Application of vestibular evoked myogenic potentials in otosclerosis patients with vertigo

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Abstract

Otosclerosis is a progressive disease with a remodeling process causing ossicular malformation and conductive hearing loss. Otosclerosis patients with vertigo can present with abnormalities of ocular and/or cervical vestibular evoked myogenic potentials (VEMPs) due to pathological damage of the utricle, saccule, semicircular canals and cochlea. These abnormalities are more common than those after caloric testing and bone-conducted hearing thresholds and their relative frequency reflects the degree of the aforementioned damage. Air- and bone-conducted pure-tone average VEMPs can be elicited in ears with otosclerosis. The evaluation of air-conducted VEMP thresholds can be added to the diagnostic work-up of otosclerosis in case of doubt thus improving the differential diagnosis in patients with air-bone gaps. As saccule has the closest anatomical proximity to the sclerotic foci, it is the most prone vestibular structure to otosclerotic damage. A study of saccular function suggests that a vestibular dysfunction is due to the direct biotoxic effect of the materials released from the otosclerosis foci on saccular receptors. Another investigation using bone-conducted VEMPs elucidates the origin of balance troubles in otosclerosis patients. Nine of ten patients complaining of dizziness and/or vertigo show abnormal results on this testing. Recent research convincingly demonstrates a considerable diagnostic effectiveness and reliability of VEMPs in otosclerosis. This study aimed at revising the scientific literature addressing the main techniques used to generate vestibular-evoked myogenic potentials and their clinical applications in otosclerosis patients with vertigo.

Keywords: otosclerosis, vertigo, vestibular evoked myogenic potentials (VEMPs)

Introduction

Otosclerosis is an osseous dysplasia, limited to the human otic capsule. It is characterized by enzyme-mediated bone resorption and bone redeposition and from a histologic point of view, the disorder is characterized by alternating phases of bone resorption and formation involving osteoblasts and osteoclasts in the temporal bone with a primary localization of otosclerotic foci around the otic capsule, between the cochlea and the vestibule just anterior to the stapes footplate (Derks 2001, Manzari 2009, Singbartle 2006). However, bony invasion could also occur in other areas of the labyrinthine capsule, leading to sensorineural hearing loss and vestibular symptoms (Derks 2001, Igarashi 1982).

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 (Manzari 2009). It is known that approximately 20–37% of patients have accompanying dizziness or vertigo (Gros 2003, Hayashi 2006), but the pathogenesis of balance problems remains unclear.

The possibility of these conditions to occur depends on the location, size and histological features of the pathologically involved area (Manzari 2009).

Symptoms pertaining to vestibular disturbances have long been observed in otoscle-

rotic patients; Approximately 3-35% of otosclerosis patients has been reported to have vestibular involvement (Igarashi 1982, Panda 2001).

Vestibular-evoked myogenic potential (VEMP) is an electrophysiological method used to assess integration of the otolith organs and vestibular nerves with the brainstem and the muscular system. Therefore, it is a complementary examination that presents the differential of evaluating the central vestibular function, and it is related to a disynaptic reflex that has been considered to investigate brainstem function (Kantner 2012, Silva 2016). The VEMP is generated from the muscle reflex responses resulted of the vestibulo-ocular, the vestibulomasseteric and the vestibulospinal reflexes. These reflexes depend on the functional integrity of the utricular and saccular maculae, the inferior and superior vestibular nerves, the vestibular nuclei, the central vestibular pathways, and the neuromuscular plaques (2, Panda 2001). Changes in the VEMP are observed if any of the listed structures present injury. The VEMP has been utilized to study a variety of vestibular diseases.

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 (Salvinelli 2007, Singbartle 2006, Tribukait 1998, Trivelli 2010).

In a previous study investigating VEMPs in otosclerotic patients authors used air-conducted stimuli to elicit a VEMP response but there was an otosclerotic middle ear conduction block. (Park 2010)

The VEMP can be generated through auditory or galvanic stimulation and evoked responses can be obtained from several muscles such as extraocular, cervical, masseter, intercostal, brachialis, soleus, or gastrocnemius. The basic principle is the action of the muscular response in the postural control, either through vestibulo-ocular, vestibulocollic, or vestibulospinal reflex (Cunha 2014, Saka 2012). With this approach, VEMP application varies according to the type of stimulation and the electromyographic muscular response (Chang 2017, Kantner 2012). In its several modalities, this test presents characteristics favorable to its use in clinical practice: objectivity, non-invasiveness, easy execution, low cost, rapidity, and minimal discomfort for the patient. As any other electrophysiological examination, the examiner's experience is a determining factor for the test reliability (Kantner 2012).

This study aimed at revising the scientific literature addressing the main techniques used to generate vestibular-evoked myogenic potentials (VEMP) and their clinical applications in otosclerosis patients with vertigo.

Material e Methods

A systematic review of the literature was conducted. A search was conducted in the PubMed, Web of Science, MEDLINE and Scopus electronic databases for articles published between January 2012 and December 2019

Results

Tsung-Lin Yang and Yi-Ho Young (Yang 2007) tested fifteen patients with otosclerosis (21 ears) without operation and 10 healthy subjects (20 ears) underwent VEMP test using air-conducted (AC) and bone-conducted (BC) tone-burst stimulation (Yang 2007). The clinical information in the patients with otosclerosis and vertigo is presented in Table 1.

Table 1. Clinical information in the patients with otosclerosis and vertigo

Sex	Age (years)	Side	AC-VEMP	BC-VEMP
Female	52	Right	+	+
Male	54	Left	-	+
Female	57	Left	-	+
Female	22	Left	-	-
Female	45	Bilateral	-	-

The purpose of their study was to investigate whether vestibular-evoked myogenic potential (VEMP) correlates with the progression of otosclerosis. By using tone-burst stimulation, the response rates of present AC-VEMPs and present BC-VEMPs were 24% and 76% in 21 otosclerotic ears; 89% and 100% in 9 opposite unaffected ears, respectively. A significant difference existed in the response rate of otosclerotic ears between AC- and BC-VEMPs ($P < 0.01$, Fisher exact test). Comparing the AC/BC-VEMPs between otosclerotic and healthy ears in response rates, mean latencies of peaks p13 and n23, and p13 to n23 amplitude exhibited no significant difference. There were 5 ears with the presence of both AC- and BC-VEMPs, 11 ears showing absent AC-VEMPs but present BC-VEMPs, and 5 ears had absence of both AC- and BC-VEMPs. Comparing the occurrence of air-bone gap greater than 30 dB among the three groups, a significant difference was exhibited. Similarly, a significant relationship existed between types of conductive HL and the presences of AC- and BC-VEMPs. The VEMPs in otosclerotic ears can be elicited by AC and BC tone-burst stimulation with the response rates of 24% and 76%, respectively. The presence of an ACVEMP may indicate an earlier stage of the disease, whereas absent BC-VEMP infers a later stage. Restated, AC-VEMPs may complement the results obtained with BC-VEMPs to classify the stage of otosclerosis.

Saka et al. (Saka 2012) examined 25 patients who were diagnosed with non-operated otosclerosis. 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 (Saka 2012). In BC-VEMP testing, 9 of 10 (90%) patients in the disequilibrium group and 2 of 15 (13%) patients in the non-disequilibrium 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 disequilibrium group, caloric testing did not show abnormal results but BC-VEMP did. 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 disequilibrium 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 complained of positional dizziness and four patients of disequilibrium during up-and-down movement (Table 2).

Table 2. Summary of 10 otosclerosis patients with vertigo/dizziness

Sex	Age (years)	Side	BC-VEMP*		Vertigo/ Dizziness	Balance problems		
			Right	Left		Duration	Recurrence	Trigger
Female	56	bilateral	0.00	0.69	dizziness	seconds	recurrence	positional
Female	36	left	1.06	0.00	dizziness	seconds	recurrence	-
Female	49	bilateral	0.00	1.86	dizziness	seconds	recurrence	up-and-down
Female	44	bilateral	1.30	1.05	vertigo	minutes	once	up-and-down
Male	60	left	0.82	0.00	dizziness	days	once	-
Female	42	bilateral	0.00	0.00	dizziness	minutes	recurrence	positional
Male	52	bilateral	0.88	0.00	dizziness	hours	recurrence	-
Female	39	bilateral	0.70	0.00	vertigo	minutes	twice	up-and-down
Female	62	bilateral	0.00	0.00	vertigo + dizziness	hours	once	-
Female	55	left	0.57	0.00	vertigo + dizziness	minutes	recurrence	up-and-down

*0.00 – Abnormal results

In the study of Tramontani et al., (Tramontani 2014) 24 (32.4%) of 74 patients presented with symptoms of dizziness in the form of vertigo or disequilibrium (after carefully completing a medical questionnaire, only patients with symptoms compatible with labyrinthine origin were found in the dizziness group). The combination of the 2 tests (AC-VEMP and BC-VEMP) in a total of 109 ears shows that the response rates of present AC-VEMPs and present BC-VEMPs were 29.36% (32 ears) and 44.03% (48 ears) respectively. Chi-square revealed a strong correlation between these 2 investigations; when AC-VEMP was present, it tended to be the BC-VEMP; but when AC-VEMP was absent, so was the BC-VEMP (χ^2=29.365; p<0.001). No statistical relationship was found between AC/BC-VEMP presence and dizziness. (χ^2, p=0.06 for AC-VEMP, p=0.598 for BC-VEMP) (Table 3).

Table 3. Comparison of results of vestibular examination between dizziness group and non-dizziness group

VEMP	Dizziness group (42 ears)	Non-dizziness group (84 ears)	Chi-square (χ^2)	P value
BC - VEMP			0.258	0.598
Present	17/40.47%	38/45.23%		
Absent	25/59.52%	46/54.76%		
AC-VEMP			3.404	0.06
Present	7/16.70%	27/32.10%		
Absent	35/83.30%	57/67.90%		

Discussion

Results of BC-VEMP for patients with otosclerosis were previously reported in two papers. Singbartle et al. (Singbartle 2006) reported 3 patients complaining of dizziness out of 23 patients with otosclerosis, and all 3 patients showed normal BC-VEMP. In 11 patients (44%), VEMPs with regular (N1/P1) potentials with respect to latencies (mean P1, 15.0; N1, 23.1) and age-related amplitude/tonic SCM activity ratio were recorded preoperatively. The preoperative mean SNHL was 32.5 (T 11.8) dB). There was no statistically significant correlation between the preoperative SNHL (Fig. 1) or age and the occurrence of VEMPs. The postoperative mean SNHL amounted to be 28.6 T 10.7 dB (i.e., an increase of about 3.9 dB compared with the preoperative data). In three other cases (12%) of VEMPs reappeared after surgery, which were absent before. However, the mean SNHL was improved (by 3 dB) in only one of those cases. In total, 14 ears presented with regular VEMPs postoperatively with respect to latencies (mean P1, 15.8; N1, 24.3) and to the age-related amplitude/tonic activity ratio in comparison to normative data. On the other hand, Yang and Young (Yang 2007) 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. Saka et al. 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. (Saka 2012)

Seo et al. (Seo 2008) 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.

About one-third of patients with otosclerosis presented with vertiginous symptoms. A possible relationship of vertigo and otosclerosis is an understandable assumption,

because otosclerosis is a disease affecting structures proximal to the vestibule (Igarashi 1982), but until now, sufficient and concrete evidence supporting this has been lacking. Any vertiginous patient can have a normally functioning labyrinth with symptoms due to incomplete central compensation or migrainous vertigo.

The different methods related to the parameters used to perform VEMP and the presentation of the results limited the comparison among studies. On the other hand, the importance of using different VEMP recording methods to assess otolith function and vestibular pathway is the diversity of vestibular diseases that can be evaluated through VEMP. Therefore, in vestibular electrophysiology research, VEMP has emerged as an outstanding complementary examination to assess vestibular function. The use of VEMP, coupled with other vestibular tests, enables a more comprehensive evaluation and, consequently, a better knowledge about the structures contained in the labyrinth and their neural pathways.

Conclusions

Although the origin of balance problems in patients with otosclerosis is not caused by a single factor, 9 of 10 patients in the disequilibrium group showed abnormal results on BC-VEMP testing in the study of Saka et al. Six of them did not show abnormal results except for BC-VEMP. Therefore, in the 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. It can be concluded that BC-VEMP testing is useful for detection of the origin of balance problems in patients with otosclerosis. The few patients in the study of Singbartl et al. (Singbartle 2006) who complained of vertigo preoperatively had regular VEMPs so that a saccular impairment is highly unlikely. Even the patients with preoperative absent VEMPs in their study complained of no vertigo, which might be because of the slow progress and the accompanying central vestibular compensation. Authors concluded that using VEMPs indicates that the close neuroanatomic neighborhood of the saccule to the oval window niche and its otosclerotic foci can lead to a spread of the disorder to this vestibular receptor (56% in their study), but that the patients affected do not necessarily experience vertiginous complaints. VEMPs reappeared after stapedotomy in 12% of the cases reported in the study.

Vertiginous symptoms should not be attributed to otosclerosis itself, but to causes affecting the semicircular canals. Perhaps further investigations into otolithic disturbances (such as subjective visual vertical and horizontal) and a questionnaire more oriented to otolithic vertigo symptoms could reveal possible clinical impacts of utricular and saccular involvement in the disease.

A postoperative increase in the resting activity of the utricular signal was described in a study of Tribukait et al. (Tribukait 1998). The subjective visual vertical test for utricular testing was done in patients before and after stapedotomy with no clinically apparent vertigo.

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