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Original Article

Audiometric Evaluation of the Relationship between Sensorineural Hearing Loss and Chronic Glaucoma

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Abstract

Objectives: To assess hearing function in chronic glaucoma patients in comparison to healthy individuals.

Materials and Methods: This cross-sectional study included 24 primary open-angle glaucoma (POAG) patients (24 ears) and 22 pseudoexfoliative glaucoma (PEG) patients (22 ears) who were followed for at least 5 years in the Afyonkarahisar Health Sciences University Ophthalmology Department, as well as 21 age- and gender-matched healthy individuals (21 ears, control group). Following a thorough ophthalmological examination that included visual acuity and intraocular pressure measurements, as well as anterior and posterior slit-lamp biomicroscopy, audiometry was performed in all participants to determine hearing function.

Results: Mean ages in the POAG, PEG, and control groups were 64.50±7, 66.90±4.51, and 64.38±4.36 years, respectively. The mean deviation in standard automated perimetry was -14.47±2.89 in the POAG group and -15.02±2.87 in the PEG group (p=0.306). When compared with the control group, the POAG group had significantly higher hearing thresholds at 500 (p=0.011) and 1,000 Hz (p=0.003), while the PEG group had significantly higher hearing thresholds at 250 (p=0.009), 500 (p=0.009), 1,000 (p=0.001), 2,000 (p=0.005), 4,000 (p=0.001), 8000 (p=0.010), and 10,000 Hz (p=0.009).

Conclusion: Both glaucoma and hearing loss are common chronic diseases that have an impact on the well-being of older people. Potential hearing problems in chronic glaucoma patients make routine ocular and otolaryngology examinations in older patients critical for prompt diagnosis and treatment.

Keywords: Primary open-angle glaucoma, pseudoexfoliative glaucoma, sensorineural hearing loss, audiometry, standard automated perimetry

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Introduction

Sensorineural hearing loss (SNHL) refers to hearing problems directly caused by cochlear, labyrinth, and central nervous system damage.[1] This disorder usually involves multiple pathologies not only in the inner ear, but also the auditory nerve. Hearing impairment refers to a hearing threshold of 21 decibels (dB) or higher in either ear. As a result, a person with normal hearing should have a sensitivity range of 0-20 dB across all frequencies, and it should be consistent at all ages.[2] SNHL is more common in people over the age of 65, with a prevalence of over 60%.[3,4] It may be associated with various etiological factors, including autoimmune ear disease, vascular diseases, noise, infection, and drug toxicity.[5] SNHL may also manifest features of vestibular schwannoma, which can only be ruled out by magnetic resonance imaging.[6] Most neurological diseases have the clinical presentation of a neurodegenerative mechanism that is nearly identical to SNHL. As a result, these patients may experience general neurological dysfunction that affects other organs.[7,8,9]

Glaucoma is a progressive optic neuropathy primarily associated with both visual field defects and high intraocular pressure (IOP).[10] Aside from primary open-angle glaucoma (POAG), there are several other types of open-angle glaucoma, including pigmentary glaucoma and pseudoexfoliative glaucoma (PEG).[11] POAG is a group of eye diseases with characteristic progressive changes in the optic nerve head and/or visual field loss.[12] POAG has no obvious cause, and glaucomatous changes may be directly related to high IOP or can also occur with IOPs lower than the population average. High IOP, advanced age, African ancestry, and a genetic predisposition to POAG are the most commonly reported risk factors.[13,14]

The most recognizable cause of secondary open-angle glaucoma is pseudoexfoliation (PEX) syndrome, which causes the deposition and accumulation of PEX material on the lens, iris, and other intraocular surfaces.[15] Although PEX syndrome is not always associated with glaucoma, patients with PEG have higher IOP at diagnosis than those with POAG, making the treatment of PEG relatively more difficult.[16]

Glaucoma patients have an increased risk of optic disc and retinal nerve tissue degeneration.[17] There is also some evidence of an association between SNHL and glaucoma.[3] As both diseases have related neurological degeneration characteristics, it is assumed that these conditions are more likely to coexist in a specific group of people. Therefore, the current study was designed primarily to assess hearing function in chronic glaucoma patients and compare the results with those of age- and gender-matched healthy individuals.

Materials and Methods

Study Participants

In this cross-sectional study, hearing function was assessed in 24 POAG patients (24 ears) and 22 PEG patients (22 ears) who had a mean deviation value lower than -12 dB in the Humphrey visual field test and had been followed for at least 5 years in the glaucoma unit of the Afyonkarahisar Health Sciences University Faculty of Medicine, Department of Ophthalmology. Hearing data from these groups were compared to those of 21 age- and gender-matched healthy individuals (21 ears, control group). The study procedure conformed to the ethical standards of the Helsinki Declaration and was approved by the Afyonkarahisar Health Sciences University Ethics Committee (approval number: 2020/520). All participants provided written informed consent prior to the study.

Inclusion and Exclusion Criteria

Participants aged 45 to 70 years old with best corrected visual acuity (BCVA) of 0.2 LogMAR or worse in each eye were referred to an otolaryngology clinic for an otological examination and hearing assessment. The study group consisted of pseudophakic or phakic male and female adults who had chronic POAG and PEG in either eye and no other ocular or systemic disease affecting visual system and who did not smoke or drink alcohol. Patients were also questioned about their history of glaucoma treatment, including both medical and surgical treatments. Subjects in the control group had IOP values lower than 21 mmHg in two readings and no ocular and/or systemic disease that could impair visual performance.

Exclusion criteria were: (a) the presence of any other type of glaucoma apart from POAG and PEG or any ocular or systemic condition associated with hearing physiology; (b) history of ear infection, surgery, tympanic membrane perforation, or exposure to ototoxic drugs or heavy noise; (c) the presence of an upper respiratory tract infection at the time of assessment; and (d) an evident perimetric sensitivity loss within the central 10° of the visual field according to pattern deviation plot.

Ocular Examination and Glaucoma Diagnosis

All participants underwent full ophthalmologic examination, including autorefraction (Canon R-F10m; Canon Inc., Tokyo, Japan), BCVA, and applanation tonometry (Goldmann; Haag-Streit AG, Köniz, Switzerland) measurements, as well as anterior and posterior slit-lamp biomicroscopy. All examinations were performed between 8:00 and 12:00 AM.

Glaucoma was diagnosed according to the International Society of Geographic and Epidemiological Ophthalmology (ISGEO) criteria.[18] POAG patients were classified as those who had an open and normal anterior chamber angle and met the ISGEO criteria. PEX syndrome was defined as the presence of PEX material in the anterior chamber angle and/or on the lens surface after pupil dilation, and PEG was defined as the presence of IOP greater than 21 mmHg as well as glaucomatous changes in both the optic nerve and visual field.

Standard automated perimetry (SAP) was performed with the Humphrey Field Analyzer HFAII (Carl Zeiss Meditec Inc, Dublin, CA, USA) using a 30-2 threshold program with Swedish Interactive Threshold Algorithm (SITA) standard strategy. The test was repeated a second time if the initial test was invalid. Test results were interpreted by comparison with the manufacturer's internal normative database. The results for visual field locations

were grouped into probability levels according to age-corrected normative values, shown on a grey scale. An irregular test result was defined as the presence of at least one low-sensitivity test point with p<1%, p<0.5%, or "not seen at maximum" on the total deviation plot.

Otolaryngologic and Audiometric Assessment

The hearing threshold for a specified ear was assessed with respect to ipsilateral ocular findings (i.e., the ear on the same side as the worse eye in POAG and the location of PEX in PEG). All participants were subjected to audiometry and noise annoyance tests to assess hearing function, and only ears with low hearing level were then studied. An otological examination was performed by an experienced otolaryngologist using a 4-mm 0-degree rigid endoscope (Xion GmbH, Berlin, Germany) and ML-150 light source (JRMed Trade Co., Seoul, South Korea). Hearing was assessed using the pure-tone average of thresholds at 250, 500, 1,000, 2,000, 4,000, 8,000, and 10,000 Hz. Hearing loss was defined as a dB level above 40 dB in one ear. All participants were asked if they had a history of noise exposure. Occupational noise exposure was defined as a history of loud noise (requiring a raised voice to be heard) at work for more than 3 months. Environmental noise exposure was defined as exposure to loud noise for more than 5 hours/week in any non-work setting.

Statistical Analysis

Statistical analysis was carried out using SPSS software (version 22, IBM Corp., Armonk, NY, USA). The Kruskal-Wallis test was used to compare the three independent groups because the study data did not show a normal distribution according to the Shapiro-Wilk test. In addition, the non-parametric Mann-Whitney U test with Bonferroni correction was used in pairwise comparisons to determine differences between groups in mean dB hearing levels at specific audiometric frequencies. Mann-Whitney U tests with p<0.0167 after Bonferroni correction were considered statistically significantly different.

Results

The mean ages of the POAG (64.50±7.45 years), PEG (66.90±4.51 years), and control (64.38±4.36 years) groups did not differ significantly (p>0.05) (**Table 1**). Eleven patients (45.8%) in the POAG group and 12 (54.5%) in the PEG group were pseudophakic (p=0.384). Two patients (8.3%) in the POAG group and 3 patients (14%) in the PEG group had a history of glaucoma filtration surgery (p=0.543). The mean logMAR BCVA values in the POAG and PEG groups were 0.61±0.49 and 0.69±0.51, respectively (p=0.217). When compared with the glaucoma groups, the control group had a significantly better logMAR BCVA of 0.00±0.00 (p<0.001 for both). Mean IOP did not differ statistically between the POAG and PEG groups (17.00±2.36 mmHg vs. 17.59±2.74 mmHg, p=0.202) but was significantly lower in the control group compared to both glaucoma groups (12.00±1.97 mmHg; p<0.001 for both). In the SAP analysis, the mean deviations were -14.47±2.89 and -15.02±2.87 in the POAG and PEG groups, respectively (p=0.306).

Audiometric Analysis

There were statistically significant differences among the three groups in hearing thresholds at 250 (p=0.039), 500 (p=0.012), 1,000 (p=0.002), 2,000 (p=0.012), 4,000 (p=0.004), 8,000 (p=0.003), and 10,000 Hz (p=0.021). In pairwise comparisons with the control group, the POAG group had significantly higher hearing thresholds at 500 (p=0.011) and 1,000 Hz (p=0.003), while the PEG group had higher hearing thresholds at all frequencies: 250 (p=0.009), 500 (p=0.009), 1,000 (p=0.001), 2,000 (p=0.005), 4,000 (p=0.001), 8,000 (p=0.010), and 10,000 Hz (p=0.009). The PEG group also had a higher hearing threshold at 8,000 Hz than the POAG group (p=0.002). There were no statistically significant differences in noise annoyance values among the three groups.

Discussion

This study demonstrated a significantly increased likelihood of SNHL in association with glaucoma. This relationship was significantly more pronounced in PEG than POAG patients, despite the fact that there was no age difference between them.

The relationship between glaucoma and SNHL is controversial. Although some studies reported a relationship between these two degenerative disorders, others reported no evidence of such a relationship.[19] One study found a significantly higher prevalence of SNHL in normotensive glaucoma patients.[20] In another study looking at the relationship between ocular diseases and SNHL, the prevalence of POAG was higher in the SNHL population, but SNHL was not significantly associated with increased glaucoma risk in covariate-adjusted models.[21] This is consistent with the current study findings that POAG patients had significantly higher hearing thresholds at 500 and 1,000 Hz in comparison to healthy individuals, suggesting a higher prevalence of concomitant hearing problems in these patients.

POAG is becoming more universally acknowledged as an age-related neurodegenerative disorder that can affect individuals predisposed to global neural damage. Optic and retinal nerve tissue degeneration is the most widely accepted glaucomatous feature. Furthermore, spiral ganglion neuron degeneration appears to be more closely connected to glaucoma development, because ganglion neurons are reduced in glaucoma patients while sensory cells are not.[22] Both POAG and SNHL appear to have common risk factors, neurodegenerative characteristics, and comorbidities. This suggests that SNHL patients may have a more vulnerable nervous system and an optic nerve more susceptible to damage than in healthy individuals, potentially leading to glaucoma progression.

A relationship between PEG and SNHL has also been reported.[23,24,25,26] However, no significant difference in hearing was observed between adults with PEG and age-matched controls in a study investigating the genetic and environmental causes of disease in older adults.[27] The authors of that study concluded by refuting Paliobei et al.'s[28] suggestion of adopting a multidisciplinary approach involving ear, nose, and throat

Table 1. Demographics of the study groups				
	POAG (n=24)	**PEG (n=22)**	**Control (n=21)**	**p value**
Age (years), mean ± SD (median, IQR)	64.50±7.45 (66, 58-72)	66.90±4.51 (66, 65-72)	64.38±4.36 (67, 62-67)	0.587*
Male:female ratio	12:12	11:11	12:9	0.863†

*Kruskal-Wallis test result, †Chi-square test result; n: Number of participants, POAG: Primary open-angle glaucoma, PEG: Pseudoexfoliative glaucoma, SD: Standard deviation, IQR: Interquartile range

specialists in the treatment of PEG and POAG patients. This contradicts the current study findings, particularly the increased likelihood of SNHL in association with PEG. Additionally, there is a much larger gap in mean ages between the current study and the study by Tryggvason et al.,[27] in which the mean ages were 77.4 years in PEG patients, 77.9 years in POAG patients, and 77.9 years in healthy individuals. The much older population in the Tryggvason et al.[27] study may explain their essentially insignificant and contradictory findings.

The general characteristic features of all types of glaucoma consist of retinal ganglion cell depletion, retinal nerve fiber layer thinning, and optic disc cupping.[29] The cell loss is not always limited to retinal ganglion cells, but may also extend to the lateral geniculate nucleus and visual cortex.[30,31] Previous studies reported that the loss of retinal ganglion cells and their axons as a result of glaucoma was followed by changes in glial cell, astrocyte, and retinal microglia cell counts.[32,33] Age-related SNHL was found to occur at a relatively high rate in age-related macular degeneration.[34] In addition, optic neuropathy and SNHL were shown to arise from more or less the same genetic defect.[35] However, few studies have focused on the relationship between glaucoma and SNHL. By taking into account the closely related features of these disorders in terms of neurological degeneration, the current study found an increased prevalence of SNHL in patients with glaucoma, most notably PEG, as opposed to only a minor manifestation in POAG. Given the concomitant neurological degeneration, this finding appears to support the early hypothesis of a clear relationship between these disorders.

POAG is characterized by unrestricted flow of aqueous humor to the trabecular meshwork and Schlemm's canal at the anterior chamber angle. In contrast, secondary open-angle glaucoma has a distinctive elevated outflow resistance through the trabecular meshwork and Schlemm's canal. The cause of this resistance is observable, as in pigmentary open-angle glaucoma and PEG, which can be identified by examining the ocular anterior segment.[36] PEX syndrome is an age-related disorder resulting in the formation and deposition of irregular extracellular fibrillar products.[37] Ocular PEX is now recognized as a part of a systemic disorder, as PEX material has been found in other body parts, including the skin, vasculature, and visceral organs such as the inner ear.[15] Thus, SNHL could be another extraocular symptom of PEX syndrome.

Analogous to the ocular anterior segment, the tectorial and basilar membranes of the inner ear are all products of the neuroectoderm. As such, accumulation of PEX materials on the tectorial and basilary membranes is also possible in PEX syndrome.[38] An abundance of PEX material on these structures can lead to elevated hearing threshold levels as a result of inner ear mechanoreceptor dysfunction, inevitably leading to hearing loss. Although SNHL has been linked to a variety of etiologies, the precise mechanism remains unknown. PEX materials that cause dysfunction of the mechanoreceptors of the inner ear have also been identified in the organ of Corti.[38] Precipitation of these materials may lead to significant changes in sound-induced vibration and impair the hearing process.[39] Yazdani et al.[26] reported a higher incidence of SNHL in PEX patients than in control subjects. Similarly, a high prevalence of SNHL in patients with PEX syndrome has been identified previously.[2,25,26,40] The current study supports prior findings regarding the prevalence of SNHL in PEX, specifically PEG. Furthermore, the current study has revealed a completely new finding: PEX syndrome was associated with a significant higher prevalence of SNHL at high frequency levels. SNHL seems to be associated with the presence of PEX material rather than glaucoma. If ocular PEX is representative of widespread PEX fibril distribution, then fibril deposition in the inner ear could demonstrate the association between PEX syndrome and SNHL. The presence of PEX fibrils in the organ of Corti may account for the clear relationship between PEX and the high hearing thresholds observed in this study.

The current study methodology has advantages as well, as more stringent participant exclusion criteria were used, and audiometric tests included a wide band of frequencies, encompassing the entire audible frequency spectrum. By revealing a higher likelihood of SNHL in PEG patients, the current study supports prior findings indicating that PEX syndrome may be a systemic disease affecting multiple tissues and organs.

Glaucoma subgroup analysis in a study by Chien et al.[3] revealed a significantly higher incidence of normotensive glaucoma and angle closure glaucoma in the SNHL group, while the incidence of POAG was only marginally increased. Steroids are a key alternative therapy for SNHL.[41] Hence, POAG is expected to become more common as a result of the IOP-raising effect of steroids, which is known as steroid-induced glaucoma.[42] Despite this, it was observed that the proportion of POAG patients who also had SNHL was not significantly higher, whereas patients with normotensive glaucoma were more prevalent in the SNHL group.[3] In the current study, however, there was a significant relationship between PEG and SNHL.

Similar to earlier studies, we found that SNHL and POAG coexisted less frequently. The preferential manifestation of SNHL and PEG is further evidence of the systemic nature of PEX syndrome. This finding lends support to the theory that a higher rate of glaucoma in SNHL patients is caused by a compromised nervous system rather than a result of steroid-related glaucoma.

Study Limitations

The current study has some limitations. First, the cross-sectional study design curtailed our ability to discover the processes underlying the relationship between hearing loss and glaucoma. Second, although we did not include patients with any ocular or systemic condition associated with hearing physiology, history of ear infection or surgery, tympanic membrane rupture, exposure to ototoxic drugs or heavy noise, and upper respiratory tract infection at the time of evaluation, there can sometimes be insufficient distinction between conductive hearing loss and SNHL. Therefore, we could not be completely certain that all patients with conductive hearing loss were excluded from the study. Third, residual confounding factors may have caused unexplained bias in the analysis. Fourth, although glaucoma patients were tested using Humphrey field analysis, which is a preferred approach for visual field testing, frequency-doubling technology is a quick, reliable, and large-scale screening technique sensitive enough to detect glaucomatous visual field abnormalities relatively earlier than SAP.[43] Fifth, participants were recruited based on ophthalmological examination using slit-lamp biomicroscopy. However, Kivelä et al.[44] stated that in some PEX cases, the accumulation of fibrillar products is not clinically observable but can be detected by histopathological examination. This fact could have contributed to some errors in control group sampling. Finally, the study population was just not large enough to improve the efficacy of the study.

While the current study has some drawbacks, it also has some advantages. So far as we know, this may be the first study to simultaneously evaluate seven different frequencies (250, 500, 1,000, 2,000, 4,000, 8,000, and 10,000 Hz) to determine pure-tone averages in the sample, which included patients and controls all of the same ethnicity. Ethnicity is an important factor in the selection of patients and controls, although an extensive investigation of this has not yet been conducted. In this case, European and American organizations have implemented international standards.[23] Based on the comparative findings of the current study and others globally that have shown comparable rates of SNHL in PEX patients, these standard systems appear to also be completely consistent with our population. Thus, there seems to be no need to set up study groups that include audiometric control measures in future Turkish studies. A high average age of study participants can be expected to influence hearing threshold results due to presbycusis. Fortunately, all of the groups in this study were roughly the same age, which might have mitigated the inherent bias in our results to some degree.

Conclusion

The current study has reaffirmed the relationship between SNHL and chronic glaucoma. Identifying concomitant hearing loss, particularly in chronic PEG patients, is essential for improving quality of life and thereby reducing the social burden of this patient group, whose quality of life is deteriorating due to long-term glaucoma therapy and irreversible visual loss. Routine ophthalmology and otolaryngology examinations in older adults may be critical for the early diagnosis and treatment of these disorders.

Ethics

Ethics Committee Approval: The study procedure conformed to the ethical standards of the Helsinki Declaration and was approved by the Afyonkarahisar Health Sciences University Ethics Committee (approval number: 2020/520).

Informed Consent: All participants provided written informed consent prior to the study.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Concept: F.F.G., M.D., M.C.S., H.H.G., A.K., Ş.U., Design: F.F.G., M.D., M.C.S., H.H.G., A.K., Ş.U., Data Collection or Processing: F.F.G., M.D., M.C.S., H.H.G., A.K., Ş.U., Analysis or Interpretation: F.F.G., M.D., M.C.S., H.H.G., A.K., Ş.U., Literature Search: F.F.G., M.D., M.C.S., H.H.G., A.K., Ş.U., Writing: F.F.G., M.D., M.C.S., H.H.G., A.K., Ş.U.

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