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Type 2 diabetes and hearing loss in personnel of the Self-Defense Forces

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Abstract

The association of type 2 diabetes with hearing loss was evaluated in middle-aged male personnel of the Self-Defense Forces (SDFs). Hearing loss was defined as the pure-tone average (PTA) of the thresholds frequency at 0.5, 1, 2, and 4 kHz greater than 25 dB hearing levels (HL) in the worse ear. Diabetes status was determined by self-report of physician-diagnosed diabetes or by oral glucose tolerance test (OGTT). Of 699 subjects studied (age 52.9 ± 1.0 years), 103 subjects were classified as having type 2 diabetes. Fasting plasma glucose of diabetic subjects was 120 ± 19 mg/dl. Hearing loss levels were (worse) higher among diabetic subjects compared with subjects with normal glucose tolerance (NGT) (30.7 ± 13.0 dB versus 27.4 ± 12.3 dB, $P = 0.014$). Hearing loss was more prevalent among diabetic subjects than among subjects with normal glucose tolerance (60.2% versus 45.2%, $P = 0.006$). The odds ratio (OR) of type 2 diabetes for the presence of hearing loss was 1.87 (95% confidence interval 1.20–2.91, $P = 0.006$) in a logistic regression analysis adjusted for age, rank, cigarette smoking and ethanol consumption. These results suggest that type 2 diabetes is associated with hearing loss independently of lifestyle factors in middle-aged men.

Keywords: Hearing loss; Diabetes; Cholesterol; Triglyceride; Ethanol

1. Introduction

It is controversial whether hearing loss is more prevalent in type 2 diabetic patients than in non-diabetic subjects. Some reports support the hypothesis [1,2], but the other reports do not [3,4]. A recent large scale study of Dalton et al. [2] shows a significant association between type 2 diabetes and hearing loss (odds ratio (OR), 1.41), although the association became insignificant when age, sex, smoking status and the other potential confounders are taken into account. Ishii et al. [5] showed that type 2 diabetes is associated with severe noise-induced hearing loss (NIHL) in an occupationally noise-exposed subjects (OR 3.9). Subjects studied in these reports are relatively old with mean age of 66 and 63 years, respectively. On the other hand, there are few studies which show the association between type 2 diabetes and hearing loss in middle-aged subjects. In the present study, we analyzed the association between type 2 diabetes and hearing loss in middle-aged male personnel of the Self-Defense Forces (SDFs) with mean age of 53 years (range 51–59).

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2. Methods and materials

Middle-aged male personnel of SDFs who underwent retirement health check were studied ($n = 699$). Serum total cholesterol, triglyceride, creatinine, and γ-glutamyl transferase levels were measured. Oral 75 g glucose tolerance test (OGTT) was done. Body mass index (BMI) was calculated. Blood pressure was measured after at rest in a sitting position with a mercury sphygmomanometer. Subjects with total cholesterol of higher than 220 mg/dl or having medication for it were defined as hypercholesterolemia. Subjects with triglyceride of higher than 200 mg/dl or having medication for it were defined as hypertriglyceridemia. In terms of the new criteria of obesity for Japanese population [6], obesity was defined as BMI of 26.4 kg/m^2 or more, and overweight as BMI of 25.0–26.3 kg/m^2.

Diabetes status was determined by self-report of physician-diagnosed diabetes or by 75 g OGTT. Criteria of the World Health Organization was used to diagnose type 2 diabetes [7]. There were no subjects who were subject to insulin therapy. Of 699 subjects studied (age 52.9 ± 1.0 years), 103 subjects (14.7%) were classified as being type 2 diabetes, 154 subjects (22.0%) as impaired glucose tolerance (IGT), and 442 subjects (63.2%) as normal glucose tolerance (NGT). Diabetic subjects were defined as complicating diabetic neuropathy if they show typical symptom of diabetic neuropathy and impaired vibratory sensation or if ankle jerks were absent. Diabetic retinopathy was diagnosed by ophthalmologists of the hospital. Overt diabetic nephropathy was defined as showing serum creatinine levels of more than 1.2 mg/dl. No subjects studied population fulfilled the definition of diabetic retinopathy, neuropathy or overt nephropathy.

Information about current daily number of cigarettes smoked, physical activity and daily volume of alcoholic beverage consumed was collected using self-administrating questionnaire. Current daily ethanol consumption (milliliters ethanol per day) was calculated from consumed volume of each type of alcoholic beverage. Subjects were categorized into alcohol abstainer, light drinkers (≤30.0 ml ethanol per day), moderate drinkers (30.1–60.0 ml ethanol per day) and heavy drinkers (>60.0 ml ethanol per day) due to daily ethanol consumption. Rank in SDFs was categorized into five categories as previously reported [8], and the rank categories (1–5) used as continuous variables in the logistic regression analysis.

Pure-tone air- and bone-conduction audiometry was performed for each ear at 0.25, 0.5, 1, 2, 3, 4, 6 and 8 kHz was calculated for each ear. Hearing loss was defined as a pure-tone average (PTA) of the thresholds at 0.5, 1, 2 and 4 kHz of >25 dB hearing level (HL) in the worse ear. Low frequency hearing loss was defined as PTA of the thresholds at 0.25, 0.5 and 1 kHz of >25 dB HL in the worse ear. High frequency hearing loss was defined as the PTA of the thresholds at 3, 4 and 6 kHz of >25 dB in the worse ear. Informed consent was obtained to participate in the study. The study protocol was approved by the ethics committee of the hospital.

Table 1
Descriptive characteristic of the subjects

	Subjects with NGT	Subjects with IGT	Subjects with DM	ANOVA *P*-values
n	442	154	103	
Age (years)	52.8 ± 1.0	53.0 ± 1.1	52.9 ± 0.9	0.177
Lifestyle factors				
No. of cigarettes smoked (/day)	10.6 ± 12.4	8.7 ± 13.4	11.6 ± 11.7	0.142
Ethanol consumption (ml/day)	33.2 ± 30.5	32.2 ± 28.2	31.1 ± 23.6	0.784
Metabolic parameters				
Body mass index (kg/m^2)	23.3 ± 2.3	24.2 ± 2.2	24.5 ± 2.8^a	<0.001
Fasting glucose (mg/dl)	97 ± 6	102 ± 11^a	120 ± 19^a	<0.001
Glucose (OGTT, 2 h) (mg/dl)	111 ± 21	157 ± 13^a	227 ± 67^a	<0.001
Total cholesterol (mg/dl)	212 ± 32	214 ± 30	224 ± 37^a	0.002
Triglyceride (mg/dl)	129 ± 59	155 ± 82^a	174 ± 92^a	<0.001
Systolic blood pressure (mmHg)	120 ± 13	124 ± 13^b	125 ± 13^b	<0.001
Serum creatinine (mg/dl)	0.86 ± 0.12	0.87 ± 0.13	0.82 ± 0.14^a	0.001
γ-Glutamyl transferase (IU/l)	45 ± 37	57 ± 61	97 ± 165^a	<0.001
Presence of metabolic disorders				
Obese	9.0%	14.9%	26.2%^{a}	
Obese or overweight	20.6%	35.7%^{a}	47.6%^{a}	
Hypercholesterolemia	38.5%	44.2%	50.5%^{c}	
Hypertriglyceridemia	10.6%	18.2%^{c}	31.1%^{a}	
Hypertension	19.9%	24.0%	24.3%	

Abbreviation: NGT, normal glucose tolerance; IGT, impaired glucose tolerance; DM, type 2 diabetes; OGTT, oral glucose tolerance test.
[a] $P < 0.001$ for subjects with NGT.
[b] $P < 0.01$ for subjects with NGT.
[c] $P < 0.05$ for subjects with NGT.

Table 2
Logistic regression analysis of the association between selected lifestyle factors and presence of hearing loss ($n = 699$)

Selected lifestyle factors	OR (95% CI)	*P*-values
Current smoking	0.99 (0.74–1.35)	0.992
No. of cigarettes smoked, Δ10/day	1.03(0.92–1.16)	0.620
Ethanol consumption		
Ethanol abstainer (0 ml/day)	1.21 (0.76–1.92)	0.416
Light drinker (≤30.0 ml/day)	1.00 (reference)	–
Moderate drinker (30.1–60.0 ml/day)	1.12 (0.95–2.11)	0.087
Heavy drinker (>60.0 ml/day)	1.69 (1.14–2.52)	0.010
Higher rank in Self-Defense Forces	0.91 (0.81–1.02)	0.104

Abbreviation: OR, odds ratio; CI, confidence interval.

A logistic regression analysis was performed with the presence of lifestyle factors and metabolic disorders as independent variables and the presence of hearing loss as dependent variables. A linear regression analysis was performed to analyze the association between hearing loss and metabolic parameters. Comparison of mean values between multiple pairs of groups were accomplished by application of Fisher's protected least-significant (PLSD) post hoc test, if there were differences by one-way ANOVA. Continuous variables were presented as mean ± S.D. Statistical analysis was done using Stat View, version 5.0 (SAS Institute Inc., Cary, IL, USA).

3. Results

Descriptive characteristics of the subjects were shown in Table 1. Body mass index, fasting and 2 h (OGTT) plasma glucose, total cholesterol, triglyceride, γ-glutamyl transferase and systolic blood pressure of diabetic subjects were higher than those of subjects with NGT, respectively (Table 1). There were no significant differences in age or lifestyle factors between NGT subjects, IGT subjects and diabetic subjects.

Association between lifestyle factors and the presence of hearing loss was analyzed in a logistic regression model. Neither current smoking status nor number of cigarettes smoked was associated with the presence of hearing loss (Table 2). Light drinking (≤30.0 ml ethanol per day) showed protective effects against hearing loss. The height of rank in SDFs was inversely but insignificantly associated with the presence of hearing loss.

In a simple logistic regression analysis, prevalence of type 2 diabetes but not IGT was associated with the presence of hearing loss (Table 3). Hypertriglyceridemia was significantly and hypercholesterolemia was marginally associated with the presence of hearing loss. None of overweight, obesity or hypertension was associated with the presence of hearing loss. Similar results were obtained in a logistic regression model adjusted for age, rank in SDFs, daily number of cigarettes smoked and daily ethanol consumption (Table 3).

In a linear regression analysis, 2 h (OGTT) plasma glucose and serum γ-glutamyl transferase activity, a marker of oxidative stress [9], but not fasting plasma glucose, BMI or systolic blood pressure correlated with levels of hearing loss (dB) (Table 4). Serum total cholesterol and triglyceride marginally correlated with levels of hearing loss (dB).

Levels of hearing loss (dB) was greater among diabetic subjects than among NGT subjects (Table 5). Levels of hearing loss (dB) were more than 3 dB larger at high frequency range (2–8 kHz) among diabetic subjects than among NGT subjects, whereas the differences were smaller in lower frequency range (0.25–1 kHz) (Fig. 1).

Table 3
Logistic regression analysis of the association between presence of metabolic disorders and presence of hearing loss ($n = 699$)

Metabolic disorders	OR (95% CI)	*P*-values	[a]OR (95% CI)	[a]*P*-values
Glucose tolerance				
IGT	1.12 (0.78–1.62)	0.548	1.16 (0.80–1.68)	0.433
Type 2 diabetes	1.83 (1.18–2.83)	0.007	1.87 (1.20–2.91)	0.006
Obesity				
Overweight	1.09 (0.77–1.54)	0.631	1.10 (0.77–1.55)	0.602
Obese	0.97 (0.61–1.52)	0.878	1.04 (0.65–1.64)	0.882
Hypercholesterolemia	1.35 (1.00–1.82)	0.053	1.33 (0.98–1.81)	0.063
Hypertriglyceridemia	1.60 (1.05–2.43)	0.027	1.58 (1.04–2.40)	0.034
Hypertension	1.07 (0.74–1.53)	0.727	1.04 (0.72–1.49)	0.851

Abbreviation: OR, odds ratio; CI, confidence interval; IGT, impaired glucose tolerance.
[a] Values were adjusted for age, rank in the Self-Defense Forces and lifestyle factors including daily number of cigarettes smoked and daily ethanol consumption.

Table 4
Linear regression analysis of the association between metabolic parameters and hearing loss levels (dB) ($n = 699$)

Metabolic parameters	Standard regression coefficient	*P*-values	[a]Standard regression coefficient	[a]*P*-values
Fasting plasma glucose	0.052	0.171	0.045	0.243
Glucose (OGTT, 2 h)	0.078	0.044	0.077	0.046
Body mass index	0.002	0.956	0.003	0.934
Total cholesterol	0.073	0.053	0.071	0.061
Triglyceride	0.071	0.061	0.064	0.093
Systolic blood pressure	0.016	0.669	0.010	0.790
γ-Glutamyl transferase	0.093	0.014	0.077	0.046

[a] Values were adjusted for age, rank in the Self-Defense Forces and lifestyle factors including daily number of cigarettes smoked and daily ethanol consumption.

Table 5
Comparison of degree and prevalence of hearing loss among subjects with normal glucose tolerance (NGT), impaired glucose tolerance (IGT), and type 2 diabetes (DM)

	Subjects with NGT $n = 442$	Subjects with IGT $n = 154$	Subjects with DM $n = 103$	ANOVA *P*-values
Hearing loss (average thresholds in the worse ear, dB)				
Hearing loss	27.4 ± 12.3	27.8 ± 11.6	30.7 ± 13.0*	0.048
High frequency hearing loss	39.3 ± 20.3	39.8 ± 20.7	43.7 ± 21.3	0.146
Low frequency hearing loss	23.0 ± 10.5	22.6 ± 9.5	25.0 ± 11.0	0.157
Prevalence of hearing loss (average thresholds >25 dB in the worse ear)				
Hearing loss	45.2%	48.1%	60.2%*	
High frequency hearing loss	67.4%	70.1%	76.7%	
Low frequency hearing loss	24.4%	24.7%	34.0%*	

* $P < 0.05$ for subjects with NGT.

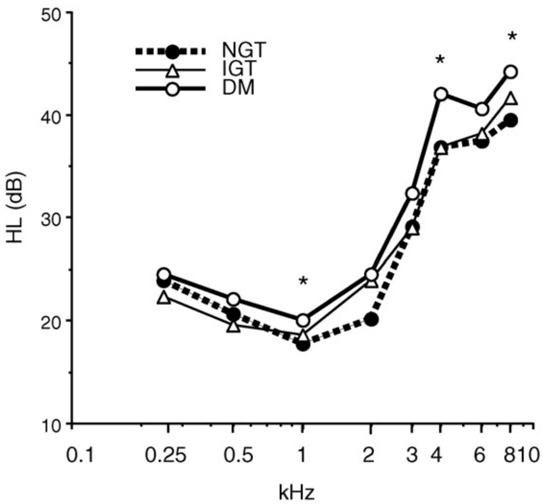

Fig. 1. Frequency thresholds of subjects with normal glucose tolerance (NGT, $n = 442$), impaired glucose tolerance (IGT, $n = 154$), and type 2 diabetes (DM, $n = 103$). The thresholds show average values of right and left ears. Hearing loss was more than 3 dB larger among diabetic subjects than among NGT subjects, at 2, 3, 4, 6 and 8 kHz. *$P < 0.05$ for subjects with NGT.

Prevalence rate of hearing loss was higher among diabetic subjects than among NGT subjects (Table 5).

4. Discussion

The results of the present study suggest that type 2 diabetes is associated with the presence of hearing loss independently of age, rank and lifestyle factors in middle-aged Japanese men who belong to SDFs. The differences in hearing loss (dB) were larger in the high frequencies (Table 4 and Fig. 1). There are several studies which examined the association between type 2 diabetes and hearing loss [1,2,5]. In those studies, however, subjects are relatively old (mean age ≥ 63 years) [2,5] or subjects size are relatively small ($n = 60$) [1]. Thus, the present report appears to be the only report which showed the association between type 2 diabetes and hearing loss in middle-aged men in a relatively large scale. In addition, as far as we know, this is the first report which showed that hypertriglyceridemia is associated with the presence of hearing loss independently of age. The results are consistent with the previous report by others [10].

Several studies show that control status of diabetes [11], and presence of diabetic retinopathy [12,13], nephropathy [2] and neuropathy [14] are associated with hearing loss. But, at the same time negative findings have been reported as to the association of hearing loss with control status [2], retinopathy [2,15,16], nephropathy [16] and neuropathy [16]. In the present study, no diabetic subjects showed overt diabetic retinopathy, neuropathy or overt nephropathy. But, it is not negligible that subclinical complications might contribute to the association between diabetes and hearing loss, because the criteria of diabetic neuropathy and nephropathy adopted in the present study were not strict ones. We could not clarify the association between control status of diabetes and hearing loss, because HbA_{1c} levels were not estimated. It is possible, however, that post-prandial hyperglycemia contribute to the development of hearing loss, because 2 h (OGTT) plasma glucose correlated with the levels of hearing loss (dB) (Table 4). Insulin resistance does not appear to contribute to the pathogenesis of the hearing loss, because IGT was not associated with the presence of hearing loss (Table 3).

The mechanism by which diabetic subjects show higher prevalence rate of hearing loss is not clear. Diabetes is associated with a number of microvascular complications affecting commonly the eyes and kidneys of the diabetic patients. Microvascular abnormalities may also affect the ears and hearing of individuals with diabetes. Because, it has been shown that basement membrane thickening consistent with diabetic microangiopathy was observed in insulin-dependent diabetic rats but not in non-diabetic rats [17], and that diabetic sensorineural hearing loss results from microangiopathic involvement of endolymphatic sac and/or basilar membrane vessels [18]. It is also reported that combination of non-insulin-dependent diabetes and noise exposure is associated with the microangiopathy in the inner ear [19]. Because most SDFs personnel are exposed to noise at work, they have higher risk of acquiring noise-induced hearing loss compared with unexposed subjects. Indeed, hearing loss was larger in the high frequencies in this population (Fig. 1). The effects of diabetes on hearing loss levels (dB) were larger among diabetic subjects than among subjects with NGT in the high frequencies (Fig. 1). These results suggest that diabetes facilitates the development of hearing loss in noise-exposed personnel. The findings are consistent with the previous report which shows that occupationally noise-exposed diabetic subjects are more likely to develop severe NIHL than non-diabetic noise-exposed controls [5].

We cannot specify the legion which is responsible for the diabetes-associated hearing loss. Although auditory brainstem potentials were not examined in the present study, it is conceivable that both cochlea and the central auditory pathways are included in the pathogenesis, because both cites are implicated for the hearing impairment in diabetic subjects [20–22] and for the development of NIHL [23].

Elevated plasma glucose [24,25] and serum triglyceride [26,27] are associated with increased oxidative stress, whereas oxidative stress is implicated for the pathogenesis of NIHL [28–31]. The association between diabetes, hypertriglyceridemia and NIHL might be explained by oxidative stress, which is reported to be increased in subjects with diabetes [24] and subjects with hypertriglyceridemia [26,27]. In the present study, both serum triglyceride and 2 h (OGTT) plasma glucose correlated with the levels of hearing loss (dB) (Table 4), and with serum γ-glutamyl transferase (data not shown), a marker of oxidative stress [9]. Interestingly, serum γ-glutamyl transferase activity correlated with the levels of hearing loss (dB) (Table 4).

Patients with maternally inherited diabetes and deafness (MIDD) and those with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) [32,33] show both diabetes and hearing loss, due to a point mutation of mitochondrial DNA (A3243G). These syndromes may partly explain the observed association between diabetes and hearing loss. Contribution of this mechanism, however, appears to be minimal, because the prevalence rate of MIDD in diabetic patients is estimated to be no more than 0.9% in Japanese [34].

Merit of the present study is the homogeneity of the subjects in terms of age, gender, ethnicity and occupational background. They were all 50s and relatively healthy, and most subjects are exposed to noise associated with military activity. The homogeneity of the subjects studied would make the interpretation of the results somewhat clearer.

One of the limitations of the present study is that individual history of noise exposure was not collected or taken into account. The difference in individual noise exposure may confound the association between diabetes and hearing loss. Another limitation of the present study is its modality. Because of the cross-sectional design, we could not clarify cause–effect relationship. Thus, longitudinal studies are necessary to confirm the observed temporal relationship between diabetes and hearing loss. The results of the present study may not be simply extrapolated to other populations, because the studied population exclusively consist of occupationally noise-exposed personnel.

In conclusion, type 2 diabetes was associated with hearing loss in middle-aged male personnel of SDFs independently of age, rank and lifestyle factors.

References

[1] M. Kurien, K. Thomas, T.S. Bhanu, Hearing threshold in patients with diabetes mellitus, J. Laryngol. Otol. 103 (1989) 164–168.

[2] D.S. Dalton, K.J. Cruickshanks, R. Klein, B.E. Klein, T.L. Wiley, Association of NIDDM and hearing loss, Diabetes Care 21 (1998) 1540–1544.

[3] K.P. Gibbin, C.G. Davis, A hearing survey in diabetes mellitus, Clin. Otolaryngol. Allied Sci. 6 (1981) 345–350.

[4] M.J. Hodgson, E. Talbott, J.C. Helmkamp, L.H. Kuller, Diabetes, noise exposure, and hearing loss, J. Occup. Med. 29 (1987) 576–579.

[5] E.K. Ishii, E.O. Talbott, R.C. Findlay, J.A. D'Antonio, L.H. Kuller, Is NIDDM a risk factor for noise-induced hearing loss in an occupationally noise exposed cohort? Sci. Total Environ. 127 (1992) 155–165.

[6] The Examination Committee of Criteria for 'Obesity Disease' in Japan. Japan Society for the Study of Obesity, New criteria for 'Obesity Disease' in Japan, Circ. J. 66 (2002) 987–992.

[7] WHO Consultation, Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Geneva, Switzerland, World Health Organization, 1999.

[8] H. Sakuta, T. Suzuki, Rank in Self-Defense Forces and risk factors for atherosclerotic disease, Mil. Med. 170 (2005) 820–823.

[9] J.B. Whitfield, Gamma glutamyl transferase, Crit. Rev. Clin. Lab. Sci. 38 (2001) 263–355.

[10] N.S. Jones, A. Davis, A retrospective case-controlled study of 1490 consecutive patients presenting to a neuro-otology clinic to examine the relationship between blood lipid levels and sensorioneural hearing loss, Clin. Otolaryngol. Allied Sci. 25 (2000) 511–517.

[11] V. Kakarlapudi, R. Sawyer, H. Staecker, The effect of diabetes on sensorioneural hearing loss, Otol. Neurotol. 24 (2003) 382–386.

[12] S.A. Axelsson, S.E. Fagerberg, Auditory function in diabetics, Acta Otolaryngol. 66 (1968) 49–64.

[13] J.P. Ferrer, O. Biurrun, J. Lorente, J.I. Conget, R. de Espana, E. Esmatjes, et al., Auditory function in young patients with type 1 diabetes mellitus, Diabetes Res. Clin. Pract. 11 (1991) 17–22.

[14] S.A. Friedman, R.H. Schulman, S. Weiss, Hearing and diabetic neuropathy, Arch. Intern. Med. 135 (1975) 573–576.

[15] R.P. Stolk, L.J. Boomsma, Prevalence of deafness is increased in patients with type 2 diabetes in the Netherlands, Diabetes Care 22 (1999) 180.

[16] A.S. Kashyap, S. Kashyap, Increased prevalence of impaired hearing in patients with type 2 diabetes in western India, Postgrad. Med. J. 76 (2000) 38.

[17] T.L. Smith, E. Raynor, J. Prazma, J.E. Buenting, H.C. Pillsbury, Insulin-dependent diabetic microangiopathy in the inner ear, Laryngoscope 105 (1995) 236–240.

[18] P.A. Wackym, F.H. Linthicum Jr., Diabetes mellitus and hearing loss: clinical and histopathologic relationships, Am. J. Otol. 7 (1986) 176–182.

[19] C.T. McQueen, A. Baxter, T.L. Smith, E. Raynor, S.M. Yoon, J. Prazma, et al., Non-insulin-dependent diabetic microangiopathy in the inner ear, J. Laryngol. Otol. 113 (1999) 13–18.

[20] G. Lisowska, G. Namyslowski, K. Morawski, K. Strojek, Early identification of hearing impariement in patients with type 1 diabetes mellitus, Otol. Neurotol. 22 (2001) 316–320.

[21] F.C. Sasso, T. Salvatore, G. Tranchino, D. Cozzolino, A.A. Caruso, M. Persico, et al., Cochlear dysfunction in type 2 diabetes: a complication independent of neuropathy and acute hyperglycemia, Metabolism 48 (1999) 1346–1350.

[22] Y.M. Huang, C.Y. Pan, R. Gu, X.H. Cai, L.M. Yu, C.Y. Qiu, Hearing impairment in diabetics, Chin. Med. J. 105 (1992) 44–48.

[23] M. Fabiani, A. Mattioni, M. Saponara, A. Cordier, Auditory evoked potentials for the assessment of noise induced hearing loss, Scand. Audiol. Suppl. 48 (1998) 147–153.

[24] A. Ceriello, F. Mercuri, L. Quagliaro, R. Assaloni, E. Motz, L. Tonutti, et al., Detection of nitrotyrosine in the diabetic plasma: evidence of oxidative stress, Diabetologia 44 (2001) 834–838.

[25] H. Kawano, T. Motoyama, O. Hirashima, N. Hirai, Y. Miyao, T. Sakamoto, et al., Hyperglycemia rapidly suppresses flow-mediated endothelium-dependent vasodilation of brachial artery, J. Am. Coll. Cardiol. 34 (1999) 146–154.

[26] J.H. Bae, E. Bassenge, K.B. Kim, Y.N. Kim, K.S. Kim, H.J. Lee, et al., Postprandial hypertriglyceridemia impairs endothelial function by enhanced oxidant stress, Atherosclerosis 155 (2001) 517–523.

[27] A. Ceriello, L. Quagliaro, L. Piconi, R. Assaloni, R. Da Ros, A. Maier, et al., Effect of postprandial hypertriglyceridemia and hyperglycemia on circulating adhesion molecules and oxidative stress generation and the possible role of simvastatin treatment, Diabetes 53 (2004) 701–710.

[28] R.D. Kopke, J.K. Coleman, J. Liu, K.C. Campbell, R.H. Riffenburgh, Candidate's thesis: enhancing intrinsic cochlear stress defenses to reduce noise-induced hearing loss, Laryngoscope 112 (2002) 1515–1532.

[29] I. Kaygusuz, A. Ozturk, B. Ustundag, S. Yalcin, Role of free oxygen radicals in noise-related hearing impairment, Hear Res. 162 (2001) 43–47.

[30] L.D. Fechter, S.F. Klis, N.A. Shirwany, T.G. Moore, D.B. Rao, Acrylonitrile produces transient cochlear function loss and potentiates permanent noise-induced hearing loss, Toxicol. Sci. 75 (2003) 117–123.

[31] T. Yamasoba, A. Pourbakht, T. Sakamoto, M. Suzuki, Ebselen prevents noise-induced excitotoxicity and temporary threshold shift, Neurosci. Lett. 380 (2005) 234–238.

[32] T. Takeshima, K. Nakashima, MIDD and MELAS: a clinical spectrum, Intern. Med. 44 (2005) 276–277.

[33] P.J. Guillausseau, P. Massin, D. Dubois-LaForgue, J. Timsit, M. Virally, H. Gin, et al., Maternally inherited diabetes and deafness: a multicenter study, Ann. Intern. Med. 134 (2001) 721–728.

[34] S. Otabe, H. Sakura, K. Shimokawa, Y. Mori, H. Kadowaki, K. Yasuda, et al., The high prevalence of the diabetic patients with a mutation in the mitochondrial gene in Japan, J. Clin. Endocrinol. Metab. 79 (1994) 768–771.