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RESEARCH

HEARING IMPAIRMENT AND TINNITUS SEVERITY IN PARKINSON'S DISEASE

ABSTRACT

Introduction: Our main objective in this study was to evaluate hearing impairment and the severity of tinnitus in patients with Parkinson's disease as well as to compare the results with healthy controls.

Materials and Methods: This study involved 43 patients with Parkinson's disease and a control group of 45 healthy age- and sex-matched individuals. Audiological examination was conducted using pure-tone audiometer and tinnitus severity was assessed by tinnitus severity index. Air conduction thresholds and tinnitus severity index scores were compared statistically.

Results: Compared with the control group, the Parkinson's disease group had significantly elevated pure-tone audiometer thresholds in 6000 and 8000 Hz, but there were no significant differences at other frequencies. The tinnitus severity index scores were significantly higher in the Parkinson's disease group than the control group ($p<0.001$).

Conclusion: The increased prevalence of hearing loss at higher frequencies and the greater severity of tinnitus among patients with Parkinson's disease were the most notable findings. We recommend that these patients be monitored more closely for auditory dysfunction, and appropriate therapy should be provided. Our results show that auditory dysfunction may be considered a non-motor symptom of Parkinson's disease.

Key Words: Hearing Loss; Tinnitus; Parkinson Disease; Presbycusis.



ARAŞTIRMA

PARKİNSON HASTALIĞINDA İŞİTME AZLIĞI VE KULAK ÇINLAMASI ŞİDDETİ

Öz

Giriş: Bu çalışmanın temel amacı, Parkinson hastalarında işitme bozukluğu ve kulak çınlaması şiddetini değerlendirmek ve elde edilen sonuçları sağlıklı kontrollerle karşılaştırmaktır.

Gereç ve Yöntem: Çalışmaya, Parkinson hastalığı tanısı almış 43 hasta ile benzer yaş ve cinsiyette 45 sağlıklı gönüllü alındı. Odyolojik değerlendirme saf ses odyometrisi ile, kulak çınlaması şiddeti tinnitus şiddet indeksi ile değerlendirildi. Hava yolu eşikleri ve kulak çınlaması şiddet skorları istatistiksel olarak karşılaştırıldı.

Bulgular: Parkinson hastalarında, 6000 ve 8000 Hz saf ses odyometrisi eşiklerinde belirgin yükselme saptanırken diğer frekanslarda anlamlı bir fark yoktu. Parkinson hastalarında kulak çınlaması şiddet skoru kontrol grubuna göre anlamlı olarak yüksek bulundu ($p<0.001$).

Sonuç: Çalışmada en dikkat çekici bulgu Parkinson hastalarında, yüksek frekanslarda saptanan işitme kaybı ve daha şiddetli kulak çınlamasıdır. Parkinson hastaları işitsel bozukluklar açısından izlenmeli, bu hastalara gerekli ve uygun tedavi sağlanmalıdır. Bu sonuçlar, işitsel disfonksiyonun Parkinson hastalığının non-motor belirtilerinden biri olabileceğini göstermektedir.

Anahtar Sözcükler: İşitme Azlığı; Kulak Çınlaması; Parkinson Hastalığı; Presbiakuzi.



INTRODUCTION

Parkinson's disease (PD) is a degenerative disorder of the central nervous system that mainly affects motor function. Mostly affecting the elderly, PD usually begins between the ages of 50 and 65, and its major symptoms result from loss of dopamine-secreting cells in the pars compacta region of the substantia nigra (1,2). However, cell degeneration in PD is not only restricted to the substantia nigra and locus ceruleus but also occurs in thalamus, cerebral cortex, autonomic nervous system and auditory system (3).

Dopamine also suppresses spontaneous and sound-evoked activity in the cochlear nerve fibers and helps to protect cochlea from noise-induced damage. Thus, dopamine deficiency can lead to damage to the cochlea and consequently to hearing loss and tinnitus (4,5), both of which are important conditions affecting the elderly. These phenomena can, in turn, lead to communication problems, insomnia, loneliness and decrease in social activities (6). Tinnitus, which is the perception of sound within the human ear or head when no external sound is present, affects about 15% of the world population and 33% of the individuals older than 60 years (7). Many aspects of the pathophysiology of tinnitus are still unclear. However, it has been postulated that damage to, or irregularities of, the cochlear hair cells and neural and central auditory pathways may be causative (8). To date hearing impairment in PD has received little attention, while to our knowledge, the severity of tinnitus in PD has never been investigated.

The aim of the present study was to evaluate the hearing impairment and tinnitus severity in patients with PD, and to compare the results with healthy age and sex-matched controls.

MATERIALS AND METHOD

This study was performed in accordance with the Helsinki Declaration of the World Medical Association. Informed consent was obtained from all participants, and the study was approved by the Research Ethics Committee of our tertiary referral center (no. 2016/4).

This cross-sectional study involved 43 consecutive patients diagnosed with PD, and a control group of 45 healthy age- and sex-matched individuals. All patients with PD were required to have stage II or III disease according to the Hoehn and Yahr classification system (Table 1), which is a widely used clinical rating scale that defines broad categories of motor function and disease progression in PD (9). Of the 43 Par-

Table 1— Parkinson's Disease Severity According to the Hoehn and Yahr Staging System

Stage	Definition
1	Unilateral disease
2	Bilateral disease with recovery on the pull test
3	Mild-to moderate bilateral disease with postural instability; physically independent
4	Severe disability; still able to work or stand independently
5	Wheelchair bound or bedridden unless aided

kinson's patients in the study, 26 patients were showing mild symptoms. 15 of these patients were taking rasagiline (monoamine oxidase-B inhibitor) treatment, other 11 were taking lower doses of dopamine agonists. The remaining 17 patients had mild symptoms of PD with mild walking impairment, they were taking combination therapy of rasagiline and a dopamine agonist. Patients with PD did not receive any treatment of levodopa in the study. The exclusion criteria were as follows: hearing loss other than sensorineural loss; otitis media or middle ear effusion in the previous 4 weeks; acoustic trauma or barotrauma in the previous 6 months; otologic surgery; neurological disorders consistent with a diagnosis of atypical parkinsonism, such as multiple system atrophy, progressive supranuclear palsy, multiple sclerosis, and corticobasal degeneration; and systemic conditions known to negatively affect hearing and neurological functions, such as thyroid disease, diabetes, hypertension, renal failure, hyperlipidemia, and chronic obstructive pulmonary disease. Patients who could not adapt to testing by audiometry were also excluded.

Detailed investigation was performed in all subjects by a neurologist and otolaryngologist. Data were collected by individualized follow-up, telephone calls, and reference to our hospital database. We performed full clinical otorhinolaryngological examination followed by assessment using pure-tone audiometer (PTA) and the tinnitus severity index (TSI). PTA was performed with an AC40 clinical audiometer (Interacoustics, Middelfart, Denmark), and we determined air conduction thresholds at 500, 1000, 2000, 4000, 6000 and 8000 Hz. The PTA in the better-hearing ear was used for subsequent analyses. TSI is an assessment questionnaire consisting of 12 questions and a rating system that scores each question from 0 to 5, giving a maximum possible score of 60 points. Scoring boundaries were as follows: 1-12 points was classified as very mild, 13-24 as mild, 25-36 as moderate, 37-48 as severe, 49-60 as catastrophic (10).

**Table 2**— Pure-tone Audiometer Thresholds (decibel) of the Control and Parkinson's Disease Groups.

Pure-tone Audiometer Thresholds (Decibel)	Control Group (n=45)	Parkinson's Disease Group (n=43)	p
500 Hz	19±9.1	22±10.8	0.11
1000 Hz	18 ±8.7	21±9.3	0.18
2000 Hz	28±9.8	30±11.4	0.35
4000 Hz	30±11.3	33±13.2	0.27
6000 Hz	36±13.4	49±18.3	0.038
8000 Hz	49±17.4	65±21.5	0.015

Values are mean±sd

Data were analyzed using IBM SPSS for Windows, Version 23 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as means±standard deviation and categorical variables as percentages. Hearing thresholds at each frequency and the TSI scores among the control and PD groups were compared using two-tailed t-test. A p-value<0.05 was taken to indicate statistical significance.

RESULTS

In the PD group, 20 patients were female and 23 were male, and the mean age was 63±7.9 years (range, 54–88). In the control group, 22 participants were female and 23 were male, and the mean age was 59±7.1 years (range, 51–82). The age and sex distributions in PD and control groups were comparable.

Compared with the control group, patients with PD showed significant elevations in PTA thresholds at 6000 and 8000 Hz (both, p< 0.05), but there were no significant differences at 250, 500, 1000, 2000, or 4000 Hz (all p > 0.05) (Table 2).

The TSI scores in the control and PD groups were 14.8±5.4 (range: 0-32), 31.4±11.2 (range: 8-60), respectively. The mean TSI score in PD group was significantly higher than that in the control group (p<0.001).

DISCUSSION

Auditory function has previously been investigated in patients with PD. Previous studies reported that patients with PD have worse hearing than age-matched control subjects (11) they also suggested prolonged latencies in auditory brainstem response (12,13). In a study, it was reported that hearing loss correlates with an increased risk of PD in the elderly (14). In addition, although PD has been shown to be associated with significantly high PTA thresholds at 4000 and

8000 Hz, but not at thresholds of 250, 500, 1000, or 2000 Hz (13), other research has found no significant difference in PTA results between the frequencies 500 and 8000 Hz when comparing patients with PD and healthy subjects (15).

Our data are consistent with the research showing significant hearing impairment at 6000 and 8000 Hz in patients with PD when compared with controls. Similarly, tinnitus severity was significantly higher in patients with PD. Together, these results show that auditory dysfunction could be a non-motor symptom of PD. Indeed, Vitale et al. (11) have previously emphasized that auditory dysfunction should be included among the sensory symptoms of PD. To understand the pathophysiology of cochlear damage that causes hearing impairment and tinnitus to be more severe in PD, it is essential to review the molecular mechanisms.

The prevalence of sensorineural hearing loss and tinnitus are increasing worldwide, mainly because of ageing and increased exposure to noise, degenerative disorders, and cardiovascular risk factors (6,16). Several studies have investigated the mechanisms underlying the primary causes of impaired hearing and tinnitus, including the damage and loss of auditory hair cells; however, very little is known the pathophysiology at a molecular level or of the protective mechanisms (17). Glutamate is the main afferent neurotransmitter within the cochlear hair cells, and massive glutamate release may result in excitotoxicity, irreversible cell death, and neurotoxicity. Dopamine, by contrast, is an inhibitory transmitter that reduces the stiffness of the outer hair cells, increases their motility and protects the cochlea from excitotoxicity. Thus, excitatory glutamatergic transmission is under the inhibitory control of dopamine (5,18-20). Because the modulation of these molecular interactions is important to both the regulation and protection of cochlear and auditory pathways, their metabolic alterations that occur in PD could profoundly increase the likelihood of damage to cochlear auditory cells. In our study, the loss of dopaminergic inhibition may have led to increases in



glutamatergic activity and inevitable cochlear damage. In these patients, the cochlear damage may have caused presentation with clinical signs that were more severe than simple presbycusis (age-related hearing deterioration). Our results indicate that PD affects cochlear and auditory pathways. In the present study, PD patients were at early stage (stage II or III according to the Hoehn and Yahr classification), thus they were receiving lower doses of monoamine oxidase inhibitor and/or a dopamine agonist, none was taking levodopa treatment. Therefore, we did not have the opportunity to determine whether dopamine treatment caused a positive or negative effect on cochlear functions.

Hearing loss and severe tinnitus may contribute to communication deficits, insomnia, loneliness and decrease in social activities among patients with PD. These patients therefore require appropriate therapy to prevent functional decline, which is typically by multidisciplinary evaluation and early intervention, including specific audiological rehabilitation programs, hearing devices, tinnitus masking devices and drug therapy. A comprehensive approach could significantly improve the quality of life of PD patients. We contend that including auditory dysfunction and tinnitus as sensory symptoms of PD may improve the detection and treatment rates.

The main strength of our study is that, to the best of our knowledge, this was the first time tinnitus severity has been assessed in PD. However, we included a relatively small number of patients, and larger population-based studies with long-term clinical follow-up data will be needed to verify our results.

Conflict of Interest

The authors have no conflicts of interest or financial ties to disclose in regard to this study.

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