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Original Article

Evaluation of the Vestibulocochlear System in Patients with Pseudoexfoliation Syndrome

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Abstract

Objectives: Patients with pseudoexfoliation syndrome (PES) can also have sensorineural hearing loss as well as balance problems. Our aim was to evaluate vestibulocochlear system involvement in PES patients.

Materials and Methods: The study included 16 subjects with PES (study group) with a mean age of 66.12±5.64 years and 17 healthy subjects (control group) with a mean age of 61.70±8.46 years. Both groups underwent ophthalmological, neuro-otological, audiological, and vestibular evaluation. Pure-tone audiometry and tympanometry were performed as audiological tests and bithermal caloric test and vestibular-evoked myogenic potential (VEMP) testing were used as vestibular tests. The Romberg, tandem Romberg, and Unterberger tests were also performed.

Results: In the PES group, bithermal caloric tests revealed right canal paresis in 6 patients, left canal paresis in 3 patients, and bilateral stimulation loss in 2 patients, despite no clinical evidence of balance loss. Paresis was not detected in any of the control subjects. Unilateral VEMP responses could not be obtained in 3 patients in the PES group. The ocular PES patients whose VEMP waves were obtained differed significantly from the control group ($p<0.05$). In office tests for vestibular evaluation, pathologic findings were found in 7 of 16 patients in the study group and only 4 subjects in the control group. Audiological evaluation with pure-tone thresholds revealed sensorineural decline at 4000 and 8000 Hertz in the PES patients. A statistically significant difference was found between the study group and the control group ($p<0.05$).

Conclusion: Patients with PES showed elevation in pure-tone thresholds and a decrease in superior and inferior vestibular nerve function, demonstrating that the vestibular system as well as the auditory system are affected in PES.

Keywords: Pseudoexfoliation syndrome, vestibular diseases, vestibular function tests, vestibular evoked myogenic potentials

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Introduction

Pseudoexfoliation syndrome (PES), first described by Lindberg[1] in 1917, is a systemic disorder characterized by excessive synthesis and accumulation of fibrillary material in the ocular and extraocular tissues. This pseudoexfoliative material is believed to have many sources and occur secondary to abnormal basement membrane constituents produced by aging epithelial cells.[2]

Pseudoexfoliation fibrils can accumulate in the anterior segment structures of the eye such as the conjunctiva, corneal endothelium, anterior lens capsule, trabeculum, iris, zonules, and ciliary body, leading to glaucoma and subsequent progressive vision loss.[3] Light and electron microscopic analyses and immunohistochemical methods have also demonstrated the presence and accumulation of pseudoexfoliative material in the inner ear, as well as the extracellular matrices of systemic organs such as the skin, heart, lung, and liver.[4,5] In addition, the detection of material accumulation in the connective tissue layers of the skin and internal organs, the periphery of blood vessels, the smooth and striated muscle layers of the internal organs, and the cardiac muscle indicates that PES is a multisystemic disorder rather than just an ocular disease.[6,7] Its association with diseases that cause high mortality and morbidity, particularly cardiovascular and cerebrovascular diseases, further increases the importance of PES.[8]

The decline in hearing in PES patients at advanced ages has been attributed to the fibrillary material accumulated in the cochlea preventing the conversion of sound energy to electrical energy.[9,10,11] Several studies have shown that pseudoexfoliation fibrils accumulate in the basilar membrane, tectorial membrane, and stria vascularis of the inner ear. Embryologically, the ocular anterior segment and inner ear originate from the same germ layer.[12] However, there are few studies in the literature demonstrating the involvement of the vestibular apparatus, which constitutes another part of the inner ear.[13]

Balance is provided mainly by the visual, vestibular, and proprioceptive systems. The central nervous system integrates information from the relevant peripheral organs, then maintains balance via the necessary reflexes.[14]

In this study, we planned to investigate whether PES also affects the balance system to the same degree as the auditory system due to the likely accumulation of pseudoexfoliation fibrils.

Materials and Methods

A prospective, case-controlled study was conducted. Approval was obtained from the Eskişehir Osmangazi University Ethics Committee. Informed consent forms were obtained from the patients.

Sixteen individuals with ocular PES (study group) and 17 healthy subjects (control group) were included.

Of the 16 patients in the study group, 10 were male and 6 were female. Of the 17 healthy volunteers in the control group, 12 were male and 5 were female. Ophthalmological, neurological, audiological, and vestibular evaluations were performed in both groups. Ophthalmological examination for all patients consisted of corrected visual acuity, biomicroscopy, intraocular pressure measurement, and fundus examination.

Vestibular evaluation was performed in both groups using vestibular-evoked myogenic potential (VEMP) testing, bithermal caloric test, and office vestibular tests; audiological evaluation was performed using pure-tone audiometry and tympanometric examination. The Romberg, tandem Romberg, Unterberger, and Dix-Hallpike tests were performed as office vestibular tests. Video electronystagmography, another vestibular test, was not used because it does not give reliable results in ocular pathologies.

VEMP Test

The cervical VEMP test is based on measuring the electromyographic activity of the sternocleidomastoid muscle in response to high-intensity acoustic stimuli to the saccular macula. It is generally used to determine whether the saccule, inferior vestibular nerve, and central connections are working normally. The VEMP pathway is formed by the saccule, inferior vestibular nerve, lateral vestibular nucleus, medial vestibulospinal pathway, and sternocleidomastoid muscle after auditory stimulation of the saccule. VEMP tracings were recorded with a Medelec Synergy device. The first positive wave was taken as p13 and the first negative wave as n23. The p13 and n23 latencies and the amplitude between the two waves (p13-n23) were measured. The latency and amplitude values of the patient group were compared with normative data obtained from the control group.[15]

Bithermal Caloric Test

Bitermal caloric test recordings were performed using a CHARTR water caloric stimulator, model NCI-480. Subjects were placed in supine position with the head at 30° anteroflexion during the test. The test was performed by administering water at two temperatures, 7°C above and below body temperature (30/44°C), to the external auditory canal. Activation is measured in the lateral semicircular canal, which is the most superficial and easiest to reach. This test can also provide information about the superior vestibular nerve. The test results were evaluated in terms of canal paresis and directional superiority. A 25% difference in the durations of nystagmus occurring with hot and cold stimuli in both canals was regarded as canal paresis.[16]

Romberg Test

While standing with feet together, head upright, and arms at their sides, the subject was asked to close their eyes. After thus eliminating the auxiliary role of vision in balance, the subject's balance is observed and any vestibular system disorders are revealed. Movement in small circles suggested a central origin, while tilting backward or to the side was considered more suggestive of a cerebellar disorder.[16]

Unterberger Test

Subjects were asked to take 40-50 steps in place with their hands outstretched in front of them. Rotational deviation

to either side that did not disappear with repeated tests was interpreted as indicating vestibular pathology on that side.[16]

Dix-Hallpike Test

In this test, the subject is quickly placed in supine position with the head facing one side and slightly extended. Rotary nystagmus associated with dizziness after a latency of 4-5 seconds after supine positioning was considered pathological.[16]

Audiological Evaluation

Tympanometry

Tympanometry was performed using a 256 Hz probe tone.[17]

Odiometry

Pure-tone threshold audiometry was performed using an InterCoustics AC-40 Audiometer and the results were recorded. In pure-tone audiometry, the average bone-conduction pathway thresholds at 500, 1000, 2000, and 4000 Hz and the air-conduction thresholds at 500-8000 Hz were included in the evaluation. Thresholds of 0-20 decibels were evaluated as normal hearing, 21-40 decibels as mild hearing loss, 41-60 decibels as moderate hearing loss, 61-80 decibels as moderate to severe hearing loss, and 81-100 decibels as severe hearing loss.[16]

Exclusion criteria for both groups were conductive hearing loss, family history of hearing loss, problems in the neck muscles, high noise exposure, acute or chronic ear infection, tympanic membrane perforation, otologic surgery, head trauma, active upper respiratory tract infection, history of drugs and systemic diseases that affect balance, and diagnosed or suspected glaucoma. Inclusion criteria were age over 40 years for both groups and for the study group, biomicroscopy findings of pseudoexfoliation not associated with glaucoma.

Statistical Analysis

Statistical analysis was performed using SPSS version 15.0 software (SPSS Inc, Chicago, IL). Comparisons of measured variables between the groups were performed using Student's t-test for independent samples. Comparisons of categorical variables between the groups were performed with chi-square (χ^2) analysis. P value <0.05 was accepted as significant.

Results

The study included 16 ocular PES patients with a mean age of 66.12±5.64 years (study group) and 17 healthy individuals with a mean age of 61.70±8.46 years (control group). All 66 ears of the total 33 subjects were included in the evaluation.

In audiological evaluation, the PES patients were found to have sensorineural hearing loss at 4000 and 8000 Hz compared to controls in pure-tone threshold testing. The difference between the two groups was statistically significant ($p<0.05$). Tympanometric peak values were lower in the patient group than the control group.

Bithermal caloric testing in the PES group showed right canal paresis in 6 patients, left canal paresis in 3 patients, and bilateral low signal in 2 patients. Paresis was not detected on caloric tests in the control group.

VEMP testing was performed in all 16 PES patients, but unilateral VEMP waves could not be obtained in 3 patients. The p13, n23, and amplitude values of the 29 ears with VEMP waves from the patient group were compared with those of the 34 ears with VEMP waves in the control group. Comparison of the control subjects and PES patients with VEMP waves revealed significant differences in right amplitude, left p13, and left n23 values ($p<0.05$) but no significant differences in right p13, right n23, and left amplitude ($p>0.05$) (Table 1).

In the vestibular office tests, pathological findings were detected in 7 of 16 patients in the study group (positive Romberg test in 2 patients and positive Unterberger test in 5 patients) and only 4 subjects in the control group (Unterberger test).

Discussion

In many embryological studies conducted to date, it has been reported that the inner ear and ocular anterior segment originate from the same germ layer.[12] In patients with PES, it is known that the accumulation of pseudoexfoliation material in the ocular anterior segment causes glaucoma and that accumulation of the same material in the cochlea leads to sensorineural hearing loss.[9,10,11,12]

Detorakis et al.[18] reported that PES patients had lower tympanometric peak values and suggested that this was caused by fibrillar deposits in the middle ear impairing middle ear elasticity. We observed similar findings on the tympanograms obtained in our study. The tympanometric peaks were also low in our study, although the decrease in these values may also be due to age-related loss of middle ear elasticity. However, Stenklev et al.[19] found no significant difference in tympanometric peaks with age.

Numerous other studies have also indicated that the cochlea is affected in patients with ocular PES and that these patients have significant sensorineural decline compared to age-matched control groups. Samarai et al.[11] attributed this to impairment of the mechanism by which hair cells convert sound to electrical energy as a result of the accumulation of pseudoexfoliation fibrils in both the tectorial and basement membranes. Yazdani et al.[9] supported this view in their study of 166 patients and 83 controls with the same findings and the same mechanism.

Many studies have shown that PES is associated with vascular disease and that fibrillary material accumulates in various organs and tissues.[10,11,12] This study was planned considering that the accumulation of fibrillary deposits in the vessel walls may affect the end arteries feeding the cochlea and vestibular apparatus, which may result in ischemia and the development of high-frequency hearing loss and balance problems. In our study, significant sensorineural hearing loss was observed at 4000 and 8000 Hz in the study group compared to the control group. In addition, although we observed pathological findings in VEMP and bitermal caloric tests, patients did not have balance problems.

Significant degeneration occurs in all structures of the vestibular system with age. Different studies have indicated

Table 1. Visual-evoked myogenic potential (VEMP) values in the patient and control groups			
	Patients	**Control mean ± SD**	**P value**
Right p13	13.22±1.18	13.10±1.22	0.781
Right n23	20.18±5.39	22.01±1.81	0.200
Right amplitude	118.64±66.98	181.40±43.39	0.004
Left p13	14.68±1.99	12.67±1.32	0.002
Left n23	23.05±1.33	21.65±1.43	0.008
Left amplitude	153.58±72.82	191.65±46.63	0.085
Age (years)	66.12±5.64	61.70±8.46	0.090
SD: Standard deviation, *: Student's t test			

different ages for the onset of this degeneration.[20,21,22] Each decade, an average of 3% of the vestibular hair cells are lost.[20,21,22] Despite histological changes, these individuals generally do not have a problem with balance in their daily lives. This has been attributed to strong central compensation. There are studies showing no significant age-related differences in vestibular assessment tests.[23]

Turgut et al.[13] included vestibular assessment in the tests performed on patients with PES. The study group consisted of 34 patients and the control group consisted of 40 individuals. Vestibular function was assessed using the Romberg test, gait test, Dix-Hallpike test, and bitermal caloric test. Although impairment was detected in the vestibular tests of the patients in the study group, they had no complaints of balance problems. To explain this, they stated that balance is supported by the vestibular apparatus as well as the visual system and the proprioceptive system. They observed that even if vestibular functions were impaired, central compensation occurred over time and patients did not develop problems such as loss of balance.[13]

In our study, significant differences in VEMP parameters were detected between the study and control groups ($p<0.05$). In addition, responses were low unilaterally in 9 patients and bilaterally in 2 patients. Despite these vestibular system findings and the significant visual system involvement in patients with PES, they did not report significant difficulty in daily life. Although the number of patients is small, this finding is due to central vestibular system activation to offset the gradual deterioration caused by pseudoexfoliative material accumulation in the vestibular system, and the individual adaptating to their new state. As we age, however, aging of the vestibular system is inevitable, and the proprioceptive system is also affected. As a result, balance disorders and associated falls and injuries are important in aging societies. In a study conducted in our country with 1078 people over 50 years of age, 3.4% of the individuals reported a fall in the last 6 months. In that study, dizziness was identified as a risk factor in 25.1% of those under 65 years of age and 26.2% of those over 65 years of age.[24,25] Therefore, it would be beneficial to inform patients with PES about balance problems, to perform vestibular tests, and to make home and environmental modifications for patients whose vestibular system is affected and include them in appropriate rehabilitation programs.

Study Limitations

Limitations of our study are the small size of the patient and control groups and the fact that we did not perform a comparison between PES patients with and without glaucoma.

Conclusion

Our study showed that among the systems responsible for balance, both the visual and vestibular systems are affected in patients with PES. In the light of the literature, it is important that ophthalmologists who follow-up PES patients keep in mind that the cochlear and vestibular compartments of the inner ear may be affected and ensure that these patients are examined periodically by an otorhinolaryngologist.

Ethics

Ethics Committee Approval: Approval was obtained from the Eskişehir Osmangazi University Ethics Committee.

Informed Consent: Informed consent forms were obtained from the patients.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: M.D.B., N.E.K., L.B., A.İ., N.Y., Concept: M.D.B., N.E.K., L.B., A.İ., N.Y., Design: M.D.B., N.E.K., L.B., A.İ., N.Y., Data Collection or Processing: M.D.B., N.E.K., L.B., A.İ., N.Y., M.D.B., N.E.K., L.B., A.İ., N.Y., Analysis or Interpretation: Literature Search: M.D.B., N.E.K., L.B., A.İ., N.Y., Writing: M.D.B., N.E.K., L.B., A.İ., N.Y.,

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