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Original Article

DPOAEs: Cochlear OHC Functions in Patients with Definite Vestibular Migraine

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OBJECTIVE: Vestibular migraine is vertigo caused directly by migraine. Otoacoustic emission (OAE) is a low sound generated in the cochlea and measured in the outer ear canal. The purpose of this study was to determine whether vestibular migraine with normal pure tone audiometry has abnormal changes in cochlear (OHC) function measured by distortion product otoacoustic emissions (DPOAEs).

MATERIALS and METHODS: DPOAEs were measured from 34 definite vestibular migraine patients with normal peripheral hearing sensitivity (11 males and 23 females), and they were compared to the results of 30 normal subjects (12 males and 18 females).

RESULTS: The mean emission amplitudes across the DPOAE-measured frequencies in both ears of patients with definite vestibular migraine were lower than that of the normal subjects but statistically non-significant (p>0.05).

CONCLUSION: The emission amplitudes that were reduced could be attributed to the patho-physiologic mechanism encountered in the ears of those patients, in spite of being of non-statically significant values. Our results suggest that definite vestibular migraine patients with normal peripheral hearing sensitivity may have subclinical cochlear affection associated with this disease.

KEY WORDS: DPOAEs, distortion product otoacoustic emissions, vertigo, vestibular migraine, definite vestibular migraine, migraine

INTRODUCTION

Migraine is a common clinical syndrome characterized by episodic headache and is associated with numerous other neurologic symptoms. There is increasing recognition of a syndrome called vestibular migraine, which is vertigo caused directly by migraine [1]. Vestibular migraine, also known as migraine-associated vertigo, is a common cause of dizziness in adults [2]. Its mechanism remains unknown [3].

In migraine, headache frequently coexists with symptoms of vestibular dysfunction, which include dizziness/vertigo, motion sickness, and gait instability [4, 5]. They often show a higher prevalence of peripheral vestibular dysfunction than would be expected in patients with purely central vestibular abnormalities [6, 7]. In the symptom-free interval, vestibular testing adds little to the diagnosis, as findings are mostly minor and non-specific [1].

Clinically, vestibular migraine presents with attacks of spontaneous or positional vertigo lasting seconds to days. Migrainous accompaniments, such as headache, phonophobia, photophobia, or auras, are common but not mandatory. Cochlear symptoms may be associated but are mostly mild and non-progressive (Table 1). During acute attacks, one may find central spontaneous or positional nystagmus and, less commonly, unilateral vestibular hypofunction [8].

Otoacoustic emission (OAE) is a low sound generated in the cochlea and can be measured in the outer ear canal. It provides information on cochlear status with special respect to outer hair cell (OHC) function. It has been classified into two types: spontaneous and evoked, which could be a transiently evoked distortion product and stimulus frequency OAEs. The test offers a fast, inexpensive, easy-to-perform, and noninvasive maneuver [9].

Distortion product otoacoustic emissions (DPOAEs) have frequently been used for clinical assessment of cochlear function in patients with hearing disorders, because their measurement can provide frequency-specific information on OHCS function in an objective and non-invasive manner [10]. Different sound pressure levels can be used for f1 and f2 to elicit it. The two levels are called L1 and L2, for f1 and f2, respectively. Stronger responses are elicited when L1 is at least 10 dB greater than L2 [11]. Also, it has been described that moderately intense stimulus tones for L1 and L2 give better information about OHC function [12], and 1.2 is the optimum ratio utilized for f2/f1 [13].

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Although many combination DPOAEs can be detected, the largest DPOAEs in human are measured at the frequency calculated by 2f1-f2 [14]. Currently, the site of origin for the 2f1-f2 DPOAEs is thought to be at or near the cochlear tonotopic site for the f2 primary [15].

The purpose of this study is to investigate whether vestibular migraine with normal hearing has abnormal changes in DPOAE response and to analyze and compare them with the results of normal subjects.

MATERIALS and METHODS

Participants

This prospective study was conducted in the outpatient ENT and audiology clinics in our hospital from May 2011 to February 2012 after approval of the hospital research committee. The patients, as well as the control group, gave their informed consent to participate in this study. Participants were subjected to a complete history, ENT, and medical and neurological examination to rule out any associated medical or other neurological disorders. They were subjected to tympanometry, pure tone audiometry, and DPOAE measurements.

The study group consisted of 34 patients (23 females and 11 males) diagnosed as definite vestibular migraine (age range 21–59 years). The patients fulfilled the diagnostic criteria of definite vestibular migraine (Table 1). Family history of migraine was reported in 8 patients. Patients who had exclusively mild head motion intolerance, hearing loss, and unspecific non-vestibular dizziness were excluded. DPOAEs were assessed when vestibular migraine was first diagnosed [16].

Table 1. Diagnostic criteria for vestibular migraine[8]

Definite migrainous vertigo		
A	Recurrent episodic vestibular symptoms of at least moderate severity*	
B	Current or previous history of migraine according to the criteria of the International Headache Society	
C	One of the following migrainous symptoms during at least two vertiginous attacks: migrainous headache, photophobia, phonophobia, visual or other auras	
D	Other causes ruled out by appropriate investigations	
Probable migrainous vertigo		
A	Recurrent episodic vestibular symptoms of at least moderate severity	
B	One of the following:	
	1	Current or previous history of migraine according to the criteria of the International Headache Society
	2	Migrainous symptoms during ≥ 2 attacks of vertigo
	3	Migraine precipitants before vertigo in more than 50% of attacks: food triggers, sleep irregularities, hormonal changes
	4	Response to migraine medications in more than 50% of attacks
C	Other causes ruled out by appropriate investigations	

*Vestibular symptoms are rotational vertigo or another illusory self or object motion. They may be spontaneous or positional or may be provoked or aggravated by head motion (head motion intolerance). Vestibular symptoms are moderate if they interfere with but do not prohibit daily activities and are severe if patients can not continue daily activities.

The control group consisted of 30 age- and sex-matched subjects (18 females and 12 males). Their age ranged from 20 to 60 years with no history of otologic or vestibular system affection, with normal otoscopy and normal hearing sensitivity in the standard audiometric test measurement by conventional pure tone audiometry.

Diagnostic Procedure

Apparatus

A Bio-logic® Scout Otoacoustic Emissions (OAE) System, Version 3.45.00 (Natus Medical, Inc., San Carlos, CA, USA), with a Scout SPORT module interfaced with a personal computer was used to gather DPOAEs. The probe uses two sound delivery tubes to deliver the two stimulus tones independently in the external ear canal and a microphone module to receive the resulting DPOAEs. DPOAEs were measured in a sound-treated room.

A pure tone audiometer (Interacoustic Clinical Audiometer AC 40, DK-5610, Assens, Denmark) was used for testing both air and bone conduction at frequency ranges for octaves from 250 to 8000 Hz for air conduction and from 500 to 4000 Hz for bone conduction to obtain results from both ears of each participant. A tympanometer (Interacoustic Impedance Audiometer AZ 26, DK-5610, Assens, Denmark) was used for testing the middle ear functional status for both the study and control group.

Procedure

For collection of the DPOAEs, participants sat upright comfortably and were given instructions to remain as quiet as possible for the duration of the test. After the instructions were given, an appropriately sized probe ear tip was placed on the probe assembly for each patient's test and positioned securely into the ear canal with a good seal.

Distortion product otoacoustic emissions at 2f1-f2 were measured with stimulus frequencies for f2 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz. An f2/f1 ratio of 1.22 was used with the primary tones to evoke DPOAEs. The unequal levels were used for the primaries; it was 65 dBSPL (L1) and 55 dBSPL (L2) for f1 and f2, respectively.

Distortion product otoacoustic emissions were collected and displayed in the form of a distortion product frequency profile (DPOAE audiogram). The test was begun after placement of the probe. DPOAEs were estimated as the amplitude in the frequency bin for the cubic distortion product 2f1-f2. The recording stopped automatically after it ran through the recording frequencies. At each of the f2 frequencies, averages were obtained from data that were lower than the artifact rejection criterion.

Emissions were regarded to be present when the signal exceeded the local noise level and had a minimum amplitude of -12 dBSPL. A sequential signal presentation and time domain averaging for DPOAE data collection were used. Frame rejection was ensured if L1 and L2 were out of tolerance by±5 dB and/or ambient noise levels exceeded 30 dBSPL.

Statistical Analysis

Descriptive statistics, including means, standard deviations, and t-test, were used for the control and study groups. Pure tone audiogram and DPdB amplitude in the dBSPL was compared for the control group and vestibular migraine. The criterion for statistical significance was set at p<0.05, and a statistically nonsignificant difference was when p>0.05.

RESULTS

In this study, the mean age did not differ between the patients with vestibular migraine and normal subjects. Females were more common than males for vestibular migraine patients; they constituted 67.6%.

The mean age for the control group was 39.4±9.9 years, while it was 38±10.2 years for the study group. There was no statistically significant difference between male and female age with vestibular migraine (t-test value =0.69, p>0.05). Figure 1 shows the age distribution for the vestibular migraine patients. In our study, the duration of the disease for vestibular migraine was 7.3±2.4 years.

The mean pure-tone audiogram for vestibular migraine patients and normal subjects at frequencies of 0.25, 0.5, 1, 2, 4, and 8 kHz as a function of hearing threshold level in dBHL is displayed in Figure 2. Although the threshold of hearing for vestibular migraine patients was lower than that of the control, it was statistically non-significant (t-test values=0.25, 0.15, 0.83, 0.12, 0.33, and 0.32 for 0.25, 0.5, 1, 2, 4, and 8 kHz, respectively, p>0.05).

Table 2 presents the mean amplitudes of DPOAEs as a function of f2 frequencies for the patient group. When amplitudes of DPOAEs obtained from males were compared to those of obtained from females, only at a frequency of 1 kHz was a statistically significant difference found. However, the interpretation of this finding is difficult, as DPOAE recordings at low frequencies below 1 kHz due to the noise floor are not clearly obvious, and the responses are difficult to be revealed.

Figures 3, 4, and 5 show that although there were no statistically significant differences between vestibular migraine patients and the normal subjects (t-test values at Table 4, p>0.05), it was noticed that there was a slight increase in DPOAE amplitude in the normal subjects versus that of the vestibular migraine patients.

In Table 3, the mean DPOAE/noise levels as a function of each f2 frequency, which is suggested to be the location of the generator of the

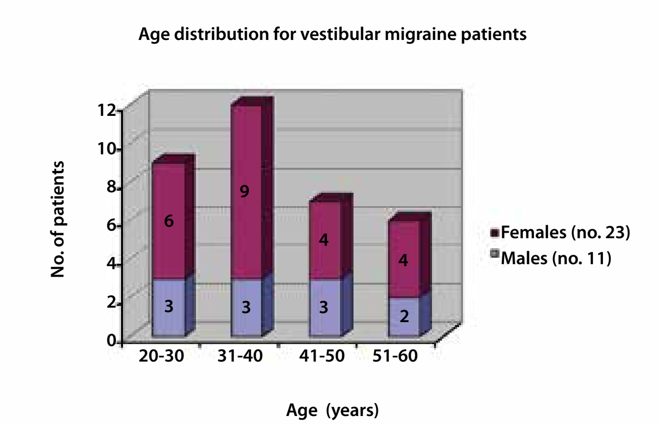

Figure 1. Age distribution for male and female vestibular migraine patients

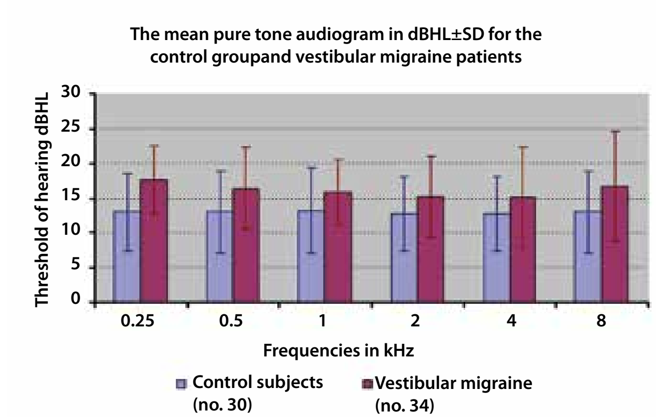

Figure 2. The mean pure tone audiogram in dBHL of the control group and vestibular migraine patients. Error bars represent 1 SD above and below the mean

Table 2. The mean DPdBSPL and NFdBSPL±SD for the females, males, right and left vestibular migraine patients

Gender	750	1000	1500	2000	3000	4000	6000	8000
Females								
DPdB	12.17±9.6	12.04±9.3	8.63±7.5	5.8±4.6	4.47±6.6	3.86±6	1.78±7.1	0.58±7.1
NFdB	2.82±9.5	2.71±10	-0.41±8.3	-4.26±4.5	-9.17±3.1	-11.97±2.8	-11.12±4.2	-10.73±3
Males								
DPdB	5.63±6.3	3.45±7.1	2.18±7.3	4.18±8	1.9±6.9	1.45±8.3	-3.09±8.4	-3.45±9.5
NFdB	-1.36±8.6	-3.27±7.3	-5.72±7.1	-7.72±3.3	-11.36±3.6	-12.63±3.3	-12.78±5.1	-10.58±11.3
Side								
Right								
DPdB	8.5±8.1	9.52±8	6.82±6.1	5.38±4.6	4.11±4.3	4.08±5.1	-0.05±7	0.58±5.3
NFdB	-0.44±8.4	-0.91±9.4	-2.5±7.5	-5.61±3.8	-9.79±3.4	-12.32±3.2	-13.23±3.8	-12.22±2.5
Left								
DPdB	11.61±9.9	9±10.9	6.26±9.6	5.17±7	3.17±8.6	2.08±8.2	0.47±8.7	-2.02±10.1
NFdB	3.38±10	2.47±9.7	-1.76±9.1	-5.14±5.1	-9.97±3.4	-12.7±2.9	-13.16±5.3	-10.94±9.3

cubic distortion product (2f1-f2), are shown for gender and side of the vestibular migraine in patients and normal subjects. The standard deviation was mentioned at each tested frequency for the DPOAE amplitude/noise level. It was noticed in this study that there were no significant statistical differences between genders or sides (right and left) in those patients (Table 4).

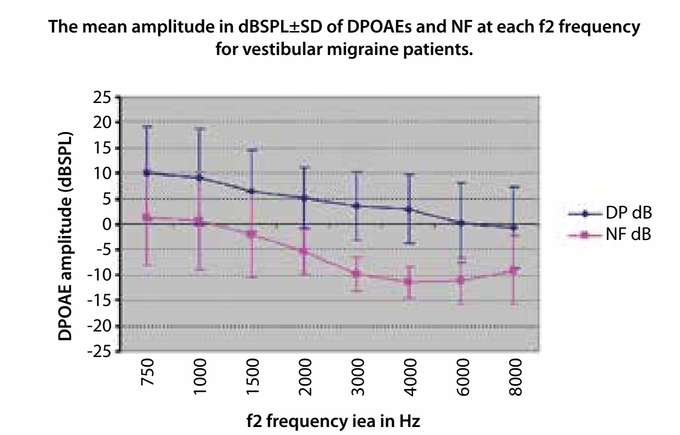

Figure 3. The mean amplitude in dBSPL of DPOAEs and noise floor at each f2 frequency for vestibular migraine patients. Error bars represent 1 SD above and below the mean

DISCUSSION

If patients with definite vestibular migraine have vestibular system dysfunction, subsequent to migraine vascular patho-physiology, we can assume that the same process can take place in the cochlear division of the audio-vestibular system and probably the OHC part. Furthermore, evidence that supports this hypothesis comes from the supposition that hair cell loss in the vestibular division can also take place in the auditory system, with special consideration to the cochlear OHCs.

In our study, the ratio between males and females was 1:2.1, with a higher incidence in women. The mean age of the patients was 38 years. The middle age between 31 to 40 years has a high risk of developing the disease. Family history was observed in 23.5% of the study group. In population-based studies, the prevalence of migraine was suggested to be 4% to 6% in men and 11.2% to 17.2% in women, with a prevalence of about 20% among women aged 30 to 49 years [17]. Studies showed that women were affected two to three times more than men [1].

Like migraine itself, vestibular migraine is diagnosed on the basis of clinical information, as there are no specific biological markers. A preliminary classification, using operational clinical criteria modeled on the International Classification of Headache Disorders (ICHD),

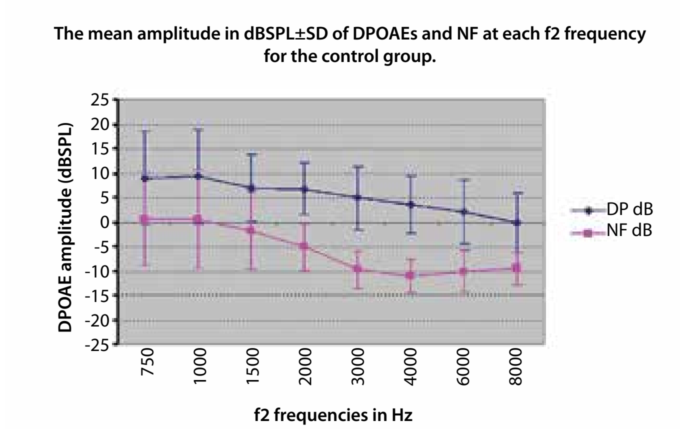

Figure 4. The mean amplitude in dBSPL for DPOAEs and noise floor at each f2 frequency for the control group. Error bars represent 1 SD above and below the mean

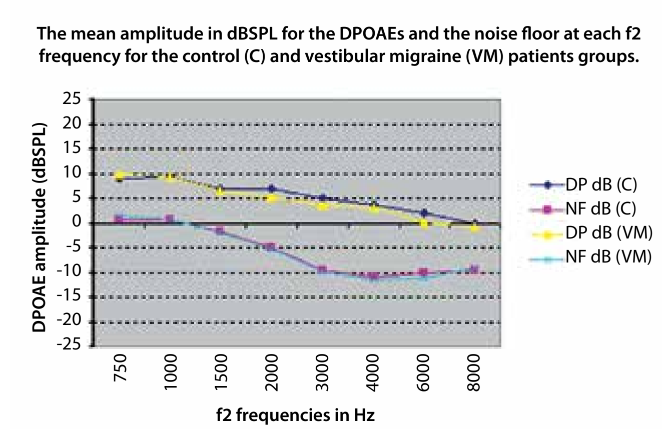

Figure 5. The mean amplitude in dBSPL for DPOAEs and noise floor at each f2 frequency for the control group. Error bars represent 1 SD above and below the mean

Table 3. The mean DPOAE/ noise levels±SD for the control, vestibular migraine (VM) patients and females, males, right and left side vestibular migraine patients

	750	1000	1500	2000	3000	4000	6000	8000
DPOAE/noise level								
Control	11.86±9.5	12.14±9.3	10.24±5.4	12.29±5.7	14.63±5.8	15.86±6.5	15.4±5.4	15.31±6.3
VM	9.55±5.5	8.97±5.2	8.94±4.6	10.29±5.5	13.82±6.5	15.86±6.6	14.42±6.7	16.11±6.7
Gender								
Females	10.34±6.1	10.08±6.5	9.08±4.2	9.97±4.7	14.13±6.1	15.89±5.9	15.1±6.5	16.81±6.9
Males	7.91±3.8	7.27±4.6	8.63±5.4	10.95±7.1	13.36±7.1	15.81±7.8	13±6.9	14.63±5.9
Side								
Right	9.64±5.4	10.82±6.9	9.26±4.5	10.44±4.6	14.26±5.5	16.41±6.2	13.14±6.3	17.67±5.6
Left	9.47±5.8	7.52±4.6	8.61±4.8	10.14±6.3	13.5±7.2	15.32±6.8	15.71±6.9	14.17±7.9

VM: vestibular migraine; DPOAEs: distortion product otoacoustic emissions

Table 4. T test of DPOAEs amplitude and DPOAE/ noise levels for control vs vestibular migraine (VM), females vs males and right vs left vestibular migraine patients

	750	1000	1500	2000	3000	4000	6000	8000
DPOAE amplitude								
Control vs VM	0.527	0.939	0.673	0.113	0.254	0.594	0.131	0.587
Females vs males	0.001	0.0001	0.001	0.387	0.156	0.235	0.024	0.087
Right vs left	0.163	0.821	0.776	0.887	0.572	0.236	0.784	0.189
DPOAE/ noise levels								
Conrol vs VM	0.102	0.021	0.147	0.047	0.453	0.999	0.360	0.491
Females vs males	0.897	0.025	0.570	0.829	0.627	0.497	0.115	0.041
Right vs left	0.897	0.025	0.570	0.829	0.627	0.497	0.115	0.041

VM: vestibular migraine; DPOAEs: distortion product otoacoustic emissions

proposed two separate diagnostic categories: definite vestibular migraine and the more sensitive but less specific probable vestibular migraine [4]. In this study, 34 patients fulfilled the criteria of definite migraine disease.

DPOAEs are an objective sensitive preneural measurement of cochlear OHC function that can monitor any dysfunction, even before significant cochlear hearing loss occurs. The reduction in the amplitude of DPOAEs in the study group relative to normal subjects, although it was non-significant, suggests the correlation of affection in both cochlear and vestibular OHCs. So, it is not possible to exclude this correlation, since the hypothesis of OHC dysfunction in vestibular migraine could be the same process that takes over in the cochlear hair cells.

In a study by Hamed et al. [18] they suggested that subclinical changes are associated with chronic migraine in cochlear function and auditory pathways. They attribute it to the possible compromise of blood supply of the auditory system that possibly accompanies migraine disease [18]. We postulate that the same patho-physiologic mechanism could be the incriminating etiology for lower DPOAE amplitudes. In our study, there were no significant statistical differences in gender or sides (right versus left) for the DPOAE results.

Previous studies investigating patients with vestibular migraine suggest that cerebral vasospasm and vasospasm of the vascular supply to the cochlea could be the incriminating cause for the lower DPOAEs than normal subjects [1, 17]. But, one limitation for the DPOAE results in vestibular migraine is the association of endolymphatic hydrops, mainly Meniere's disease, which should be considered; another limitation is the assumption of peripheral rather than central vestibular affection in vestibular migraine, which requires further studies. Hence, it would be advisable to use DPOAEs in the test battery for the evaluation of patients with vestibular migraine to reveal OHC function in those patients.

In conclusion, DPOAEs in patients with vestibular migraine differ, with lower amplitude than normal. The reduction in the absolute amplitude and DPOAE/noise level could be attributed to the patho-physiologic mechanism and causative relation that could exist between cochlear affection and vestibular migraine disease. Also, the vasospasm of the vascular supply that is associated with migraine, especially that of the cochlea, which is sensitive to minimal blood supply reduction, could be the incriminating cause. But, further studies are required to demonstrate if a causative relation exists between cochlear affection and vestibular migraine disease.

Ethics Committe Approval: Ethics committee approval was received for this study from the ethics committee of Mansoura University Hospital and KFMMC Hospital.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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