Hearing Thresholds In Patients With Diabetes
F Salvinelli, A Miele, M Casale, F Greco, L D'Ascanio, L Firrisi, M Trivelli, T Petitti, L Aloe, P Pozzilli

Abstract
Despite a number of studies, conflicting results on hearing function in diabetic patients with well-controlled disease are described in the medical literature. Aim of this study is to investigate hearing function in well-characterised diabetic patients and to evaluate the role of potentially relevant factors. We enrolled 38 diabetic patients, 15 with type 1 diabetes and 23 with type 2. In all subjects we evaluated the disease duration, metabolic control (HbA1c) and retinopathy degree. ENT assessment and pure tone audiometry (PTA) were performed and auditory thresholds were compared to those obtained in 38 age-matched healthy controls. Patients' mean HbA1c was 7.553% and only mild-moderate non-proliferative retinopathy was observed. Auditory thresholds in both type 1 and type 2 diabetic patients did not differ from controls. Auditory function in diabetic patients was not related to the type of diabetes or duration of disease. We conclude that metabolically well-controlled diabetic patients did not show reduced hearing function, at least clinically at pure tone audiometry. Possible explanations for our data are discussed.

INTRODUCTION
Diabetes is a chronic metabolic disorder characterized by hyperglycaemia and alterations in fat and protein metabolism (Nathan, 1996). It is associated with a number of microvascular complications affecting most commonly eyes and kidneys, and with diffuse polyneuropathy involving somatic and autonomic nerve fibers (Young et al., 1986).

The relationship between diabetes and hearing thresholds deserves special attention. Despite a number of studies on hearing function in diabetic patients with well-controlled disease, conflicting data still exist on a possible association between bilateral progressive high frequency hearing loss and diabetes. Several authors reported a higher incidence of hearing loss in diabetic patients in comparison to the general population (Kurien, 1989; Cullen and Cinnamond, 1993; Axellsson and Fagerberg, 1968; Kasemsuwan et al., 2001, Tomisawa, 2000; Celik et al., 1996), whereas no difference in pure tone audiometry (PTA) between diabetic patients and controls was observed in other studies (Gibbin and Davis, 1996). Patients with severe peripheral neuropathy or retinopathy seem to have an increased risk of hearing loss (Miller et al., 1983; De Espana, 1995), though no association between duration or severity of diabetes and hearing impairment has been reported as well (Kasemsuwan et al., 2001, Gibbin and Davis, 1996). On the contrary poor metabolic control (Kasemsuwan et al., 2001, Gibbin and Davis, 1996, Dalton et al., 1998) and hypoglycemic episodes were shown not to be associated with increased hearing thresholds (Ferrer et al., 1991; Virtaniemi et al., 1994; Tay et al., 1995).

In general, hearing loss was reported to be more frequent in patients with type 1 diabetes than in those with type 2 (Tay et al., 1995).

Hearing loss in diabetes may be the result of microangiopathy in the inner ear (Tomisawa, 2000), neuronal degeneration (Toth et al., 2001) or diabetic encephalopathy, but it could also be due to deranged glucose metabolism and hyperactivity of oxygen free-radicals (Tomisawa, 2000). Rosen and Davis, who sought a possible correlation between sensorineural hearing loss and microangiopathy in diabetic patients, conclude that hearing loss is definitely common in these patients (Rosen et al., 1971). Histological studies of the temporal bones showed changes in the small blood vessels of stria vascularis and modiolus. Vascular changes in the inner ear are regarded as the most important changes in diabetes, and hypertrophy of the intima or arteriosclerosis may be the cause of blood vessels narrowing in the inner (Schuknecht, 1993; Tomisawa, 2000). On the contrary, Lisowska et al. did not find any association between microvascular alterations and cochlear dysfunction (Lisowska et al. 2001). Finally, a study...
Hearing Thresholds In Patients With Diabetes

on the insulin role on glucose uptake in the inner ear suggests that in animals insulin does not regulate glucose uptake in the Corti's organ (Shuncun and Jochen, 1990), thus indicating that, at least in animals, Corti's organ is freely permeable to glucose. Despite the number of studies so far published, no final conclusion on hearing thresholds in diabetes can be drawn.

Aim of this study is to investigate hearing function in well-characterised diabetic patients and to evaluate the role of potentially relevant factors such as type of diabetes, disease duration, metabolic control and presence of complications.

PATIENTS AND METHODS

Seventy-five consecutive patients with diagnosis of diabetes attending the ENT clinic at University Campus Bio-Medico were enrolled in the study. Criteria for exclusion were history of excessive recreational or occupational noise exposure, ototoxic drug usage, severe head injury, family history of deafness or middle ear abnormality, ear discharge, ear surgery, antiblastic chemotherapy, head or neck radiotherapy, recent (less than 1 month) high respiratory tract infection, autoimmune diseases and hypertension.

Patients with conductive or mixed-type audiometric curves with an air-bone gap higher than 15 dB were also excluded. According to the exclusion criteria, thirty-eight patients (group 1) were maintained in our study. None of our patients showed diabetic neuropathy.

Diabetic patients were sub-grouped into group 1A, type 1 diabetic subjects (15 patients; mean age 34.1 yrs), and group 1B, type 2 diabetic subjects (23 patients; mean age 66.1 yrs).

In our patients were evaluated metabolic control (according to HbA1c level with cut-off of 7.4%), duration of disease (0-2 years, 3-10 years, 11-20 years, and >21 years) and degree of retinopathy (1 = mild to moderate non-proliferative; 2 = moderate to severe non proliferative; 3 = severe and very severe non-proliferative; 4 = proliferative) (Hudson, 1996) as a sign of microangiopathy.

Clinical otological examination and pure tone audiogram (PTA) from 250 Hz to 4 KHz were performed as well. The audiometric tests were conform to the specification of ISO 8253 (“Acoustics Audiometric Test Methods: Basic pure tone and bone conduction threshold audiometry.” International Organization for Standardization Geneva Switzerland). The British Society of Audiology recommended procedures for manual audiometry were used (Ito et al., 1993).

Audiometric results in diabetic patients were compared to those obtained in the control group (group 2), consisting of 38 healthy subjects. They were sub-grouped into group 2A, group 1A age-matched controls (15 subjects; mean age 35 yrs), and group 2B, group 1B age-matched controls (23 subjects; mean age 65.8 yrs).

Data were analysed using the Statistical Package for Social Sciences Software (SPSS 10.0 for Windows, SPSS Inc., Chicago, IL, USA). Data are shown as median and interquartile range (25° and 75°) and 1.5 interquartile range. Non-parametric (Manny-Whitney) tests were used to compare different values. Scores with P<0.05 were considered as statistically significant.

RESULTS

Patients of group 1A showed median hearing thresholds between 6.25 (interquartile range 5-10) dBHL and 10 (interquartile range 5-11.87) dBHL, with poorest threshold at 4000 Hz. Those of group 2A were between 5 (interquartile range 5-10) and 10 (interquartile range 10-12.5) dBHL, with poorest threshold at 250 Hz (Fig. 1). Patients belonging to group 1B had median hearing thresholds between 10 (interquartile range 5-13.12) dBHL and 25 (interquartile range 10-30) dBHL, with poorest threshold at 4000 Hz. Those of group 2B showed median hearing thresholds between 12.5 (interquartile range 5-23.12) dBHL and 28.75 (interquartile range 15-36.25) dBHL, with poorest threshold at 4000 Hz (Fig. 2).

Figure 1

Figure 1: Median hearing thresholds in type 1 diabetic patients (group 1A) and controls (group 2A).
No statistically significant difference in hearing function was found between the diabetic patients' groups (1A and 1B) and the corresponding control groups (2A and 2B respectively).

As to metabolic control, our patients' mean HbA1c was 7.553% (±1.448%). No statistical correlation was found between hearing thresholds and HbA1c. Moreover, when patients with type 1 diabetes were sub-grouped according to metabolic control, median hearing thresholds of well-controlled patients were between 5 (interquartile range 5-10) dBHL and 10 (interquartile range 7.5-12.5) dBHL, with poorest threshold at 250 Hz. The group of poorly-controlled patients showed median hearing thresholds between 7.5 (interquartile range 5-7.5) dBHL and 10 (interquartile range 7.5-10) dBHL, with poorest threshold at 250 Hz (Fig.3). However the difference was not statistically significant.

In type 2 diabetic patients, median hearing thresholds of well-controlled patients were between 10 (interquartile range 5-30) dBHL and 30 (interquartile range 11.25-32.5) dBHL, with poorest threshold at 4000 Hz. The group of poorly-controlled patients had median hearing thresholds between 10 (interquartile range 5-12.5) dBHL and 20 (interquartile range 10-25) dBHL, with poorest threshold at 4000 Hz (Fig.4). Again the difference was not statistically significant.

As to duration of disease, no significant difference was observed among median hearing thresholds in the different diabetes duration groups in both type 1 and type 2 diabetes (Fig. 5 and 6).

Only 16 patients showed diabetic retinopathy: 9 presented a degree 1 retinopathy, and 7 a degree 2; none of them...
suffered from severe angiopathy. Moreover no statistically significant difference in hearing function was found in the different retinopathy-related groups.

**DISCUSSION**

Our data did not show a clinical reduction of hearing function in diabetic patients compared to controls, in contrast to what reported by most international literature (Axelsson and Fagerberg, 1968; De Espana et al., 1995; Celik et al., 1996; Kasemsuwan et al., 2001). Moreover we did not find any correlation between duration of diabetes and hearing level, in disagreement with De Espana et al. (De Espana et al., 1995), who reported a positive correlation between hearing loss and disease duration. No correlation was observed between hearing thresholds and type of diabetes, presence of microangiopathy (retinopathy) and patients’ age.

As to glycemia evaluation, our patients showed a good metabolic control (mean HbA1c 7.553%) and none of them suffered from severe retinopathy (in a scale from 1 to 4, our patients’ maximum score was 2). Though a severe angiopathy was not noted, a possible sub-clinical inner ear microangiopathy without evident hearing function impairment can not be excluded.

Normal hearing thresholds in our diabetic patients may be related to various factors. Firstly the existence, in the inner ear, of a blood-brain-like barrier (blood-labyrinth barrier), which would maintain the constant composition of endolymph and perilymph (Carlisle et al., 1990; Ito et al., 1993). Glucose flow from endolymph to perilymph would be regulated by GLUT1 glucose transporters. It is possible that glucose transport in the endolymphatic space is an auto-regulated process protecting the inner ear from hyperglycemia (Ito et al., 1993).

Secondly, a role of neurotrophines can be proposed. A reduction of Nerve Growth Factor (NGF) in neuropathic diabetics with limitation of axonal retrograde transport and nervous fibres demyelinization has been reported (Tomlinson et al., 1996). NGF is a neurotrophic factor essential for survival, development, and maintenance of peripheral and central nervous system. It also exerts neurotrophic and biological activity on non-neural cells (Bonini et al., 1999). A NGF decrease plays an important role in the pathogenesis of diabetic neuropathy (Chiarelli et al., 2000); Recent data from our group correlate presence of sensorineural hearing loss with reduction of serum levels of NGF (Salvinelli et al., 2002); therefore a reduction of NGF may be involved in sensorineural hearing loss in diabetic patients, especially in those suffering from severe diabetic neuropathy.

**CONCLUSION**

Diabetic patients preserve a normal hearing function until diabetic neuropathy has developed; since then the nerve degeneration related to a decrease in circulating NGF leads to a progressive impairment of the auditory pathway with consequent hearing deficit. In addition, metabolically well-controlled diabetic patients do not suffer from hearing impairment, at least clinically at pure tone audiometry. However, a sub-clinical inner ear impairment, affecting the inner ear vascular microcircuit, cochlea and VIII cranial nerve, without clear hearing deficit may be possible.

Further studies are in course at our clinic to investigate subclinical ear involvement, and in particular inner ear and auditory nerve microlesions, through otocochlear emissions (TEOAES and Distortion Products) and auditory brainstem responses (ABRS), in order to evaluate the physiopathological bases of normal hearing function in metabolically well-controlled diabetic patients.

**ACKNOWLEDGEMENTS**

This work was supported by a grant from University CBM. The assistance of Mrs Jennifer Nisita is greatly acknowledged.

**CORRESPONDENCE TO**

Angela Miele, MD Area of Otolaryngology University School of Medicine ADDRESS: Campus Bio-Medico – Rome Via Longoni, 69/83 – 00155 Rome (Italy) Tel.: 0039622541740 – Fax: 0039622541456 E-mail: a.miele@unicampus.it

**References**

Hearing Thresholds In Patients With Diabetes

Hearing Thresholds In Patients With Diabetes

Author Information

Fabrizio Salvinelli, PhD
Department of Otolaryngology, University Campus Bio-Medico

Angela Miele, MD
Department of Otolaryngology, University Campus Bio-Medico

Manuele Casale, MD
Department of Otolaryngology, University Campus Bio-Medico

Fabio Greco, MD
Department of Otolaryngology, University Campus Bio-Medico

Luca D'Ascanio
Department of Otolaryngology, University Campus Bio-Medico

Luca Firrisi, MD
Department of Otolaryngology, University Campus Bio-Medico

Maurizio Trivelli, MD
Department of Otolaryngology, University Campus Bio-Medico

Tommasangelo Petitti, MD
Medical Directorate, Interdisciplinary Center for Biomedical Research (CIR), University Campus Bio-Medico

Luigi Aloe, PhD
Institute of Neurobiology and Molecular Medicine CNR

Paolo Pozzilli, PhD
Unit of Endocrinology and Diabetes, University Campus Bio-Medico