation. Differences in mean values of parameters between patient and control group was analyzed by student t-test. Furthermore, correlations between different parameters were assessed using
Pearson’s correlation test. In all statistical procedures, an instance with a $P$-value less than 0.05 was considered to be statistically significant.

**Result**

In the sample of the consecutively admitted 30 patients with otosclerosis, the mean age was 34.37 ± 12.50 years (range, 12–46 years) and for the control subjects it was 31.30 ± 6.53 years (range, 17–41 years). There was no statistically significant difference between these two groups according to sex and age ($P>0.05$).

The median duration of the disease in patients was 9 years (range, 2-15 years). 8 (26.66%) patients had a positive history of some forms of disequilibrium and 17 (56.66%) complained of tinnitus.

<table>
<thead>
<tr>
<th></th>
<th>Control subjects</th>
<th>Patients subjects</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>p13 latency</td>
<td>13.68 ± 1.1</td>
<td>15.31 ± 2.98</td>
<td>0.004</td>
</tr>
<tr>
<td>n23 latency</td>
<td>21.95 ± 2.70</td>
<td>22.82 ± 3.40</td>
<td>0.084</td>
</tr>
<tr>
<td>p13-n23 amplitude</td>
<td>2.80 ± 1.03</td>
<td>2.10 ± 1.15</td>
<td>0.012</td>
</tr>
<tr>
<td>AR</td>
<td>0.13 ± 0.11</td>
<td>0.26 ± 0.20</td>
<td>0.005</td>
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</table>

A statistically significant increase in latency of the p13 was found in the affected ears ($P=0.004$). Of the 49 otosclerotic ears, 11 (22.44%) had this finding (greater than 2.5 times the standard deviation of the mean value in normal control subjects). At the same time, differences in n23 latency did not reach a statistically significant level ($P=0.112$).

Disparities in amplitude of p13-n23 in between two study groups was statistically meaningful ($P=0.009$), indicating that the patients with otosclerosis had lower amplitudes, a findings that was noted in 8 (16.32%) otosclerotic ears. Since the calculation of AR needs the records of VEMP on both sides, this parameter was assessed just in 19 patients in which VEMP were bilaterally present. As the normal value of AR is defined as $\leq 0.34$, 6 (20%) patients had an abnormal AR.

Figure 1, shows the percentage of VEMP abnormalities in the patients group.

As far as concerns the correlation between PTA test results and VEMP, there was a statistically significant correlation between VEMP elicitation and AC and BC-PTA ($P=0.003$ and 0.000, respectively), however the correlation with ABG was not statistically meaningful ($P=0.112$).

**Discussion**

Studies concerned with vestibular involvement in otosclerosis are less numerous than those with auditory involvement. Variety of vestibular symptoms including unsteadiness, dizziness and vertigo and also vestibular tests abnormalities have been reported in these patients (13-18).

Ghorayeb and Linthicum, reported 27 otosclerotic patients with vertigo that the vertiginous symptoms improved after stapedectomies in 23 individuals (16). Fisch carried out electronystagmography investigation in otosclerosis patients and found up to 28% subjects having spontaneous or positional nystagmus (17). Morales-Garcia also pointed great percentage of caloric abnormalities in otosclerotic ears and reported that vestibular involvement might occur without the cochlea necessarily becoming involved (18).

Concordance with previous studies in the field of VEMP in otosclerosis patients, decreased VEMP response occurrence was noted in the present survey and suggesting of saccular involvement in the process of otosclerosis. The absent response was noted in 11 (36.66%) of our patients and overall in 28.57% of affected ears. Accordingly, Trivelli et al., reported 61.9% absent response in BC-VEMP in otosclerosis ear.
of their patients before stapedectomy surgery (11), this absent response was noted in 24% of otosclerosis ears in a study of Yang and Young (10).

We noted that, the correlation between duration of disease and the generation of the VEMP was positive, this trend implied that the possibility of vestibular degeneration, as measured with VEMP, was greater in a later stage of disease; Accordingly, Cody, Baker, Ghorayeb and Linthicum reported that, as the amount of sensorineural hearing loss was increased, depression of vestibular functions was enhanced, too (15,16).

Our results here also showed a delay of p13 latency in some of the patients. It was originally proposed by Richter and Schuknecht (5), that vestibular nerve fibers are vulnerable to injury where otosclerotic lesions were large enough to involve the cribrose areas, and this could be an underlying cause of the neural dysfunction in otosclerosis patients. Sando et al., found vestibular nerve atrophy in four temporal bones from patients with otosclerosis (19). Additionally, Scarpa’s ganglion cell counts also have shown reduction in these patients (8). Seemingly, abnormal increase in VEMP latency is at least partially due to these morphological changes occurring in the vestibular pathways mediating vestibulo-collic reflex and corresponding changes in the neural function.

Moreover, statistically significantly, there are more numerous cases of reduced peak to peak amplitude and abnormal AR in otosclerosis patients than in normal control subjects; The exact mechanism underlying these results are not fully understood, however, the direct biotoxic effect on saccular receptors, released from the otosclerosis foci may be responsible for such findings; As Johnsson et al., reported loss of vestibular hair cells as well as loss of dark cells in several years with severe otosclerosis (20).

Taken together, from the results of the present study along with previous investigations, it can be concluded that the possibility of vestibular dysfunction, specially the saccular pathway, is high in individuals suffering from otosclerosis and abnormally recorded parameters in VEMP correlates with the progression of disease; Additionally, VEMP, a non-invasive and simple procedure is useful in vestibular assessment of otosclerosis patients.

We recommend that a larger study using other vestibular tests such as video nystagmography (VNG) and computerized dynamic posturography (CDP) be carried out for a complete evaluation of the vestibular system in patients with otosclerosis.

References


