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Evaluation of the acoustic function in pseudoexfoliation syndrome and exfoliation glaucoma: Audiometric and tympanometric findings

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PURPOSE. *Previous studies have reported increased audiometric thresholds in patients with pseudoexfoliation syndrome (XFS), compared with normative data. This study examines mean audiometric thresholds and tympanometric peak values in patients with XFS and in a control group.*
METHODS. *This is a prospective, nonrandomized control case study. Patients with XFS in one or both eyes constituted the study group (SG). Patients without XFS in either eye constituted the control group (CG). Patients with a history of conditions affecting hearing function were excluded. The SG and the CG included 54 and 48 patients, respectively. Pure tone hearing thresholds levels were measured at 0.25, 1, 2, 3, and 8 kHz. Tympanometric peak values were also recorded. Differences in audiometric mean threshold values and tympanometric peak values between SG and CG, as well as between glaucomatous and nonglaucomatous eyes, were examined.*
RESULTS. *Bone and air audiometric thresholds were significantly increased in SG for 3 kHz and 8 kHz but not for 0.25 kHz, 1 kHz, and 2 kHz. Tympanometric peak values were significantly lower in SG compared with CG. In SG, glaucomatous patients had significantly higher air-conduction thresholds for 3 kHz and 8 kHz. Differences in bone and air audiometric findings as well as tympanometric findings between glaucomatous and nonglaucomatous patients were statistically not significant in CG.*
CONCLUSIONS. *The results agree with previous reports on sensorineural hearing loss in XFS. The reduced tympanometric peak values in SG imply impairment in the elastic properties of the middle ear in XFS. The findings provide additional evidence for the systemic nature of XFS. (Eur J Ophthalmol 2008; 18: 71-6)*

KEY WORDS. *Glaucoma, Pseudoexfoliation, Audiometry, Tympanometry, Pseudoexfoliation syndrome, Pseudoexfoliation glaucoma*

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INTRODUCTION

Pseudoexfoliation syndrome (XFS) is an age-dependent condition, characterized by the deposition of grey-white material at various anterior segment ocular structures (1, 2). There are indications that a disturbance in basement membrane synthesis may underlie XFS pathogenesis (3, 4). The detection of pseudoexfoliative material in several extraocular sites, including conjunctiva, orbit, skin, and visceral organs, has led to the assumption that XFS may

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be a systemic condition (5, 6).

XFS has been associated with several ophthalmic pathologic conditions, including glaucoma (exfoliative glaucoma, XFG) (1, 2). Some studies have reported a possible correlation between glaucoma and hearing loss, although there are controversial reports, depending on the type of glaucoma and the control population examined (7-9). Furthermore, deafness and glaucoma have been associated in a number of congenital conditions, including Alstrom and Stickler syndromes (10, 11). A previous study, employing pure-tone audiometry, has reported that sensorineural hearing loss is significantly more common in patients with XFS, compared with international standards, regardless of the presence of XFG (11). Age-related hearing loss may also result from defective elastic properties of tympanic membrane or middle-ear tissues (12). The latter is evaluated by tympanometry, a technique that assesses the mobility and immittance of tympanic membrane during pressure changes in the sealed ear canal (12, 13). The present study examines findings from air and bone audiometry and tympanometry in XFS and XFG as well as in an age-matched group of non-XFS individuals and aims at correlating results with clinical information. Findings could help in exploring the systemic manifestations of XFS and understanding the mechanism of XFS-related hearing loss.

METHODS

This is a prospective, nonrandomized control case study. Patients included were candidates for cataract or glaucoma surgery consecutively examined at the Department of Ophthalmology of the University Hospital of Alexandroupolis. Patients with a history of exposure to noisy environments, previous ear surgery or trauma, inflammations in the ear or upper respiratory tract, as well as previous use of ototoxic drugs were excluded to rule out hearing impairment related to these conditions. All patients signed a written informed consent form in accordance with the tenets of the Declaration of Helsinki.

Patients with XFS in one or both eyes constituted the Study Group (SG). The Control Group (CG) included patients without XFS features in either eye. The diagnosis of XFS was based on slit lamp examination following mydriasis as well as gonioscopic evaluation, as described elsewhere (2). The diagnosis of glaucoma was based on the combined evaluation of the intraocular pressure (IOP), optic disc (both ophthalmoscopically and with the GDx nerve fiber layer analyzer, Laser Diagnostic Technologies, San Diego, CA), and visual field testing (using the 30-2 program of the Humphrey automated perimeter, model 750, Humphrey Systems, 5160 Hacienda Drive, Dublin, CA), as described elsewhere (1).

The SG included 108 eyes of 54 patients (33 males, 61.11%) and the CG included 96 eyes of 48 patients (30 males, 62.06%). The average age (mean±SD, range) was 68.11±2.11 (57–87) years in the SG and 67.14±1.30 (69–84) years in the CG. The intraocular pressure (IOP) was 18.94±1.19 (15–25) mmHg and 17.38±0.63 (12–20) mm Hg in the eyes with SG and CG, respectively. XFS was bilateral in 34 of SG patients (62.96%). Twenty-five patients of the CG (52.08%) had been diagnosed with primary open angle glaucoma (POAG) in at least one eye. In the SG, 30 patients (55.55%) had been diagnosed with open-angle glaucoma in at least one eye (including XFG in pseudoexfoliative eyes and POAG in non-pseudoexfoliative eyes). Differences in age, gender, and IOP between patients of the SG and CG were not statistically significant (independent samples *t* test).

All patients had bilateral audiometric and tympanometric evaluations. Audiometry and tympanometry were performed by the same experienced examiner (V.D.) in all patients. Audiometry was performed with the Orbiter 922 audiometer (Madsen GN Otometrics, Taastrup, Denmark). Hearing thresholds (slightest perceptible sounds) for pure tones were measured for air-conduction in decibels hearing level (dB HL), for all octave and half-octave bands from 0.25 kHz to 8 kHz. However, only the results from 0.25, 1, 2, 3, and 8 kHz are presented for reasons of brevity and uniformity to previous reports (11). For air-conduction testing, insert earphones were used to reduce the crossover effect to the non-test ear. For bone-conduction testing, oscillators placed over the mastoid were used together with masking (constant noise) to the non-test ear to prevent crossover. Testing began approximately 60 dB above the expected threshold and continued in descending 10 dB steps below threshold. Subsequently, 5 dB-ascending steps were taken until two of four sounds were heard, as described elsewhere (9, 11). The threshold for each frequency was recorded and the entire range of audible pitches was plotted on an audiogram. Subsequently, the difference between the air-conduction threshold and the bone-conduction threshold (air-bone gap) was calculated for all examined frequencies in both SG and CG.

Tympanometry was performed with the Amplaid A724 Clinical Middle Ear Analyser (Amplifon, Milano, Italy). The tympanometer was calibrated before each use and the tips disinfected. The external auditory meatus was first inspected to rule out the presence of wax and to determine the size of the meatus for the proper selection of probe tip. The tip was then placed and sealed against the ear canal. The seal was maintained until the tympanogram was completed. The peak value of the compliance (mobility) curve (expressed in mL) was recorded.

Statistical analysis was performed with SPSS 8.0 for Windows (SPSS, Chicago, IL, USA). Statistical significance was set at 0.05. Differences in mean tympanometric peak values between SG and CG, as well as between nonglaucomatous and glaucomatous patients (i.e., those diagnosed with glaucoma in one or both eyes) in SG and CG, were examined. Differences in bone and air audiometric thresholds for each frequency between SG and CG as well as between nonglaucomatous and glaucomatous patients in SG and CG, as well as differences in the air-bone gap between SG and CG and between the glaucomatous and nonglaucomatous eyes of both SG and CG, were also examined. One-way analysis of variance (ANOVA) was employed in the comparisons of mean values. The power of the study was assessed using the G*Power statistical package (http://www.psycho.uni-duesseldorf.de/aap/projects/gpower/), assuming significance level (alpha)=0.05 and an effect size of d=0.25. According to these assumptions, a post hoc analysis for ANOVA (two groups) for a total sample size of 102 yielded a power of 0.70.

RESULTS

For both air and bone conduction, patients of SG displayed significantly higher mean audiometric thresholds, compared with patients of CG, for frequencies of 3 kHz and 8 kHz, whereas differences for frequencies of 0.25, 1, and 2 kHz were statistically not significant (Tab. I). Differences in the air-bone gap between SG and CG were not statistically significant for all examined frequencies (Tab. I).

In SG, patients diagnosed with glaucoma in one or both eyes had significantly higher audiometric hearing thresholds (compared with patients without glaucoma in either eye) for frequencies of 3 kHz and 8 kHz in air conduction. Respective differences were not statistically significant for frequencies of 0.25 kHz, 1 kHz, and 2 kHz (air conduction) as well as for all examined frequencies in bone conduction (Tab. II). The air-bone gap was also significantly higher in glaucomatous patients of the SG, compared with nonglaucomatous patients, for the frequency of 3 KHz. Respective differences in air-bone gap were not statistically significant for the other frequencies examined (Tab. II). In CG, differences in audiometric hearing thresholds between patients diagnosed with glaucoma in one or both eyes and patients without glaucoma in either eye were not statistically significant for all examined frequencies in both air and bone conduction (Tab. III). Furthermore, in CG, differences in air-bone gap between glaucomatous and nonglaucomatous patients were not statistically significant for all examined frequencies (Tab. III).

Tympanometric peak values were significantly lower in SG (0.66±0.60 mL) compared with CG (0.97±0.60 mL) (ANOVA F-value=3.41, p=0.04). In CG, differences in tympano-

TABLE I - AUDIOMETRIC THRESHOLDS (dB HL) OF AIR AND BONE CONDUCTION IN STUDY GROUP (SG) AND CONTROL GROUP (CG) IN FREQUENCIES EXAMINED, RESPECTIVE AIR-BONE GAPS, AND RESPECTIVE LEVELS OF STATISTICAL SIGNIFICANCE (one-way analysis of variance)

	Audiometric threshold (dB)								
Frequency (kHz)	Bone conduction			Air conduction			Air-bone gap		
	SG	CG	p	SG	CG	p	SG	CG	p
0.25	20.50	17.13	0.34	36.35	33.91	0.50	15.85	16.78	0.76
1	22.68	18.46	0.20	31.07	30.55	0.37	8.39	12.09	0.12
2	37.20	32.81	0.22	41.22	40.26	0.79	4.02	7.45	0.51
3	39.34	33.11	0.04	48.13	42.69	0.03	8.79	9.58	0.88
8	48.72	39.22	0.02	62.27	56.50	0.04	13.55	17.28	0.42

metric peak values between glaucomatous (1.05±0.78 mL) and nonglaucomatous patients (0.80±0.63 mL) were not statistically significant (ANOVA F-value=1.56, p=0.22). In SG, differences in tympanometric peak values between glaucomatous (0.77±0.69 mL) and nonglaucomatous patients (0.55±0.50 mL) were also not statistically significant (ANOVA F-value=3.07, p=0.09).

DISCUSSION

A previous study, based on the evaluation of pure tone audiograms, has detected sensorineural hearing loss for frequencies of 1, 2, and 3 kHz in a consecutive group of 69 patients with XFS, compared with the international standard ISO 7029, which gives values of normal age-associated hearing loss as deviations relative to the median thresholds of young otologically normal subjects (11). Other studies have also examined pure-tone audiograms in XFS and age- and gender-matched control patients and have confirmed the correlation between XFS and sensorineural hearing loss (14, 15). Results from the present study, also based on a group of pseudoexfoliative patients and on an age- and gender-matched control group, are in agreement with these reports but additionally support the possibility of XFS-associated impaired elastic properties of the middle ear, based on the impaired tympanometric peak values in the SG.

Advanced age has been significantly associated with impaired hearing acuity (16, 17). The attenuation in higher

TABLE II - AUDIOMETRIC THRESHOLDS OF AIR AND BONE CONDUCTION FOR FREQUENCIES EXAMINED IN GLAUCOMATOUS (G) AND NONGLAUCOMATOUS (NG) PATIENTS OF STUDY GROUP (SG), RESPECTIVE AIR-BONE GAPS, AND RESPECTIVE LEVELS OF STATISTICAL SIGNIFICANCE (one-way analysis of variance)

	Audiometric threshold (dB)								
Frequency (kHz)	**Bone conduction**			**Air conduction**			**Air-bone gap**		
	SG (G)	**SG (NG)**	**p**	**SG (G)**	**SG (NG)**	**p**	**SG (G)**	**SG (NG)**	**p**
0.25	15.92	24.02	0.07	36.18	36.48	0.95	20.26	12.46	0.06
1	21.25	23.75	0.58	31.22	30.98	0.29	9.97	7.23	0.06
2	40.03	35.16	0.27 4	5.26	38.30	0.15	5.23	3.14	0.26
3	42.05	37.17	0.38	56.11	42.20	≈0.00	14.06	5.03	0.02
8	50.90	47.63	0.67	69.94	57.24	0.01	19.04	9.61	0.06

TABLE III - AUDIOMETRIC THRESHOLDS OF AIR AND BONE CONDUCTION FOR FREQUENCIES EXAMINED IN GLAUCOMATOUS (G) AND NONGLAUCOMATOUS (NG) PATIENTS OF CONTROL GROUP (CG), RESPECTIVE AIR-BONE GAPS AND RESPECTIVE LEVELS OF STATISTICAL SIGNIFICANCE (one-way analysis of variance)

	Audiometric threshold (dB)								
Frequency (kHz)	**Bone conduction**			**Air conduction**			**Air-bone gap**		
	CG (G)	**CG (NG)**	**p**	**CG (G)**	**CG (NG)**	**p**	**CG (G)**	**CG (NG)**	**p**
0.25	16.00	17.66	0.77	36.07	32.93	0.54	20.07	15.27	0.44
1	19.50	18.00	0.76	34.28	28.87	0.27	14.78	10.87	0.28
2	41.76	29.06	0.14	47.50	37.00	0.16	5.74	7.94	0.67
3	32.14	33.35	0.83	44.07	41.65	0.13	11.93	8.3	0.61
8	28.33	42.82	0.11	50.80	58.69	0.31	22.47	15.87	0.38

frequency hearing is a feature of presbyacusis (age-dependent hearing loss) (16). The fact that this study detected statistically significant differences between SG and CG in audiometric thresholds of both bone and air conduction for higher frequencies (3 and 8 kHz), whereas respective differences for lower frequencies (0.25, 1, and 2, kHz) were not statistically significant, implies that XFS may enhance the effects of aging on hearing thresholds. Furthermore, the fact that all participating patients were recruited from the same population and the same hospital practice implies that CG used in the present study may be a more adequate comparison group for SG than international normative standards.

XFS-associated sensorineural hearing impairment may result from the presence of pseudoexfoliative fibrils in the organ of Corti, affecting the conduction of vibratory energy to sensory hair cells, as been previously suggested (11). In that case, findings would represent additional evidence for the systemic nature of XFS. The presence of pseudoexfoliative material may cause functional impairment in affected sites (18, 19). Therefore, the deposition of pseudoexfoliative fibers in other ear tissues, such as the middle ear conduction apparatus, including the tympanic membrane may explain the significantly reduced peak values of tympanograms in the SG compared with CG. However, biopsy specimens from middle ear would have to be examined to confirm this hypothesis. On the other hand, presbyacusis may be correlated with dietary factors affecting the role of reactive oxygen metabolites (ROMs) (9). Similar factors have been implicated in the pathogenesis of XFS (20, 21). Therefore, the association between presbyacusis and XFS may reflect common etiologic mechanisms.

Hearing thresholds were not significantly higher among patients with glaucoma in the CG, despite the fact that glaucomatous patients had higher hearing thresholds, compared with nonglaucomatous patients, in frequencies of 1 and 2 kHz for bone conduction and most examined frequencies for air conduction (except 8 kHz). This finding is in agreement with previous studies, although there are controversial reports on the correlation between glaucoma and hearing loss (22-25), possibly due to the diversity of glaucomas and different methodologies employed in various studies. In the case of glaucomatous patients with SG, air-conduction audiometric thresholds were significantly higher for frequencies of 3 kHz and 8 kHz, whereas respective differences for frequencies of 0.25 kHz, 1 kHz, and 2 kHz (air-conduction) and all examined frequencies in bone conduction were not statistically significant. This finding again supports the possibility that XFS may preferentially affect sensorineural hearing in higher frequencies and is in agreement with the fact that audiometric thresholds were significantly higher in SG, compared with CG, for 3 kHz and 8 kHz. The fact that tympanometric peak values did not differ significantly between glaucomatous and nonglaucomatous patients of both SG and CG, whereas respective differences between SG and CG were statistically significant, differentiates the associations between hearing impairment and XFS or glaucoma. Indeed, based on the present findings, it would seem more probable that XFS, rather than glaucoma, is primarily associated with hearing impairment in the patients studied.

The non-randomized design and relatively small number of patients recruited may be considered weaknesses of this study. On the other hand, the consecutive recruitment of eligible patients in both groups, which did not differ in age and gender distribution, and the fact that all hearing functional tests were performed by the same examiner enhance the validity of results. Nevertheless, larger randomized trials would be required to further clarify a potential association between hearing loss and XFS as well as between hearing loss and the glaucomas.

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