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Evaluation of the Auditory Effects in Controlled and Uncontrolled Type 2 Diabetes Mellitus Using Otoacoustic Emissions

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The hearing loss associated with both insulin dependent (Type 1 DM) or non-insulin dependent diabetes mellitus (Type 2 DM) is described as a bilateral and progressive sensorineural type hearing loss. The hearing loss in diabetic patients may be related to microangiopathy, neuronal degenerations or diabetic encephalopathy.
The purpose of this study was to establish the effect of metabolic control on the subclinical auditory disfunction related with Type 2 DM by utilizing otoacoustic emission. The metabolic control of the DM was measured by using HbA1c. Distortion product otoacoustic emissions (DPOAE) and transient evoked otoacoustic emissions (TEOAE) measurements were accomplished in metabolicolly controlled and uncontrolled diabetic patients with hearing levels better than 30 dB in both groups. Twenty-five patients with Type 2 DM were eligible to participate in the study. The patients were seperated into two groups according to the HgA1c levels. Group 1 and Group 2 consisted controlled Type 2 DM cases having HgA1c<6% and uncontrolled Type 2 DM cases with HgA1c>6%. Therefore; the effects of metabolic control of glycemia on the outer hair cells (OHCs) functions were evaluated in the Type 2 DM patients.
We aimed to investigate the possible role of metabolic control in diabetic patients on the outer hair cells (OHCs) functions.No statistically significant differences were found in the otoacoustic emission measurements of the patients who have metabolicolly controlled diabetes and uncontrolled group. In this study, by using DPOAE (DPgram and DPOAE I/O) and TEOAE measurements. There was no statistically significant effect of metabolic control on hearing loss in diabetic patients. Further comprehensive clinical investigations shoud be done to reveal the effects of metabolic control in diabetes mellitus on hearing.
Key Words: Hearing Loss; Non-Insulin Dependent Diabetes Mellitus; Metabolic Control; Otoacoustic Emission**.**

Kontrollü ve Kontrolsüz Tip 2 Diabetes Mellitusun İşitme Üzerine Etkisinin Otoakustik Emisyon İle Değerlendirilmesi

İnsülin bağımlı (Tip 1 DM) ya da bağımsız (Tip 2 DM) diabetes mellitusta görülebilen işitme kaybı, bilateral, progresif sensörinöral tip işitme kaybı olarak tanımlanmıştır. Bu işitme kaybı mikroanjiopati, nöronal dejenerasyon ya da diabetik ensefalopati ile ilişkili olabilir.
Bu çalışmanın amacı Tip 2 DM'da metabolik kontrolün subklinik işitme fonksiyonları üzerine etkisini otoakustik emisyon ölçümleri ile değerlendirmekti. Diabetes mellitusun metabolik kontrolü glikolize hemoglobin (HgA1c) ile değerlendirildi. İşitmesi normal olan (işitme eşiği ≥30dB), metabolik kontrol sağlanmış ve sağlanamamış diabetik hastalarda distorsiyon ürünü (DPOAE) ve geçici uyarılmış (TEOAE) otoakustik emisyon ölçümleri yapıldı. Bu kriterleri taşıyan 25 hasta çalışmaya dahil edildi ve hastalar HgA1c seviyelerine göre iki gruba ayrıldı. Grup 1'de metabolik kontrolü sağlanmış (HgA1c<%6) hastalar, grup 2'de ise metabolik kontrolü sağlanamamış hastalar (HgA1c>%6) yer aldı. Bu sayede Tip 2 DM'da gliseminin metabolik kontrolünün dış tüylü hücreler üzerindeki etkisinin araştırılması hedeflendi.
Bu çalışmada otoakustik emisyon ölçümleri ile insülin bağımlı olmayan diabetes mellitusta metabolik kontrolün sağlanmamış olması ya da olmamasının, dış tüylü hücre fonksiyonunu etkilemediği istatistiksel olarak gösterilmiştir. Her ne kadar çalışmamızda diabetik hastalarda metabolik kontrolün işitme kaybı üzerine etkisi olmadığı otoakustik emisyon ölçümleri ile gösterilmiş olsa da, bu konuda daha geniş çalışmaların yapılmasına ihtiyaç vardır.
Anahtar Kelimeler: İşitme Kaybı; İnsülin Bağımlı Olmayan Diabetes Mellitus; Metabolik Kontrol; Otoakustik Emisyon**.**

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Introduction

Diabetes mellitus (DM) is a chronic disease of the carbohyrate metabolism that results particular or complete insulin deficiency or resistance. The relationship between diabetes mellitus and hearing loss was first reported by Jordao.[1] and is still matter of controversy. Despite most of the studies showed bilateral progressive high frequency sensorineural hearing impairement in diabetes mellitus,[2-6] some other studies showed that hearing was not effected in diabetic patients.[7-10] In some of these clinical studies, it has been shown that there is a creeping and progressive sesorineural process that effects both of the ears similarly in diabetic patients. In one of our previous study, we detected the decreased DPOAE amplitudes only at 4 KHz in asymptomatic diabetic patients.[11] This finding is not significant, because, the decrease was compatible with the increased noise susceptibility. Hearing impairement in DM may be related to microangiopathy, neuronal degenerations or diabetic encephalopathy. Also the imbalance in glucose metabolism and the hyperactivity of the free oxygen radicals may be blamed for the hearing impairement in DM.[12] These pathological changes and metabolic disorders may cause cochlear, retrocochlear and combined type hearing loss.[13]

Material and Methods

The groups consisted of non-insulin dependent diabetes mellitus (Type 2 DM) patients. These patients were divided into two groups; patients who had provided metabolic control (patients whose HgA1c were <6%) (Group 1) and patients who had not (patients whose HgA1c were >6%) (Group 2). The patients were selected from the Endocrinology Department of the Inonu University Faculty of Medicine. All individuals involved in this study, underwent a full otolaryngological examination and a general medical examination by the same otolaryngologist and diabetologist respectively. The diagnosis of Type 2 DM was verified on the basis of a clinical history and biochemical analysis including glycolized hemoglobin (HgA1c) levels, that indicates absent or low insulin secretion capacity.

Twenty-five patients with Type 2 DM, who have no obvious angiopathic or neuropathic involvement, were eligible to participate in to the study. The study groups consisted of 12 patients (24 ears) with metabolic controlled Type 2 DM (Group 1) and 13 patients (25 ears) with metabolic uncontrolled Type 2 DM (Group 2). In the study group 13 female and 12 male, total 25 patients (49 ears) were evaluated whose age range were between 30-50 (range 44.7). Age and gender is comparable between in both groups. The patients were seperated into two groups according to the HgA1c levels (Group 1: controlled Type 2 diabetes mellitus, HgA1c<6%, Group 2: Uncontrolled Type 2 diabetes mellitus, HgA1c>6%). And hearing tests were done in both ears, only in one patient, the measurements were done only one ear, because of the middle ear pathology on the other side. Therefore; the effects of metabolic control of glycemia on the outer hair cells (OHCs) functions were evaluated in the Type 2 DM patients.

Pure tone and speech audiometry were performed in all patients at 250-8000 Hz frequencies (250-500-1000-2000-4000-8000 Hz) (Interacoustics AC 5 Clinical Audiometer, Denmark). Distortion product otoacoustic emissions (DPOAE) and transient evoked otoacoustic emissions (TEOAE) measurements were done in patients with hearing levels better than 30 dB in both groups. The tympanometric evaluation of the middle ear was done (Zodiac 901 Middle Ear Analyzer, Madsen, Denmark) and only patients with Tip A tympanogram were enrolled in the study. Then, TOAEs and DPOAEs as both DP-grams and input/output (I/O) functions at various frequencies were performed.

OAE measurement

OAE measurements were recorded in a sound-attenuated room. Stimulus presentation, data recording and spectrum analysis were carried out using an ILO 96 cochlear emissions analyzer (Otodynamics, London, UK) with an adequate software (V5 ILO OAE Research, ILO 96, Otodynamics Ltd).

DPOAE and TOAEs of the both groups were measured. All subjects were instructed to be as still as possible during the OAE recordings. Adequate positioning of the measurement probe in the external ear canal was monitored carefully at the beginning of the test by observing the ear canal response on the monitor.

DPOAEs were measured as DP gram and input/output (I/O) functions. For DP-grams the stimulus consisted of two equal pure-tone signals, at two different frequencies, called f1 and f2 (f1<f2), generated simultaneously by a two channel frequency synthesizer. The intensities of primary stimuli were set equilevel ($L_1=L_2$) at 65 dB SPL. The primary-tone frequencies (f_1 and f_2) were adjusted according too $f_2/f_1=1.21$. The f_2 frequencies evaluated in the DP-grams ranged from 1 to 6.3 kHz (1001, 1184, 1416, 1685, 2002, 2380, 2832, 3369, 4004, 4761, 5652, and 6299 Hz). And stimulus levels were setted 65 dB for f1 and 55 dB for f2. Detection threshold and supra-threshold measures in the form of I/O functions were obtained by decreasing the primary tones from 65 to 35 dB SPL in 3 dB steps. The primary tones produced by two separate ear

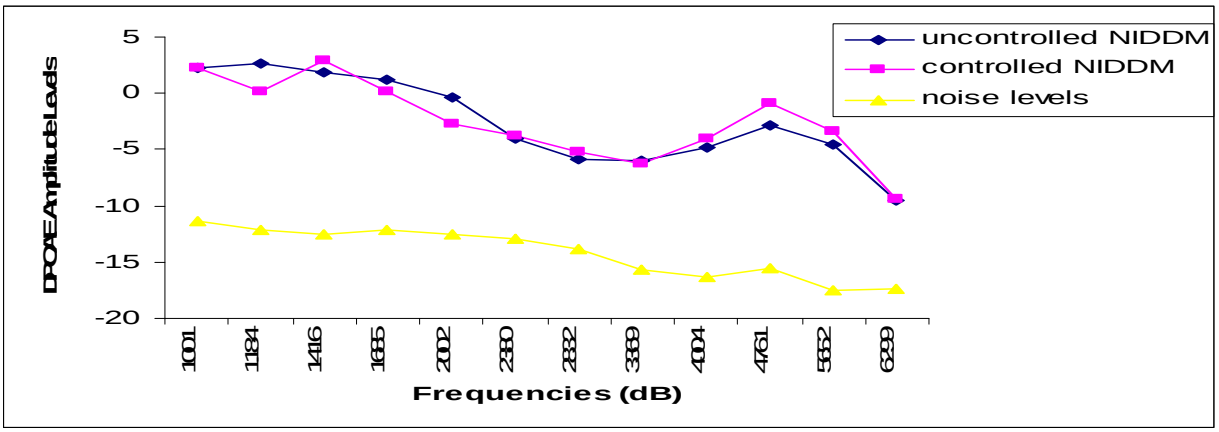
speakers were introduced to the external ear canal. The resolution of DPgram recording was obtained at three points per octave and the stimulus level in the external ear was setted at 80+/-3 dB SPL. The noise-floor level was measured at the frequency, which was 50 Hz above the DPOAE frequency. Either in the DP-gram or in I/O functions the response was accepted if the DPOAE at $2f_1$-f_2 ≥3 dB above the noise floor level at the $2f_1$-f_2+50 Hz frequency.

TEOAE measurements were done at 1, 2, 3, 4 and 5 kHz by continous click stimulus at 80µs. In the outer ear the stimulus level was setted at 80, 3 dB per SPL. The click rate was 50 per s, and post-stimulus analysis was in the range of 2 to 20 ms. A total of 260 sweeps was averaged above the noise rejection level of 47 dB. Stimuli were confered in the non-linear mode, that every fourth click stimulus is inverted and three times greater in amplitude than the three preceding clicks. A significant TEOAE was defined as a response thats amplitude was ≥3 dB above the level of the noise floor. Reproducibility percentages ≥60 percent were taken into account as acceptable for analysis at five successive frequency bands from 1 to 5 kHz.

The independent samples t-test was used to do the statistical analyzes.

Results

No statistically significant difference was found in DP-gram (Graphic 1) and DPOAE I/O (Table 1) measurements between diabetic patients with metabolicolly controlled or uncontrolled. Also, in TEOAE measurements, according to the amplitude levels at all frequencies between controlled and uncontrolled diabetic groups (p>0.05) no statistically significant differences were found.



Graphic 1. DPgram amplitudes of diabetic patients in group 1 (controlled Type 2 DM) and group 2 (uncontrolled Type 2 DM).

Table 1. DPOAE I/O results of the patients in group 1 (controlled diabetes mellitus) and group 2 (uncontrolled diabetes mellitus).

		DPOAE I/O Frequencies										
		35 dB	**38 dB**	**41 dB**	**44 dB**	**47 dB**	**50 dB**	**53 dB**	**56 dB**	**59 dB**	**62 dB**	**65 dB**
1 kHz	**Group 1**	-2,6	-3,8	-3,6	-2,5	-3,2	0,5	0,2	-0,5	1,05	1,1	2,1
	Group 2	-5,7	-4,6	-6,6	-4,6	-4,8	-4,3	-2,3	-1,4	-1,7	0,3	2,06
2 kHz	**Group 1**	-15,3	-13	-13,2	-11,1	-10,3	-7,6	-7,4	-7,1	-5	-2,2	-0,2
	Group 2	-16,7	-15,6	-14,1	-13,4	-12	-9,6	-11	-7,5	-6,9	-4,1	-0,3
3 kHz	**Group 1**	-17,1	-18,1	-14,02	-14,5	-14,1	-12,9	-12,1	-10,3	-7,9	-7,05	-2,6
	Group 2	-16,8	-14,5	-16,4	-15,2	-14,2	-12,8	-12,2	-12,6	-8,1	-6,8	-4,4
4 kHz	**Group 1**	-3,5	-5,6	-6,2	-9,08	-10,8	-12,3	-14,5	-17,1	-18,1	-17,4	-18,2
	Group 2	-4,4	-6,6	-9,4	-10,4	-13,9	-14,2	-15,4	-16,5	-19,3	-19,	-18,4
5 kHz	**Group 1**	0,5	-2,3	-5,1	-7,8	-9,9	-10,7	-13,1	-14,7	-15,3	-16,6	-16,4
	Group 2	-1,2	-4,08	-6,8	-10,7	-11	-12,4	-14,6	-15,8	-17,1	-18,9	-18,4
6 kHz	**Group 1**	-20,1	-18,6	-19,1	-21	-18,6	-17,1	-16,2	-14,4	-10,2	-7,4	-4,6
	Group 2	-17,7	-19,7	-19	-17,5	-16,3	-17,6	-12,8	-12,7	-8,5	-6,2	-3,4

Group 1: Controlled Type 2 DM, HgA1c<%6 (n=24) , **Group 2:** Uncontrolled Type 2 DM, HgA1c>%6 (n=25).

Discussion

Diabetes mellitus (DM) is a chronic disease of the carbohydrate metabolism that effects multiple organ systems. According to the pathological changes and metabolic disequilibriums in diabetes mellitus, cochlear, retro-cochlear or combined type hearing losses can be seen.[13] But the correlation between cochlear dysfunction and diabetic microangiopaty is still matters of controversy. To identify the origin of hearing loss a number of studies were done, but the location of the lesions and the mechanism of deficit is not clear. Cochlear microangiopathy, hyperglycemia of the cerebrospinal fluid or perilymph, auditory neuropathy, and diabetic encephalopathy are suggested pathogenesis for DM-associated sensorineural hearing loss.[14]

The incidence of hearing loss in DM were found in different ranges in different investigations; zero up to 93% in diabetic patients.[1,3,14-15] Hearing loss in DM has been classified as a bilateral sensorineural hearing loss predominantly affecting the high-frequency area, with a gradual onset and progression,[2,4] but the mechanism of this condition is still debating. Wackym et al.,[12] suggested that hearing loss in diabetes were related to the microangiopaty in endolenphatic sac or basillar membrane, whereas Friedman,[16] suggested neuropathic origin. In some of the studies done with otoacoustic emission measurements, the relationships between microangiopathy and cochlear dysfunction were established, most of the studies were found no correlation.

Lisowska et al.,[13] were found that the amplitudes of DPOAE were lower in Type 2 DM patients when compared with control group. However Park,[15] recorded only 8 kHz decreases on DPOAE amplitudes in diabetic patients when compared to control group. In the same study the DPOAE amplitudes of the patients with controlled and uncontrolled diabetes groups were evaluated and a significant differences were recorded at 6 and 8 kHz. In our previous study, hyperlipoprotenemia and Type 2 DM patients with normal hearing were investigated for subclinical auditory dysfunction with evoked-otoacoustic emissions. Statistically significant differences in frequencies were found only at 4 kHz ($p<0.05$). The mean DPOAE amplitudes of the hypertriglyceridemic and Type 2 DM groups were lower than control group at 4 kHz. And no differences were found in the existence of TEOAEs at all frequencies in all groups ($p>0.05$). It has been suggested that in hypertriglyceridemic and diabetic patients the lower DPOAE amplitude at 4 kHz may be demonstrative for the prospective effects of HPL and DM, that is harmonic with sensorineural hearing loss observed in the hyperviscosity and increased noise susceptibility cases.

Simoncelli et al.,[17] showed that EOAE amplitudes were lower in diabetic patients, compared with control group. Sasso,[18] were found that, in diabetic patients the decrease in EOAE amplitudes were more significant with neuropathy, when compared to patients without neuropathy and by this way he explained that the cochlear damage was correlated with the duration of illness, metabolic control levels and peripheric neropathy. In our preliminary study, in DPOAE (DPgram and DPOAE I/O) and TEOAE measurements we did not found statistically significant effect of metabolic control in diabetic patients on hearing loss.
Also in a recent study, Austin et al.,[14] reported that there was greater hearing loss especially in younger DM patients. Significant hearing differences were found at all frequencies for Type 2 DM patients. These researchers noted that HbA1c was less strongly correlated to hearing threshold.

Conclusion

The mechanism of DM on hearing function is still controversial. The most accepted theory is the hearing loss in DM was secondary to the diabetic microangiopathy. Some of the different studies were confirmed the decreases on DPOAE amplitudes, but more compherensive studies should be performed. Further studies are indicated to determine whether efforts to prevent diabetic microangiopathy in Type 2 DM patients can also prevent associated hearing loss and to reveal the effects of metabolic control in diabetes mellitus on hearing.

References

1. Smith TL, Raynor E, Prazma J et al. Insulin-dependent diabetic microangiopathy in the inner ear. Laryngoscope 1995;105:236-40.
2. Kurien M, Thomas K, Bhanu TS. Hearing threshold in patients with diabetes mellitus. J Laryngol Otol 1989;103:164-8.
3. Parving A, Elberling C, Balle V et al. Hearing disorders in patients with insulin-dependent diabetes mellitus. Audiology 1990; 29:113-21.
4. Virtaniemi J, Laakso M, Nuutinen J, et al. Hearing thresholds in insulin-dependent diabetic patients. J Laryngol Otol 1994; 108:837-41.
5. Frisina ST, Mapes F, Kim S, Frisina DR, Frisina RD. Characterization of hearing loss in aged type II diabetics. Hear Res. 2006;211:103-13.
6. Jorgensen MB, Buch NH. Studies on inner-ear function and cranial nerves in diabetics. Acta Otolaryngol 1961;53:350-64.
7. Harner SG. Hearing in adult-onset diabetes mellitus. Otolaryngol Head Neck Surg 1981;89:322-7.
8. Miller JJ, Beck L, Davis A, et al. Hearing loss in patients with diabetic retinopathy. Am J Otolaryngol 1983;4:342-6.
9. Gibbin KP, Davis CG. A hearing survey in diabetes mellitus. Clin Otolaryngol Allied Sci 1981;6:345-50.

10. Sieger A, White NH, Skinner MW, et al. Auditory function in children with diabetes mellitus. Ann Otol Rhinol Laryngol 1983;92:237-41.
11. Erdem T, Ozturan O, Miman MC, et al. Exploration of the early auditory effects of hyperlipoproteinemia and diabetes mellitus using otoacoustic emissions. Eur Arch Otorhinolaryngol 2003;260:62-6.
12. Wackym PA, Linthicum FH. Diabetes mellitus and hearing loss: clinical and histopathologic relationships. Am J Otol 1986;7:176-82.
13. Lisowska G, Namyslowski G, Morawski K, et al. Cochlear dysfunction and diabetic microangiopathy. Scand Audiol Suppl 2001;52:199-203.
14. Austin DF, Konrad-Martin D, Griest S, McMillan GP, McDermott D, Fausti S. Diabetes-related changes in hearing. Laryngoscope 2009;119:1788-96.
15. Park MS, Park SW, Choi JH. Distortion product otoacoustic emissions in diabetics with normal hearing. Scand Audiol Suppl 2001;52:148-51.
16. Friedman SA, Schulman RH, Weiss S. Hearing and diabetic neuropathy. Arch Intern Med 1975;135:573-6.
17. Simoncelli C, Ricci G, Molini E, et al. Evoked acoustic oto-emissions in patients with diabetes mellitus. Ann Otolaryngol Chir Cervicofac 1993;110:255-8.
18. Sasso FC, Salvatore T, Tranchino G, et al. Cochlear dysfunction in type 2 diabetes: a complication independent of neuropathy and acute hyperglycemia. Metabolism 1999;48:1346-50.

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