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RESEARCH ARTICLE

Assessment of functional status of outer hair cells in Type 2 diabetes by using distortion product otoacoustic emissions

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ABSTRACT

Background: Outer hair cells in the organ of Corti are not directly involved in deciding the threshold of the acoustic stimulus, but their damage will increase the hearing threshold and may even cause the neuronal deafness. Type 2 diabetes is increasing globally at an alarming rate; one of many complications of Type 2 diabetes is loss of hearing. In Type 2 diabetes, poor glycemic status is the cause for neuropathy or microangiopathy which may affect the normal hearing. **Aims and Objectives:** To observe the effect of Type 2 diabetes on the functional status of outer hair cells. To illustrate the effect of Type 2 diabetes on outer hair cells for right and left ear is same or different. **Materials and Methods:** A total of 50 Type 2 diabetic subjects, aged between 30 to 55 years, both sexes were included as test group after assessing their glycemic index. 50 age and sex matched healthy individuals are also included as control group. Functioning of outer hair cells was assessed with distortion product otoacoustic emissions (DPOAEs). **Results:** Glycosylated hemoglobin percentage among test (8.58 ± 0.83) and control group subjects (5.28 ± 0.50) is statistically significant (<0.0001). Odds of failing the DPOAEs are 7 and 15 times higher in patients with Type 2 diabetes than those without diabetes for right and left ear, respectively. **Conclusion:** There is increased risk of damage to the outer hair cells in Type 2 diabetes. The risk of damage to the outer hair cells is more in the left ear than the right ear.

KEY WORDS: Outer Hair Cells; Distortion Product Otoacoustic Emissions; Type 2 Diabetes; Glycosylated Hemoglobin

INTRODUCTION

Otoacoustic emissions (OAEs) are low-level auditory signals produced from the outer hair cells of the cochlea.[1,2] OAEs are widely used to assess the functioning of cochlea by analyzing the outer hair cell micromechanics in humans.[3] Use of higher stimulus intensities increases OAEs and can provide useful evidence of residual hair cell activity but does not probe further deep into the auditory pathway.[4] OAEs also give an indirect idea about the functional status of inner hair cells.[5] Like any other system in the body, the auditory system also requires glucose for its complex signal processing. Exposure to hyperglycemia even for short periods will trigger the cascade of metabolic reactions, such as increasing the endothelial permeability and disturbing the cochlear endolymph electrolyte homeostasis, that will affect the cochlea both functionally and morphologically.[6] OAEs are altered if there is damage to the cochlea, but they are not disturbed if the retrocochlear neural pathway is affected.[7,8] With the sensitivity of OAEs, the audiologists may identify auditory impairment before the onset of hearing loss or before the impairment progresses further to the deeper auditory structures.[9]

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Hypothesis

Type 2 diabetes alters the functional status of outer hair cells in the cochlea.

Objectives of the Study

1. To observe the effect of Type 2 diabetes on functional status of outer hair cells
2. To illustrate the effect of Type 2 diabetes on outer hair cells for right and left ear is same or different
3. To estimate the glycosylated hemoglobin (HbA1c) concentration in Type 2 diabetics and controls.

MATERIALS AND METHODS

Study Design

It is a case control study. The study was approved by the institutional ethical committee (FWA00002084 dated 16/03/2015).

Inclusion Criteria

A total of 50 Type 2 diabetic subjects of both the sex, aged between 30 to 55 years, were included in the study as cases. Age and sex matched 50 normal individuals were included as controls in the study, written informed consent was obtained from both the groups after making them to understand the objectives of the study. In test group, 32 are males and 18 are females and in the control group, 29 are males, and 21 are females.

Exclusion Criteria

Subjects were excluded from the study if they have present or past history of using ototoxic drugs, noise exposure, ear surgeries, chronic middle ear diseases, cranial trauma, metabolic disorders except for diabetes mellitus, underwent recent surgeries, any type of chronic infections, congenital hearing problems, Type 1 diabetes, smokers, and alcoholics.

Methods

HbA1c

HbA1c was estimated on the basis of latex agglutination inhibition assay using Rx imola automated analyzer. Here, the hemoglobin is hydrolyzed by the enzyme protease in the hemoglobin denaturant reagent. The reported HbA1c result is calculated as a percentage of the total hemoglobin concentration (Randox, UK). HbA1c was estimated in both the groups.

Distortion product OAEs (DPOAEs)

OAE is a conventional objective, non-invasive test protocol that assists to detect the accuracy of cochlear functioning and hearing at frequencies ranging from 1000 to 4000 Hz. From several types of OAEs, DPOAEs are used in this study.

Instrument

Biologic Scout Sport system (Natus, USA).

Recording

A probe wire that is directly connected to the instrument is placed in the patient's ear. The stimulus used includes clicks, with an intensity of 65-70 dB sound pressure level and test frequencies include 1000-4000 Hz. The results thus obtained are a numerical representation for the formula 2f1−f2 = DPOAE. Results obtained with a noise floor of more than 6 dB are noted as no response. Thus, after the compilation using the formula, the final results of the test are displayed as PASS or REFER, which in turn explain the outer hair cell functioning. PASS means normal functioning and REFER means abnormal and requires further investigation with brainstem auditory evoked potentials. In this study, if the result of OAEs is "PASS," we considered it as 1 and if the result is "REFER or FAIL" then it is considered as 2.

Statistical Analysis

Statistical analysis was conducted using MedCalc Statistical Software Version 12.7.8 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014), an unpaired *t*-test was performed to compare the mean difference between test and control group, $P < 0.05$ was considered as statistically significant. Odds ratio was calculated for both right and left ear OAEs.

RESULTS

HbA1c percentage among test group subjects (8.58 ± 0.83) and controls (5.28 ± 0.50) is statistically significant (<0.0001). We analyzed DPOAEs in test and control groups. The distribution of DPOAEs frequencies in test and control groups of both left and right ears was presented in Table 1. In the right ear DPOAEs, among the 50 control subjects, 38 (76%) were present and 12 (24%) were absent. Among the

Table 1: Odds ratio of both right and left ears DPOAEs

Results	Controls (%)	Test (%)	OR (95% CI)	*P* value
Right ear				
Pass	38 (76.0)	16 (32.0)	Reference	<0.001
Fail/refer	12 (24.0)	34 (68.0)	6.72 (2.80-16.22)	
Left ear				
Pass	41 (82.0)	13 (26.0)	Reference	<0.001
Fail/refer	9 (18.0)	37 (74.0)	12.96 (4.97-33.80)	

P<0.05 is consider significant. DPOAEs: Distortion product otoacoustic emissions, OR: Odd ratio, CI: Confidence interval

50 test subjects, 16 (32%) were present, and 34 (68%) were absent. In the left ear DPOAEs, among the 50 control subjects, 41 (82%) were present and 9 (18%) were absent. Among the 50 test subjects, 13 (26%) were present and 37 (74%) were absent. In risk analysis, there was a significant increased risk was observed in both right ($P \leq 0.001$; odd ratio [OR] 6.72; 95% confidence interval [CI] 2.80-16.22) and left ($P \leq 0.001$; OR 12.96; 95% CI 4.97-33.80) ears.

DISCUSSION

DPOAEs were absent in the majority of people with Type 2 diabetes than in the controls. It has been observed that in left ear DPOAEs are absent more than in the right for the test group but in the controls, the opposite was established. The glycemic index is high in the test group than the controls; this indicates that diabetes has a vulnerable role on the outer hair cells function, and it may cause hearing impairment in the diabetic persons. Contrary to our findings in some studies, OAEs were not affected at most frequencies in Type 2 diabetic subjects.[10,11] The contributions of hyperglycemia, insulin resistance, and hyperlipidemia could influence outer hair cell damage or other cochlear pathologies such as stria vascularis or fibrocyte damage, as a result of metabolic alterations.[12]

Decreased amplitude of DPOAEs was reported in Type 2 diabetic patients when compared with the normal individuals.[13-19] Impaired functioning of the outer row of hair cells reduces sensitivity to the acoustic stimulus.[20-23] The possible mechanisms by which glucose is affecting the outer hair cells and resulting in abnormal OAEs are; glucose is the energy source for the cochlea if glucose is disrupted then it affects the OAEs.[12,24-26] Advanced glycosylated end products in hyperglycemia causes release of more cytokines, these affect matrix metalloproteinase and damage nerve cells, it may have some negative effect over functions of outer hair cells in diabetes.[27] Outer hair cells have ion channel which are sensitive to adenosine triphosphate (ATP) as a neurotransmitter.[28-30] When ATP and its analogs were applied to the cochlear perilymph, reductions were observed in OAE amplitudes and auditory nerve compound action potentials.[31] Functional loss of outer hair cells may result in hearing impairment.[32] Some studies also reported where hearing impairment is not associated with the hair cell dysfunctioning.[33]

CONCLUSION

Functioning of outer hair cells is altered in Type 2 diabetes. Pure tone audiometry and brainstem auditory evoked potentials will help in the deeper analysis of effects of Type 2 diabetes on hearing threshold and interpeak latencies, respectively, and these results may re-establish the findings of OAEs.

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