TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2014) 44: 150-156
© TÜBİTAK
doi:10.3906/sag-1207-99

Evaluation of outer hair cell function and medial olivocochlear efferent system in patients with type II diabetes mellitus

Hayriye KARABULUT[1,*], İsmail KARABULUT[2], Muharrem DAĞLI[3], Yıldırım Ahmet BAYAZIT[4], Şule BİLEN[5], Yusuf AYDIN[6], Serdar GÜLER[7], İsmet BAYRAMOĞLU[4]

[1]Department of Otolaryngology and Audiology, Ankara Dışkapı Yıldırım Beyazıt Research and Training Hospital, Ankara, Turkey
[2]Department of Physiology, Faculty of Medicine, Hacettepe University, Ankara, Turkey
[3]Department of Otolaryngology, Ankara Dışkapı Yıldırım Beyazıt Research and Training Hospital, Ankara, Turkey
[4]Department of Otolaryngology, Faculty of Medicine, Gazi University, Ankara Turkey
[5]Department of Neurology, Ankara Numune Research and Training Hospital, Ankara, Turkey
[6]Department of Endocrinology, Faculty of Medicine, Düzce University, Düzce, Turkey
[7]Department of Endocrinology, Ankara Numune Research and Training Hospital, Ankara, Turkey

Received: 26.07.2012 • **Accepted:** 08.01.2013 • **Published Online:** 02.01.2014 • **Printed:** 24.01.2014

Aim: This study was designed to investigate the function of outer hair cells and medial olivocochlear efferents in type II diabetes mellitus (DM).

Materials and methods: There were 50 patients with type II DM and 51 age- and sex-matched healthy controls included in the study. Both groups were compared in terms of transient evoked otoacoustic emissions (TEOAEs), distortion product otoacoustic emissions (DPOAEs), and contralateral suppression of TEOAE.

Results: Pure tone thresholds of the patients with type II DM were significantly higher than in the controls ($P < 0.05$). The TEOAE amplitudes at 1 kHz and at 1.5, 2, 3, 4, and 6 kHz signal-to-noise ratio amplitudes on DPOAE testing were significantly lower in the patients than controls ($P < 0.05$). There was no significant difference between the type II DM and control groups regarding contralateral suppression test results of TEOAEs.

Conclusion: Type II DM seems to impact the auditory system at the cochlear level by affecting the functions of outer hair cells, and it results in elevation of the thresholds on audiometry and a decrease in the amplitudes of otoacoustic emissions.

Key words: Diabetes mellitus, contralateral suppression, medial olivocochlear efferent, transient evoked otoacoustic emissions, distortion product otoacoustic emissions, hearing

1. Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized genetically, which can cause a variety of metabolic, neurologic, and vascular complications (1). Although a correlation between DM and hearing loss has been show in numerous studies (2,3), there is still no consensus about the exact etiopathogenesis of hearing loss and the site of auditory system involvement (3).

The medial olivocochlear (MOC) efferents originate from the medial part of the superior olivary complex on both sides, project through the vestibular nerve, and terminate on the outer hair cells of the cochlea (4–7). Stimulation of the MOC efferents results in an inhibition of outer hair cell activity in the cochlea and, in turn, a decrease in the amplitudes of otoacoustic emissions (OAEs) (8,9). The OAEs are generated by the outer hair cells in the cochlea, either spontaneously or in response to acoustic stimuli, and can be recorded in the external ear canal noninvasively. Thus, the combination of OAEs and contralateral acoustic stimulation (CAS) allows the investigation of the efferent cochlear innervations (4,10,11). This effect is known as contralateral suppression (CLS) of OAEs and facilitates assessment of the MOC efferent system (4,11,12).

The aim of the current study was to investigate the outer hair cell function and MOC efferent system by OAE tests in patients with type II DM.

* Correspondence: hayriyekarabulut@gmail.com

2. Materials and methods

This research was performed in accordance with the principles of the Declaration of Helsinki, and approval for this study was granted by the local ethics committee. Written informed consents were obtained from the patients and controls tested in this study.

2.1. Patients and controls

There were 50 patients (100 ears) with type II DM who were diagnosed in the department of endocrinology and 51 healthy age- and sex-matched controls (102 ears) included in the study.

The mean age of patients with DM was 49.8 ± 5.1 years (range: 40–60 years). There were 34 (68%) female and 16 (32%) male patients. The mean age of the control group was 47.9 ± 4.8 years (range: 40–58 years), and there were 33 (64.7%) female and 18 (35.3%) male subjects. There was no significant difference between the ages and sexes of the patients and controls ($P > 0.05$).

None of the participants had a history of using ototoxic drugs, noise exposure, ear surgery, chronic middle ear disease, Meniere's disease, cranial trauma, metabolic diseases except for DM, otoscopic evidence of a perforated tympanic membrane or other middle ear pathology, presence of a flat tympanogram, or an air-bone gap of 5 dB or greater at any frequency.

In the patients, the mean duration of disease, glycosylated hemoglobin (HbA1c) levels, and simultaneous fasting glucose levels were recorded. In the control group, fasting glucose level was also recorded.

2.2. Audiometry and middle ear evaluation

The hearing examination included otoscopy, tympanometry, pure-tone audiometry, and speech audiometry. Pure-tone audiometry was performed at the frequencies of 250, 500, 1000, 2000, 4000, and 8000 Hz using a diagnostic audiometer (Madsen Orbiter 922-2 Clinical Audiometer, Copenhagen, Denmark) in a sound-treated cabin. Tympanometric measurements were done using a TDH-39 headset and middle ear analyzer (TympStar GSI**,** Grason-Stadler Inc**.,** Milford, NH, USA). On tympanometry, all participants had a normal peak compliance, peak pressure, gradient and ear canal volume, and acoustic reflex, as defined by American Speech Language and Hearing Association.

2.3. OAE testing

All OAE measurements were performed bilaterally and were recorded using the ILO 292 USB II OAE analyzer, version 6 (Otodynamics Ltd., London, UK), with 2 ILO UGD TE+DPOAE probes (insert phone) in a sound-proof room.

2.4. DPOAE test parameters

Distortion product otoacoustic emission (DPOAE) testing was performed bilaterally using an ILO device. The emission at 2f1–f2 was the distortion product measured. Distortion product signal amplitude and noise floor across the range of frequencies corresponding to the following frequencies values for f2 were recorded: 1000, 1500, 2000, 3000, 4000, 5000, and 6000 Hz. The test parameters for DPOAEs were the following: stimulus, f1 = 65 dB, f2 = 55 dB, and 2f2/f1 = 1.22; time out (NLo), 500 sweeps or 100 s; noise rejection level, 49.5 dB sound pressure level (SPL); point/octave, 2.

2.5. Testing contralateral suppression of TEOAEs

The transient evoked otoacoustic emissions (TEOAEs) were registered on the linear click channel. The data set from the test with CAS was designated as memory store 1, and that from the test without CAS was designated as memory store 2. The CAS consisted of continuous broad band white noise at 60 dB SPL, delivered through channel B of the ILO and presented by ILO general purpose UGD TE+DPOAE probes. All subjects were tested bilaterally in a randomized fashion. After the 2 probes were in place, TEOAEs were recorded in alternating blocks (with and without CAS) for the linear mode, always in the same order. TEOAE contralateral suppression was calculated by subtracting the TEOAE level with CAS from the TEOAE level without CAS.

In all patients, TEOAE with CAS [CAS (+)] and TEOAE without CAS [CAS (–)] were recorded in linear mode, and test frequencies were at 1000, 1500,1000,3000, and 4000 Hz. Under all conditions, the intensity of the clicks was 80 dB SPL, and a total of 260 sweeps were recorded for each ear. The measurements were averaged after 260 responses and were only accepted when stimulus stability was better than 80%. The linear TEOAE recording mode is the most sensitive at CLS.

2.6. Statistical analyses

The statistical analyses were performed using SPSS 13.0 for Windows (SPSS Inc., Chicago, IL, USA). A chi-square test was used to compare the DM and control groups regarding sex and the rate of hearing loss. The independent sample t-test was used to compare the ages and all audiological parameters of the patients and controls. Pearson correlation and linear regression analysis were used in correlation analyses of TEOAE, DPOAE, and TEOAE with and without CAS with mean duration of disease and HbA1c blood levels. $P < 0.05$ (2-tailed) was regarded as statistically significant.

3. Results

The mean duration of diabetes mellitus was 8.1 ± 5.8 years (range: 1–20 years). The mean blood level of HbA1c was 8.1 ± 2.27 (5.22–13.12) and of glucose was 171.6 ± 73.6 (75–340) mg/dL in the patient group. HbA1c was within the normal range only in 6% of the diabetic patients. The mean blood level of glucose was 92.9 ± 8.5 (66–110) mg/

dL in the control group. There was a significant difference between the mean blood glucose levels of the patients and controls (P < 0.0001, independent sample t-test). Twenty-eight percent of the diabetic patients were taking insulin in the management of their disease. The rest were taking oral antidiabetic medications or attempting to control their diabetes by diet.

As there was no air-bone gap in the participants, only air conduction thresholds were taken into consideration. Since there was no difference between the right and left ears of both groups, the results of both ears were taken into consideration in the statistical analyses. The pure-tone audiometric thresholds of the groups are shown in Table 1. There was a significant difference between the pure-tone thresholds of the patients and controls at all frequencies (P < 0.05, independent sample t-test).

The mean speech discrimination scores of the patient and control groups were 94.1 ± 6.6% (range: 68%–100%) and 96.5 ± 4.7% (range: 72%–100%), respectively (P = 0.004, independent sample t-test). The pure-tone average (PTA) of air conduction thresholds at 500, 1000, and 2000 Hz was measured separately for each ear. Hearing loss was defined as a pure-tone threshold level higher than 15 dB at any test frequency (11). The rates of hearing loss at each test frequency of the groups are shown in the Figure. There was a significant difference between the rate of sensorineural hearing loss (SNHL) of the patients and controls at all test frequencies (0.05, chi-square test).

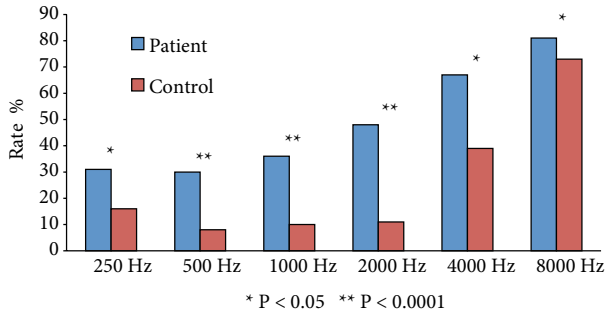

Figure. The rate of hearing loss (>15 dB) at all frequencies.

The DPOAEs, noise floor, and signal-to-noise ratio (SNR) findings of the patients and controls are shown in Table 2. There were statistically significant differences between the levels of SNR of the patients and controls at all frequencies (P < 0.05) except for the 1000 Hz results on DPOAE testing. The CAS (–) and CAS (+) TEOAE findings of the patients and controls are shown in Tables 3 and 4. There was no statistically significant difference between CLS test results of patients and controls (P > 0.05). In our study, no correlation was found between CAS (–) and CAS (+) SNR amplitudes at specific frequencies and disease duration, glucose blood level, or HbA1c and test parameters.

Table 1. Air conduction pure tone thresholds of groups.

Group	Frequency	N	Minimum dB HL	Maximum dB HL	Mean dB HL	SD dB HL
Patient	250 Hz	100	0	75	16.2	10.6
	500 Hz	100	0	60	15.3	9.5
	1000 Hz	100	0	50	16.7	9.4
	2000 Hz	100	5	50	18.0	10.2
	4000 Hz	100	0	70	24.4	13.4
	8000 Hz	100	5	85	33.2	16.6
Control	250 Hz	102	5	25	12.2	5.2
	500 Hz	102	5	30	10.7	5.4
	1000 Hz	102	0	30	10.9	5.4
	2000 Hz	102	0	30	10.8	6.0
	4000 Hz	102	0	50	16.5	11.6
	8000 Hz	102	5	85	26.3	16.2

HL = hearing level; SD = standard deviation.

Table 2. DPOAE signal and SNR findings of groups.

Frequency	Patient group			Control group		
	N	Mean	SD	N	Mean	SD
1000 Hz signal (dB SPL)	100	1	8.5	102	3.3	6.9
1000 Hz SNR (dB SPL)	100	4	9.3	102	6.2	9.5
1500 Hz signal (dB SPL)	100	1.8	9.7	102	6.1	7.8
1500 Hz SNR (dB SPL)	100	8.7	10.8	102	14	8.9
2000 Hz signal (dB SPL)	100	–1.6	11.4	102	2.4	9.1
2000 Hz SNR (dB SPL)	100	9.3	12.1	102	12.9	9.2
3000 Hz signal (dB SPL)	100	–8.7	12.7	102	–3.9	11.5
3000 Hz SNR (dB SPL)	100	4.8	12.8	102	9	11.2
4000 Hz signal (dB SPL)	100	–6.1	12.7	102	–0.3	10.7
4000 Hz SNR (dB SPL)	100	7.5	12.4	102	12.4	10.4
6000 Hz signal (dB SPL)	100	–12.6	12.7	102	–7.4	12.6
6000 Hz SNR (dB SPL)	100	–0.03	12.4	102	5.3	12.5
8000 Hz signal (dB SPL)	100	–22.6	8.6	102	–19.4	11.1
8000 Hz SNR (dB SPL)	100	–6.8	8.4	102	–4	9.5

SNR: signal-to-noise ratio; SPL: sound pressure level; SD = standard deviation.

Table 3. CAS (–) and CAS (+) TEOAE signals and noise and SNR findings for patient group.

Frequency	CAS (–) TEOAE					CS (+) TEOAE				
	N	Min.	Max.	Mean	SD	N	Min.	Max.	Mean	SD
1000 Hz signal (dB SPL)	100	–11.6	26.7	9.6	5.8	100	–12.6	26.6	9.5	5.8
1000 Hz noise (dB SPL)	100	–21.1	15	–9.2	5.1	100	–20.7	3.3	–8.9	4.4
1000 Hz SNR (dB SPL)	100	–12.7	37.4	18.9	7.4	100	–34.1	33.4	18.1	8.5
1500 Hz signal (dB SPL)	100	–9.2	20.5	9.5	5.3	100	–11.6	20.5	9.3	5.4
1500 Hz noise (dB SPL)	100	–23.5	0.4	–11.6	4.1	100	–24.2	1.5	–11.2	4.0
1500 Hz SNR (dB SPL)	100	–16	32.5	20.8	7.0	100	–17.7	31.6	20.2	7.0
2000 Hz signal (dB SPL)	100	–7.5	18	6.6	5.0	100	–16.2	17.9	6.5	5.2
2000 Hz noise (dB SPL)	100	–28	13.4	–12.2	4.1	100	–16.3	12.6	–11.7	4.0
2000 Hz SNR (dB SPL)	100	–12.1	29.6	18.8	6.2	100	–30	27.7	18.3	7.3
3000 Hz signal (dB SPL)	100	–15.9	17.3	1.8	5.9	100	–15.4	17.4	1.8	5.9
3000 Hz noise (dB SPL)	100	–30	0.3	–11.6	2.8	100	–15.2	–1.3	–11.3	2.0
3000 Hz SNR (dB SPL)	100	–19.3	28.1	13.2	6.8	100	–21.5	28.2	12.8	6.8
4000 Hz signal (dB SPL)	100	–15.1	18.8	–2.3	7.5	100	–15.7	18.8	–2.4	7.6
4000 Hz noise (dB SPL)	100	–16.2	2.5	–11.4	2.3	100	–14.6	–0.5	–11.3	1.8
4000 Hz SNR (dB SPL)	100	–3.5	28.9	9.3	7.5	100	–37.4	28.2	8.6	8.6
Total signal (dB SPL)	100	3.7	26.9	15.5	4.0	100	–15.4	26.9	15.1	4.9
Total noise (dB SPL)	100	–5.6	7.5	–0.6	2.7	100	–22	7.4	–0.5	3.5

SNR: signal-to-noise ratio; SPL: sound pressure level; Min. = minimum; Max. = maximum; SD = standard deviation.

Table 4. CAS (–) and CAS (+) TEOAE signals and noise and SNR findings for control group.

Frequency	CAS (–) TEOAE					CAS (+) TEOAE				
	N	Min.	Max.	Mean	SD	N	Min.	Max.	Mean	SD
1000 Hz signal (dB SPL)	102	–5.5	21.5	10.7	4.7	102	–1.6	21.1	10.9	4.6
1000 Hz noise (dB SPL)	102	–23.5	14.1	–9.5	4.8	102	–17.1	12	–8.8	4.6
1000 Hz SNR (dB SPL)	102	2.4	36.1	20.5	6.1	102	7.4	36	19.9	6.3
1500 Hz signal (dB SPL)	102	–1.7	22.9	10.9	4.5	102	–1.6	22.6	10.8	4.5
1500 Hz noise (dB SPL)	102	–16.9	1.7	–11.0	3.8	102	–18.1	10.8	–10.3	4.5
1500 Hz SNR (dB SPL)	102	11	35.1	22.0	5.0	102	3.5	33.2	21.4	5.7
2000 Hz signal (dB SPL)	102	–6.7	19	6.9	5.2	102	–8.4	18.8	6.7	5.2
2000 Hz noise (dB SPL)	102	–17.4	12	–11.4	4.2	102	–17	1.9	–11.5	3.4
2000 Hz SNR (dB SPL)	102	6.8	30.4	18.5	4.9	102	4.5	32.9	18.3	5.1
3000 Hz signal (dB SPL)	102	–12.5	18.3	2.7	6.2	102	–13.2	18	2.7	6.3
3000 Hz noise (dB SPL)	102	–14.8	12.5	–10.8	3.4	102	–14.6	12.6	–10.7	3.4
3000 Hz SNR (dB SPL)	102	–4.1	29.5	13.8	6.3	102	–6.4	30	13.5	6.4
4000 Hz signal (dB SPL)	102	–15.1	20.1	–1.6	6.6	102	–15.8	20	–1.8	6.6
4000 Hz noise (dB SPL)	102	–14.7	–3.3	–11.1	1.8	102	–15.1	–0.7	–11.0	1.9
4000 Hz SNR (dB SPL)	102	–5.6	32.7	9.5	6.7	102	–5.1	130	10.3	13.7
Total signal (dB SPL)	102	6.4	25.8	16.1	3.7	102	6.7	25.4	16.0	3.7
Total noise (dB SPL)	102	–5.1	7.9	–0.6	2.9	102	–5	7.9	–0.2	2.9

SNR: signal-to-noise ratio; SPL: sound pressure level; Min. = minimum; Max. = maximum; SD = standard deviation.

4. Discussion

In our study we evaluated the auditory functions not only traditionally but also by detailed audiological tests. According to our audiometric test results, there was SNHL in the diabetic patients at all test frequencies. We found a statistically significant difference between the SNR levels of the patients and controls at all frequencies except for 1000 Hz on DPOAE testing. We also found that there was no significant difference between CLS amplitudes of the patients and controls. This means that the MOC system is not affected by type II DM.

In the literature, different types of hearing losses were reported in diabetic patients, such as bilateral SNHL, affecting hearing at high frequencies.

In our study, there was SNHL that affected hearing at high frequencies in both patients and controls. This may result from presbycusis; however, hearing loss in the patients was more severe than in the controls. Although some studies reported that DM is one of the possible reasons for sudden SNHL, this had happened in none of our patients.

In our study, hearing thresholds of males at 4000 and 8000 Hz were higher than those of females in both patients and controls, and there was no correlation between hearing loss and age. Cullen and Cinnamond reported that hearing loss is more prominent in male diabetics than female diabetics, which is possibly due to males being exposed to environmental noise more frequently than females (14). Age is another factor leading to hearing loss, and the presence of DM accelerates age-related hearing loss, or presbycusis, by synergistic action (14). In our study the relationship between disease duration and hearing loss is a matter of controversy. Ottaviani et al. (16) did not find a correlation among the disease duration, HbA1c, OAE amplitudes, and neuropathy in their regression analysis model.

In our study we found that there was a statistically significant difference between the levels of SNR of the patients and controls at all frequencies except for 1000 Hz on DPOAE testing. This study confirms that cochlear function is affected at all frequency regions in DM patients. Measurement of DPOAEs corresponds closely

to the physiological state of the outer hair cells of the cochlea (16). DPOAEs are mainly used in the assessment of cochlear function to determine the site of pathology associated with SNHL. DPOAEs, if normal, provide extremely strong evidence of normal cochlear function, regardless of the audiometric data (17).

We did not find any significant difference between CLS amplitudes of the patients and controls. Namyslowski et al. (19) and Ugur et al. (20) reported that there was a significant decrease in the TEOAE suppression amplitudes in children with DM. The lack or reduction of CLS amplitude is a pathologic state implicating auditory neuropathy or dyssynchrony (20). The cochlea is innervated by the olivocochlear efferent system, and the thick and myelinated MOC efferent fibers originate from the medial part of the superior olivary complex on both sides (20) and project through the inferior vestibular nerve (4,21,22).

In our study the patients and controls were middle-aged, between 40 and 60 years old. Many studies confirmed that the suppression effect on the MOC system decreases with age, and auditory pathway structures begin to degenerate at 40 years of age (23,24). This may explain our results with the decrease of olivocochlear system function. The preference of stimulus is important in OAE test procedures because the appropriate stimulus can provide better results, especially in some specific measurements. Linear stimulation is more sensitive in detecting shifts in the TEOAEs recorded in the presence of competitive noise than in those recorded without competitive environmental noise (25,26). However, it has some technical limitations, and therefore some authors recommend using the nonlinear mode of stimulation in detecting CLS of TEOAEs in clinical settings (18–20). In our study, we used the linear stimulus mode, which was more sensitive. In the literature, although several clinical and experimental studies exist about evaluation of the MOC function in patients with type I DM (18,19,27), we did not find any clinical study performed in patients with type II DM, and the current study is the first of this topic.

Makashima and Tanaka described atrophy of spiral ganglion neurons and demyelination of the eighth cranial nerve in 4 DM subjects. Histopathological studies of the inner ear in the patients with DM showed a thickening in the walls of capillaries in the stria vascularis and degeneration in the organ of Corti and outer hair cells (28). Additionally, abnormal auditory brainstem response results can also suggest impairment in the central neural conduction process of the auditory system in DM (28,29).

In conclusion, audiological results suggest that type II DM seems to have an important impact on outer hair cells in the auditory system. The audiometric thresholds at all test frequencies increased, and except for at 1000 Hz, the amplitudes of DPOAEs at all frequencies decreased in diabetic patients. Our results suggest that an impairment of the outer hair cells is evident in the cochlea. The MOC efferent system was not affected in type II diabetic patients.

References

1. Giniş Z, Öztürk G, Sırmalı R, Yalçındağ A, Dülgeroğlu Y, Delibaşı T, Delibaş N. The role of HbA1c as a screening and diagnostic test for diabetes mellitus in Ankara. Turk J Med Sci 2012; 42 (Suppl. 2): 1430–1436.
2. Wu HP, Guo YL, Cheng TJ, Hsu CJ. Chronological changes in compromised olivocochlear activity and the effect of insulin in diabetic Wistar rats. Hear Res 2010; 270: 173–178.
3. Austin DF, Konrad-Martin D, Griest S, McMillan GP, McDermott D, Fausti S. Diabetes-related changes in hearing. Laryngoscope 2009; 119: 1788–1796.
4. Maia CA, Campos CA. Diabetes mellitus as etiological factor of hearing loss. Braz J Otorhinolaryngol 2005; 71: 208–214.
5. Guinan JJ Jr. Olivocochlear efferents: anatomy, physiology, function, and the measurement of efferent effects in humans. Ear Hear 2006; 27: 589–607.
6. Al-Mana D, Ceranic B, Djahanbakhch O, Luxon LM. Hormones and the auditory system: a review of physiology and pathophysiology. Neuroscience 2008; 153: 881–900.
7. Brown MC, Levine JL. Dendrites of medial olivocochlear neurons in mouse. Neuroscience 2008; 154: 147–159.
8. Maison SF, Liberman MC. Predicting vulnerability to acoustic injury with a noninvasive assay of olivocochlear reflex strength. J Neurosci 2000; 20: 4701–4707.
9. Hall JW. Handbook of Otoacoustic Emissions. San Diego, CA, USA: Singular Thomson Learning, 2000.
10. Yost WA. Fundamentals of Hearing. San Diego, CA, USA: Academic Press, 2000.
11. Berlin CI, Hood LJ, Cecola RP, Jackson DF, Szabo P. Does type I afferent neuron dysfunction reveal itself through lack of efferent suppression? Hear Res 1993; 65: 40–50.
12. Collet L. Use of otoacoustic emissions to explore the medial olivocochlear system in humans. Br J Audiol 1993; 27: 155–159.
13. Harrell RW. Puretone evaluation. In: Katz J, editor. Handbook of Clinical Audiology. Philadelphia: Lippincott Williams Wilkins, 2002. pp. 71–87.
14. Cullen JR, Cinnamond MJ. Hearing loss in diabetics. J Laryngol Otol 1993; 107: 179–182.
15. Axelsson A, Sigroth K, Vertes D. Hearing in diabetics. Acta Otolaryngol Suppl 1978; 356: 1–23.

16. Ottaviani F, Dozio N, Neglia CB, Riccio S, Scavini M. Absence of otoacoustic emissions in insulin-dependent diabetic patients: is there evidence for diabetic cochleopathy? J Diabetes Complications 2002; 16: 338–343.

17. Karabulut H, Dagli M, Ates A, Karaaslan Y. Results for audiology and distortion product and transient evoked otoacoustic emissions in patients with systemic lupus erythematosus. J Laryngol Otol 2010; 124: 137–140.

18. Korres SG, Balatsouras DG, Economou C, Ferekidis E, Kandiloros D, Adamopoulos G. Effect of the number of averaged responses in transient evoked otoacoustic emissions on the results of neonatal hearing screening. Audiology 2000; 39: 293–299.

19. Namyslowski G, Morawski K, Kossowska I, Lisowska G, Koehler B, Jarosz-Chobot P. Contralateral suppression of TEOAE in diabetic children. Effects of 1.0 kHz and 2.0 kHz pure tone stimulation--preliminary study. Scand Audiol Suppl 2001; 126–129.

20. Ugur AK, Kemaloglu YK, Ugur MB, Gunduz B, Saridogan C, Yesilkaya E, Bideci A, Cinaz P, Goksu N. Otoacoustic emissions and effects of contralateral white noise stimulation on transient evoked otoacoustic emissions in diabetic children. Int J Pediatr Otorhinolaryngol 2009; 73: 555–559.

21. Hood LJ, Berlin CI, Bordelon J, Rose K. Patients with auditory neuropathy/dys-synchrony lack efferent suppression of transient evoked otoacoustic emissions. J Am Acad Audiol 2003; 14: 302–313.

22. Göksoy C, Utkuçal R. Contralateral white noise-induced enhancement in the guinea pigs MLR: a possible link to directional hearing. Turk J Med Sci 2000; 30: 433–439.

23. Maison S, Micheyl C, Collet L. Sinusoidal amplitude modulation alters contralateral noise suppression of evoked otoacoustic emissions in humans. Neuroscience 1999; 91: 133–138.

24. Gkoritsa E, Korres S, Segas I, Xenelis I, Apostolopoulos N, Ferekidis E. Maturation of the auditory system: 2. Transient otoacoustic emission suppression as an index of the medial olivocochlear bundle maturation. Int J Audiol 2007; 46: 277–286.

25. Oliveira JR, Fernandes JC, Costa Filho OA. Age impact on the efferent system activities in cochlear mechanical properties in normal hearing individuals. Braz J Otorhinolaryngol 2009; 75: 340–344.

26. Berlin CI, Hood LJ, Hurley AE, Wen H, Kemp DT. Binaural noise suppresses linear click-evoked otoacoustic emissions more than ipsilateral or contralateral noise. Hear Res 1995; 87: 96–103.

27. Karabulut H, Hizli S, Dagli M, Karabulut I, Acar B, Celik E, Abaci A, Ozdemir O, Karasen RM. Audiological findings in celiac disease. ORL J Otorhinolaryngol Relat Spec 2011; 73: 82–87.

28. Makishima K, Tanaka K. Pathological changes of the inner ear and central auditory pathway in diabetics. Ann Otol Rhinol Laryngol 1971; 80: 218–228.

29. Bayazit Y, Yilmaz M, Kepekci Y, Mumbuc S, Kanlikama M. Use of the auditory brainstem response testing in the clinical evaluation of the patients with diabetes mellitus. J Neurol Sci 2000; 181: 29–32.