Cochlear and Brainstem Audiologic Findings in Normal Hearing Tinnitus Subjects in Comparison with Non-Tinnitus Control Group

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Abstract- While most tinnitus cases have some degree of hearing impairment, a small percent of the patients admitted to Ear, Nose and Throat Clinics or Hearing Evaluation Centers are those who complain of tinnitus despite having normal hearing thresholds. Present study was performed in order to better understanding of the probable causes of tinnitus and to investigate possible changes in the cochlear and auditory brainstem function in normal hearing patients with chronic tinnitus. Altogether, 63 ears (31 ears with tinnitus and 32 ears without tinnitus) were examined. The prevalence of transient evoked otoacoustic emissions and characteristics of the auditory brainstem response components including wave latencies and wave amplitudes was determined in the two groups and analyzed with appropriate statistical methods. There was no difference between the prevalence of transient evoked emissions in the two groups. The mean difference between absolute latencies of waves I, III and V was less than 0.1 ms between the two groups that were not statistically significant. Also, the interpeak latency values of I-III, III-V and I-V in both groups had no significant difference. Only the V/I amplitude ratio in the tinnitus group was significantly larger than the other group (p =0.04). The changes observed in amplitude of waves, especially in the later ones, can be considered as an Audiologic finding in normal hearing tinnitus subjects and its possible role in generation of tinnitus in these patients must be investigated.

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Introduction

Tinnitus is defined as the perception of sound without any external physical stimuli. In most cases, it is not audible for the examiner and called as "subjective tinnitus" (1). The "chronic" tinnitus is a term that usually used when the tinnitus lasts more than 3 months (2). This symptom can generally be seen in conditions that there is a possibility of hearing loss including noise exposure, presbycusis, ototoxic medications, middle ear infections, inner ear diseases, Etc. Therefore, About 90% of tinnitus patients show some degrees of hearing impairment (2,3). A small percent of patients admitted to Ear, Nose and Throat Clinics or Hearing Evaluation Centers are those who complain of tinnitus despite having normal hearing thresholds. It seems that the source of tinnitus generation is not limited to the peripheral auditory system. However, there are evidences of abnormalities of the central auditory system in tinnitus patients (4,5).

Transient evoked otoacoustic emissions (TEOAEs) are sounds of cochlear origin that are highly sensitive to cochlear pathology (6). Auditory Evoked Potentials (AEPs) including Auditory Brainstem Responses (ABRs) are one of techniques that used for the evaluation of synchronization of neural activity and identification of abnormal neural activity in the auditory brainstem pathways and centers. Many studies have used these techniques to investigate the origin of tinnitus and the role of peripheral and central auditory system in its generation. In these studies there are reports such as increased interpeak and absolute latency of waves,

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changes in wave amplitude and abnormalities in OAE responses (4, 7-9). However, there are few studies that have exclusively examined the tinnitus in normal hearing population (10-12). On the other hand, the researches using Functional Magnetic Resonance Imaging (fMRI) techniques in tinnitus patients have shown increased neural activity in response to acoustic stimuli in the auditory brainstem regions (13). In regard to this, and in order to better understanding the probable causes of tinnitus in normal hearing subjects, this study was conducted and analyzed the results of TEOAE and ABR tests and compared them between normal hearing tinnitus and non-tinnitus subjects.

Materials and Methods

In a cross-sectional, descriptive and analytic study, the subjects were chosen from patients admitted to the otorhinolaryngology clinic in Amiralmomenin hospital-Rasht, over a period of 11 months from April 2011 until March 2012. The case group consists of 19 subjects with unilateral and 6 subjects with bilateral tinnitus (total of 31 ears), including 9 men and 16 women whom aged 20 to 57 years (Mean, 34.4 years; SD, 12.2 years). The subjects in the control group were selected in such ways that have a close match in terms of age and gender and the status of the hearing. The inclusion criteria were existence of non- pulsating tinnitus for more than 3 months, age range of 18 to 59 years, hearing thresholds better than 25 dB hearing level (HL) in the frequency range 250 to 8000 Hz and normal (type A) tympanograms, no history of exposure to hazardous levels of noise, no history of ear surgery or ototoxic medications. A written consent was taken from all subjects, and this study was approved by the ethics committee of the Guilan University of Medical Sciences.

Pure tone hearing thresholds and middle ear function were evaluated using a calibrated Madsen Astera audiometer and Madsen Zodiac 901 tympanometer respectively. TEOAE recordings were conducted using the Madsen Capella OAE System. To perform the TEOAE recordings we presented 1000 click stimuli at 80 dB sound pressure level (SPL) in each ear. Response reproducibility of 70% (or more) and signal to noise ratio ≥6dB in at least three of the four frequencies tested (1500, 2000, 3000, and 4000 Hz) was considered as a criterion for the existence of TEOAE response. ABRs were recorded using the ICS CHARTR with a horizontal electrode montage. The stimuli were 2000 sweeps of alternating polarity clicks presented through the earphones at 90 dB SPL and a repetition rate of 11.1 clicks per second. During recording session, the subjects were in the supine position with eyes closed.

For statistical analysis, the commercial SPSS.17 software was used in 0.05 significance levels. Colmogrov-Smirnov test was used to define normal distribution of data and a χ^2 test was used to compare the two groups with respect to results of TEOAE tests. Significance of differences between the absolute peak latency values and interpeak latencies of waves in the two groups was assessed using Independent Samples t-Test. Characteristics of the amplitude of waves of the two groups were compared using Non-parametric Mann-Whitney test.

Results

This study was conducted on 25 normal hearing patients (9 men and 16 women) with chronic tinnitus. Fifteen patients (48%) had tinnitus in the right ear, 4 patients (13%) in the left ear, and 6 (39%) in both ears. A total of 31 ears were examined. The results were compared with findings of 32 ears of non-tinnitus normal subjects who were similar to those in the experimental group in respect of hearing thresholds, age and gender. In 69% of subjects in the experimental group and 66% of controls, TEOAE responses were observed. Comparison of responses in the two groups using χ^2 test showed that there was no significant difference in this respect (P>0.05). The Independent Samples t-Test was used to evaluate the significance of differences between the absolute and interpeak latency values between the two groups.

The mean difference of absolute latencies of waves I, III and V between the two groups were less than 0.056 ms that were not a statistically significant difference (P>0.05). Also, study and control groups had a difference of 0.037, 0.040, and 0.047 ms between the mean values of interpeak latencies of I-III, III-V and I-V respectively that was not statistically significant (P>0.05). The mean amplitude of waves I, III, V and the V / I and III / I amplitude ratios in the two groups are presented it table 1. Statistically larger V / I ratio was found in the test group using Mann-Whitney test (P=0.04). The case group had slightly smaller and larger mean amplitudes of wave me and V, respectively. However, there were no significant differences between these values and also the other response components including amplitude of wave III and III / I amplitude ratio (P>0.35).

Table 1. The mean amplitude of waves and mean wave ratios in the two groups

Groups	Wave I amp.	Wave III amp.	Wave V amp.	III/I amp. ratio	V/I amp, ratio
Tinnitus patients	0.28	0.35	0.58	1.75	3.44
Normal subjects	0.32	0.36	0.50	1.54	2.10
P value	0.80	0.35	0.47	0.91	0.04

amp. = amplitude (μV)

Discussion

There are several hypotheses about the pathophysiology of tinnitus which generally can be divided into three categories: aberrant activity in the peripheral auditory system, a central nervous system origin; and a combination of the central nervous system disorders and abnormalities of the peripheral input (14). To date, considerable attention has been paid to the possible involvement of cochlear mechanisms in tinnitus generation, but in recent years the interest of the scientific community has shifted towards retro-cochlear and central mechanisms (15). Existence of minor abnormalities in the outer hair cell function have suggested as a possible source of tinnitus in normal hearing adults based on studies of the OAE responses (12, 16). Studies that have examined the changes in latencies of ABR waves in tinnitus patients have reported different findings. However, in the present study the prevalence of TEOAE responses, which reflects healthy status of the cochlea, was similar between the two groups. Therefore, it seems that peripheral cochlear dysfunction has a less important role in tinnitus generation in this group of individuals, and there is more likelihood of a neural origin.

Gerken and colleagues compared results of ABR test in 9 hearing impaired tinnitus patients with that of 11 normal hearing non-tinnitus subjects. They found a significant difference between latency of wave VII in the two groups and reported that there were no significant differences in latencies of earlier waves and amplitudes of all waves between the two groups (17). Recently, Mohammadkhani and Roozbahani analyzed and compared auditory brainstem responses in 30 patients suffering from noise induced tinnitus and 30 healthy persons without tinnitus whom aged 20 to 50 years. They reported that mean interpeak latencies of III-V and I-V in ipsilateral electrode array and mean absolute latencies of waves IV and V in contralateral electrode array were significantly increased in noise induced tinnitus group relative to the control group. These authors concluded that there was some decrease in neural transmission time in brainstem and that there were some signs of involvement in lateral lemniscus and medial nuclei of olivary complex (4). Unlike the above-mentioned studies, this study was performed in subjects with normal hearing thresholds. The analysis of the wave latencies in the present study did not show significant differences between the two groups which are consistent with McKee and Barnea findings in normal hearing tinnitus patients (10,18). Considering the findings of researchers, it seems that excessive spontaneous activity in the central auditory pathways may be one of the possible causes of tinnitus in this population. However, some researchers ascribe lack of considerable difference in latencies of ABR components to the type of stimuli used in recording these responses. Due to masking effect on abnormal spontaneous activity of auditory nerve centers and pathways, using click stimuli to evoke ABR responses may lead to absolute and interpeak latencies similar to normal subjects (11,18).

The fMRI imaging and neurobiological studies have shown that increased spontaneous neural activity at the level of the auditory nerve, brainstem and cortex can be considered as central sources of tinnitus (9,13). Study of the ABR wave's amplitudes has more limited application -compared to latency evaluations- in identifying abnormalities of the auditory brainstem (11). However, since the ABR reflects activity of a limited population of neurons which are simultaneously activated in response to auditory stimuli and, compared with imaging techniques, it provides more specific information in this case, amplitude measurements can be useful in demonstrating increased activity of specific auditory pathways (8, 19). In a study on 37 tinnitus patients with auditory thresholds better than 20 dBHL and comparing the results with control group, Kehler and colleagues reported that the V / I amplitude ratio was significantly larger in the tinnitus group (11). The study of Wendy Gu showed that decreased amplitude of wave I, increased amplitude of wave V and subsequent increase in the III / I and V / I amplitude ratios are findings that may be seen in tinnitus patients (8). In this study, compared with the control group, the

amplitude of the wave I was slightly smaller, and also the amplitude of wave V was slightly larger in tinnitus group. Although this difference was not statistically significant, but comparing the V/I amplitude ratio in the groups showed that it was significantly larger in the tinnitus group. Reduction of the amplitude of the wave I in tinnitus group may be the result of "loss of higher-threshold auditory nerve fibers" that has no effect on hearing thresholds. The other possible reason for this finding could be explained by "sporadic damage to the inner hair cells" that does not cause hearing loss, but leads to reduction of the amplitude of wave I (8).

Increased spontaneous neural activity at higher levels of the auditory pathways, including dorsal and ventral cochlear nuclei and inferior colliculus, are among the theories about the origin of the tinnitus (15,20). Neuropsychological data obtained from animal studies have shown increased excitability of the auditory brainstem after noise exposure (8). Although most studies that evaluated increased neural activity in the tinnitus subjects have been performed on animal models or in cases of hearing impairment, increased V / I amplitude ratio in the present study can represent the role of auditory brainstem centers in tinnitus generation in normal hearing people. However, it seems that further studies are needed for the interpretation of the results of this study and similar studies in normal hearing subjects (11).

It seems that conduction time for a click evoked auditory potentials in normal hearing tinnitus patients do not change considerably at the level of auditory nerve and brainstem. However, the changes that have been found in the amplitude of ABR waves, especially in the later waves, can be considered as an audiologic finding that indicates increased spontaneous activity of neurons of the brainstem auditory centers. In comparison to peripheral cochlear damage, this probably has a more prominent role in the generation of tinnitus.

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