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Relationship Between Ocular Pseudoexfoliation and Sensorineural Hearing Loss

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ABSTRACT

The purpose of this study is to evaluate the air and bone conductance rates in audiogram between healthy individuals and the patients having pseudoexfoliation (PEX).
Patients with evidence of ocular PEX and controls were included in the study. Air conduction hearing thresholds (minimal perceptible sounds) were determined at frequencies of 250, 500, 1000, 2000, 4000, 6000, 8000 Hz and bone conduction hearing thresholds were determined at frequencies of 500, 1000, 2000, 4000 Hz for each ear. At these frequencies, air and bone conductance rates in audiogram were measured for patients with PEX and control group to analyze the relation between conductance rates and PEX cases.
86 participants were enrolled in this case-control study, in which 40 of them having PEX. The acquired results showed that the PEX group displayed significantly higher hearing tresholds in air conductance compared with control subjects at frequencies of 250, 500, 1000, 2000, 4000 Hz, but not at frequencies of 6000, 8000 Hz. Similar results were obtained in bone conduction thresholds as well, in terms of the tendency of decreasing significance level between the groups in higher frequencies.
In our study, we have shown that there is a statistically significant sensorineural hearing loss in PEX patients comparing age control subjects. These findings are more significant in lower frequencies, and the significance level is decreased toward the higher frequencies. Based on these findings, we speculate that endolymphatic pressure increase could have a role in the pathogenesis of PEX related sensorineural hearing loss.

Key Words: Ocular pseudoexfoliation, sensorineural hearing loss, endolymphatic pressure

Introduction

Pseudoexfoliation (PEX), which was previously described by J.G.Lindberg in 1917, is a systemic situation characterized by the accumulation of fibrillar extracellular substances (1, 2). The prevalence of this condition increases with age. PEX is found in 25.3% of the population aged over 70 (3). As a complex glycoprotein, exfoliation material tends to accumulate progressively in various organs, for instance, the heart, skin, lungs, kidney, gall bladder, and vascular structures (4). Among the eye structures, especially the iris, trabecular meshwork and lens capsule are affected by the PEX material. And it is recognized as the second most common cause of glaucoma and a well-known risk factor for intra-postoperative complications in cataract surgery due to poor pupil dilation, weak zonular fibers, and capsular fragility (4-6).

Like the Corti organ of the inner ear, the eye's anterior segment is originated from the neural ectoderm. This relationship is thought to be important in terms of the accumulation of PEX material, whereas tissues with the same embryological origin exhibit similar behavior. In some studies, PEX material has been found on the basilar and tectorial membrane (7), and it has been suggested that PEX accumulation on these membranes leads to sensorineural hearing loss due to dysfunction of the mechanoreceptors of the inner ear (8). Alternatively, it has been hypothesized that vascular compromise due to the accumulation of PEX on vessel walls may also play a role by disrupting the circulation of the inner ear basal segment (9).

The logarithmic unit of sound pressure is dB (decibel). Normal hearing threshold levels are determined to be between 0–20 dB in human (10). The 21 dB or more hearing threshold in any ear is considered as hearing impairment. Approximately 70% of the human sensory deficit is due to sensorineural hearing loss (SNHL) (11). Many studies were conducted to evaluate the association of SNHL and PEX existence in the literature. 1000 Hz, 2000 Hz, 3000 Hz frequencies, which

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are relevant for speech comprehension, were used in the majority of these studies (9, 12-15). The higher frequencies were found to be more vulnerable in the PEX patients comparing healthy subjects similar to presbycusis, which is bilateral and symmetric (16, 17).

In our study, we tried to evaluate a possible correlation between PEX and SNHL. For this purpose, the hearing quality of the patients having PEX and age-gender matched healthy subjects were compared in 250, 500, 1000, 2000, 4000, 6000, 8000 Hz frequencies. In addition, we tried to create a new perspective on the pathogenesis of the SNHL in PEX patients.

Materials and Methods

This case-control study was conducted in collaboration with the Van Yuzuncu Yil University Medical Faculty Ophthalmology and Otorhinolaryngology (ENT) Department between June and September 2020. Approval was obtained from Van Yuzuncu Yil University Clinical Research Ethics Committee. In the applied methods, the principles of the Helsinki Declaration were adhered to. All participants were informed, and informed consent forms were obtained from the participants.

Forty patients with ocular PEX and 46 healty controls with similar age and gender characteristics were included in the study. Past medical history was obtained from all of the subjects, and an ophthalmologic examination was performed, including determination of best-corrected visual acuity, biomicroscopic examination, measurement of intraocular pressure, gonioscopy, and fundus examination with a non-contact lens (90-diopter). The diagnosis of PEX was made on biomicroscopic examination by observing the white, gray colored exfoliation material on the anterior lens capsule and / or at the pupillary border in one or both eyes after dilation of the pupil with 1% tropicamide drop. Persons who did not have PEX material in their eyes during ophthalmological examination were included in the study as control group.

The exclusion criteria were evidence of external or middle ear abnormalities and upper respiratory tract infection, history of ear disease, myringosclerosis, head trauma, unilateral PEX involvement, long-term exposure to gunfire or heavy noise and using some ototoxic drugs, such as aminoglycosides.

ENT Specialist Evaluation and Audiometry Examination: All participants were referred to an otolaryngologist for physical examination. External ear examination was performed with otoscopically. The presence of middle and/or inner ear pathologies was investigated with computed tomography and magnetic resonance imaging of temporal bone.

For audiological analysis of the subjects, pure-tone audiometry (PTA) (Interacoustic Clinical Audiometer; model AC 40; Assens, Denmark) was performed by the same audiologist. Air conduction hearing thresholds (minimal perceptible sounds) were determined at frequencies of 250, 500, 1000, 2000, 4000, 6000, 8000 Hz. Bone conduction hearing thresholds were determined at frequencies of 500, 1000, 2000, 4000 Hz for each ear. Hearing loss rates and average hearing thresholds at each frequency were compared between the patient and control groups.

Statistical Analysis: The statistical analyses were performed with SPSS software for Windows (version 23.0, IBM Corp.). Descriptive statistics were used to determine the mean and standard deviations of variables of the patient and control groups. The Kolmogorov-Smirnov test was used to determine whether the data had a normal distribution. Student's t-test was used in the analysis of continuous variables, and the chi-square test was used in the analysis of categorical variables. The Independent t-test was used to compare air and bone conductance rates between groups. A p value below 0.05 was considered statistically significant.

Results

Eighty six participants were enrolled in this study in total. Fourty of the participants were patients with PEX material in their eyes and 46 were healthy subjects of similar age and sex. Regarding gender distribution, 50% of PXE group participants (n=20) were male. The control group was composed of 22 male (48%) and 24 female (52%) subjects. The mean ages of male participants were 66.03 ± 9 and 63.43 ± 10.69 years, in patients and controls, respectively (p=0.845). The mean ages of female participants were 70.4 ± 6.62 and 65 ± 10.62 years (p=0.519). Demographic characteristics are shown in Table 1.

Mean hearing threshold levels at the frequencies

Table 1. Demographic characteristics of the patient and control group

Characteristics	PEX group (mean±std) (n=40)	Control group (mean±std) (n=46)	p value
Age (years)	67.13 ± 8.6	64.04 ± 10.58	0.146
Age of males (years)	66.03 ± 9	63.43 ± 10.69	0.628
Age of females (years)	70.4 ± 6.62	65 ± 10.62	0.167
Gender (male/female)	20/20	22/24	0.613

PEX: Pseudoexfoliation, STD: Standard Deviation

Table 2. Air Conduction Hearing Levels of PEX and Control Groups

Frequencies (Hz)	Air conduction hearing levels in dB (mean±std)		p value
	PEX group (n=40)	Control group (n=46)	
250	35.91 ± 12.53	26.53 ± 9.84	0.001
500	34.09 ± 13.60	23.89 ± 10.49	0.001
1000	33.33 ± 15.19	22.92 ± 11.55	0.002
2000	35.45 ± 16.60	27.08 ± 14.51	0.029
4000	52.12 ± 23.91	43.47 ± 19.59	0.036
6000	57.50 ± 26.38	45.14 ± 19.32	0.151
8000	69.38 ± 27.62	62.64 ± 21.19	0.241

PEX: Pseudoexfoliation, dB: Decibel, n: Number, Hz: Hertz

Table 3. Bone conduction hearing levels of PEX and control groups

Frequencies (Hz)	Bone conduction hearing levels in dB (mean±std)		p value
	PEX group (n=40)	Control group (n=46)	
500	29.88 ± 12.01	21.52 ± 6.9	<0.001
1000	27.25 ± 13.68	18.26 ± 7.08	<0.001
2000	33.75 ± 15.51	24.02 ± 12.23	0.002
4000	36.75 ± 20.52	30.87 ± 17.39	0.154

PEX: Pseudoexfoliation, dB: Decibel, n: Number, Hz: Hertz

examined were compared in the patient and control groups. The bone and air conductance were compared in patient and control groups. The difference was more pronounced at lower frequencies; even it was not statistically significant in higher frequencies. Results showed that the PEX group displayed significantly higher HTLs in air conductance compared with healthy control subjects at frequencies of 250, 500, 1000, 2000, 4000 Hz but not at frequencies of 6000, 8000 Hz (Table 2) (Figure 1). Similar results were obtained in bone conduction thresholds as well, in terms of the tendency of decreasing significance level between the groups in higher frequencies. (Table 3) (Figure 2) In pure-tone audiometry, sensorineural hearing loss was determined in 29 right (72.5%) and 30 left (75%) ears of 40 PEX patients. The corresponding rates in the control group (n=46) were 28 right (61%) and 26 left (56.5%) ears.

Discussion

PEX syndrome is a disease that affects many organs in the body. The exact etiology is still unclear, although it is more common in older ages. The previously published studies have shown that there is a link between SNHL and PEX. Two pathophysiologic mechanisms were discussed in the literature. One of these is the dysfunction of the hearing mechanoreceptors as a result of the accumulation of PEX material in organ of Corti (8). The other one is that the PEX material that accumulates in the vascular walls of the cochlea causes malnutrition in the cochlear basal cells, thus leading a type of SNHL in which the higher frequencies are affected predominantly (9). In our study, we investigated the relationship between hearing loss and ocular PEX. In addition, we tried to claim a new insight into the pathophysiological pathway of the association of PEX and SNHL.

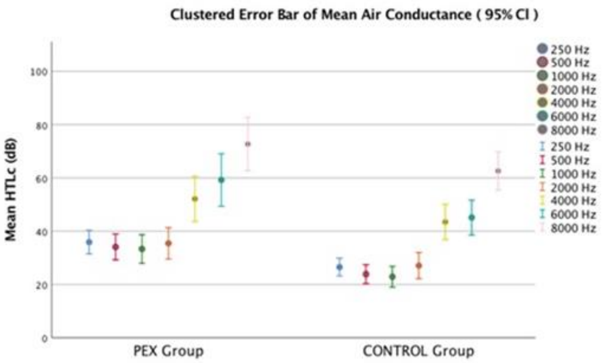

Fig 1. Clustered error bar of Mean Air Conductance (95% CI)

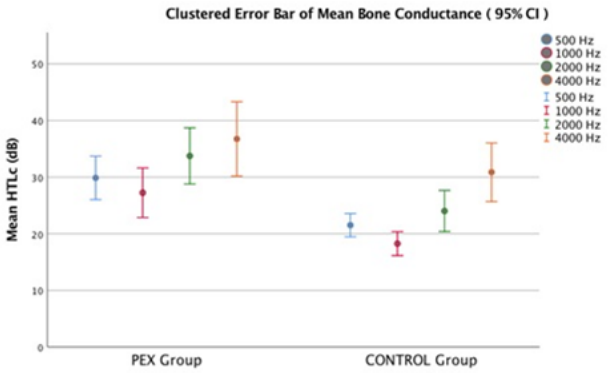

Fig 2. Clustered error bar of Mean Bone Conductance (95% CI)

There are many studies in the literature showing an increased incidence of SNHL in patients with PEX. In a study in regard to showing SNHL in PEX cases, Cahill et al. performed audiometry in 69 patients with PEX and reported SNHL existence in 73.7% of the ears (14). Shaban and Asfour reported SNHL in 36 of 41 patients (87%) with PEX, in an uncontrolled fashion. There was no correlation between the sensorineural hearing threshold level and presence of glaucoma (15). In a case-control study, Aydogan et al. reported that the mean speech frequencies were higher in PEX cases comparing healthy individuals (18). In our study, we have compared 40 PEX patients and 46 age and gender-matched individuals, and, similar to the previously mentioned studies, sensorineural hearing loss was determined in 73% and 36% of the ears of PEX and control subjects, respectively.

Afterward, multiple case-control studies were conducted to show SNHL in PEX patients, to find out any correlation between the worst-influenced eye and the worst-hearing ear and also to expose the absence or presence of glaucoma might be a predictive factor for hearing loss (8, 9, 13, 16, 19, 20). There is no strong evidence available for the correlation between glaucoma and hearing loss, and SNHL may occur in either right/left/both sides independent from the PEX orientation. In our study, we enrolled bilateral cases; thus, it could not be possible to determine the importance of PEX laterality on the severity of SNHL. The presence of glaucoma was determined in 11 of 48 PEX patients. The statistical analysis is not possible due to the unequal distribution of the groups.

Severel studies have shown that the increase in the hearing threshold in pure tone audiometry tests in patients with PEX affects the speech range, especially at a frequency of 2000 Hz (8, 9, 13, 21). Aydogan O et al. found that there was a significantly higher prevalence of hearing threshold levels at speech levels (500, 1000, and 2000 Hz) in the PEX cases when compared with controls (18). As an exception of previously mentioned studies, in a case-control study consisting of 47 PEX and 22 healthy subjects, Papadopoulos TA et al. stated that SNHL has a tendency to be significantly apparent in the PEX group comparing healthy individuals at the high frequencies (6000 and 8000 Hz) (16). In contrast to this report, we found out a reverse trend in our study. Though approximately similar demographic distribution in both studies, we determined a tendency of decrease toward higher frequencies in comparison to PEX and control group hearing thresholds. Papadopoulos TA et al. explained their findings according to vascular compromise hypothesis. In addition to the aforementioned pathogenesis of the SNHL in PEX patients, Schlötzer-Schrehardt UM et al. suggested that the underlying possible mechanism may be the cells that produce and drain endolymph inside the ear are structurally similar to the ciliary epithelium and trabecular meshwork in the eye (4). Interestingly, the obtained findings in audiometry were compatible with the findings of Meniere's disease. The most important and remarkable conclusion of our study is the statistically significant difference in lower audiometric frequencies between PEX and control subjects. These findings made us speculate on the previously mentioned pathogenesis. One of the important features of the endolymphatic hydrops, which is called Meniere's disease, is SNHL at lower frequencies. Due to declining surface area toward the apex of the cochlea, the increased endolymphatic pressure leads to early degeneration of the hair cells, which are responsible for perceiving lower frequencies.

One of the important features of endolymphatic hydrops is a vestibular disturbance. In a study which was conducted by Turgut B et al.(22), 34 patients with PEX were involved. While 21 (61.8%) patients with clinical imbalance had significant pathological findings in vestibular function tests (P = 0.05), only 3 (7.5%) of 40 subjects in the control group had pathological findings in vestibular function tests. Thus they concluded that there may be a vestibular involvement in the pathological level in inner ear. We could not have evaluated vestibular functions in our study group. But the very last mentioned pathogenesis might be important when we combined these findings. One of the few limitations of our study is we did not take vestibular functions into account. The other limitation of our study is we did not perform endolymphatic sac MRI for supporting our findings.

The results of our study have indirectly suggested that PEX can accumulate in the eye and ear, as in studys showing that its systemically accumulates in various organs and tissues in the body. The SNHL in PEX patients is a well-known symptom, but the exact pathogenesis is still unknown. In our study, we have shown that there is a statistically significant SNHL in PEX patients comparing age and gender-matched control subjects. These findings are more significant in lower frequencies, and the significance level is decreased toward the higher frequencies. Based on these findings, we speculate that endolymphatic pressure increase could have a role in the pathogenesis of PEX related SNHL. But further investigations, for instance, endolymphatic sac MRI, are needed to focus on enlightening the role of endolymphatic pressure on the pathogenesis of PEX related SNHL.

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