· Clinical research ·

Should the ophthalmologic examination be performed in presbyacusis patients for early diagnosis of pseudoexfoliation syndrome?

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Abstract

• AIM: To find out if presbyacusis is a predictive clinical parameter for early diagnosis of pseudoexfoliation syndrome (PES).

• METHODS: This is a prospective, case-control study. 30 patients with PES in one or both eyes constituted the study group and the other 30 presbyacusis patients were in control group. Pure-tone hearing threshold levels (HTLs) were measured at 0.5, 1, 2, and 4 kHz. Tympanometric peak values and transient evoked otoacoustic emissions (TEOAE) testing results were also recorded. All subjects underwent a detailed ophthalmic examination.

• RESULTS: Distribution of the hearing levels was different between the study group and control group. Mild hearing loss (21-40 dB) was higher in control group than that in study group. Mean hearing thresholds at each of the examined frequencies were compared directly between the two groups. Clinically significant differences were found when we compared mean pure-tone HTLs between the 2 ears of the two groups. However, there was not a statistically and clinically significant difference between the 2 ears mean pure-tone HTLs at high frequency (4 kHz).

• CONCLUSION: We concluded that patients who are diagnosed with presbyacusis in ear, nose, and throat should not be performed any ophthalmic examinations, which would save time and money in daily clinical practice.

• KEYWORDS: presbyacusis; pseudoexfoliation syndrome; transient evoked otoacoustic emissions; early diagnosis
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INTRODUCTION

The term presbyacusis refers to sensorineural hearing impairment in elderly individuals. Characteristically, presbyacusis involves bilateral high-frequency hearing loss associated with difficulty in speech discrimination and central auditory processing of information. Feldmann[1] first described the association between advanced age and high-tone deafness in 1899. Since then, extensive research has attempted to determine the pathologic changes of presbyacusis. Although the precise etiology of presbyacusis is not known currently, the cause of presbyacusis is generally agreed to be multi-factorial. Proposed causes include arteriosclerosis, noise exposure, stress, genetic, diet, metabolism, drug and environmental chemical exposure, disease of the ear, and systemic diseases.

Lindberg[2] first described pseudoexfoliation syndrome (PES) in 1917 in a Finnish population. This syndrome is recognized to be a systemic disorder. It is the most common identifiable cause of glaucoma, which has now been termed pseudoexfoliation glaucoma (PESG)[3]. A protein-like material of the lens, iris, and various other anterior ocular structures characterizes the exfoliation syndrome, a relatively common disorder among older individuals and within certain ethnic populations. It is recognized clinically by the typical appearance of the exfoliative material on the anterior lens capsule. Ocular PES is characterized by white fibrillar deposits on the anterior capsule surface of the lens and/or pupil margin. Features other than PES include endothelial pigmentation, loss of pupillary ruff, iris sphincter transillumination, Sampaolesi's line, and pigment deposition in the trabecular meshwork[4].

There is increasing evidence that pseudoexfoliation not only affects ocular anterior segment structures, but may also be a systemic disease. The pseudoexfoliation material mainly localized to connective-tissue portions or septa traversing the various organs. PES materials can also be observed in the skin, lung, heart, liver, gall bladder, kidneys, blood vessels, extraocular muscles, and meninges[5]. Additionally, there is evidence of association between pseudoexfoliation and systemic vascular disorders[6]. For these reasons, considering the possible adverse effect of abnormal deposits and/or vascular abnormalities on the hearing organs, that can cause hearing loss. In this study, we aimed to find out whether an

association exists between presbyacusis and PES and to determine if presbyacusis is a predictive clinical parameter for early diagnosis of PES.

MATERIALS AND METHODS

Materials This study was conducted between January 2008 and April 2010 in the Faculty of Medicine University of Cumhuriyet, Sivas, Turkey and approved by the Ethical Committee of the University of Cumhuriyet Faculty of Medicine in accordance with the Declaration of Helsinki. This prospective case-control study was performed in patients of both groups. All patients were informed of the audiometric testing and examination process. Informed consent and full medical history was obtained from each participant.

Patients of study group were recruited from the eye clinic. Consequently, all of the patients diagnosed with PES were referred to the Department of Ear, Nose and Throat (ENT) for a complete otological assessment. Patients of control group were recruited from the ENT clinic and referred to the Department of Ophthalmology for a complete ophthalmologic assessment.

Exclusion criteria were history of ear surgery, acute or chronic otitis media, history of tympanic membrane perforation, ear or head trauma, upper respiratory tract infection during the examination, intake of oto-toxic drugs, employment in a noisy environment, history of intraocular surgery (except PES and PESG or any other eye disease), and systemic diseases like hypertension and diabetes mellitus.

Methods All subjects underwent a detailed ophthalmic examination by the same investigator, including visual acuity, biomicroscopy, gonioscopy, Goldmann applanation tonometry, and dilated fundoscopy with a +90 diopter noncontact lens. Ocular hypertension was diagnosed as presence of intraocular pressure >21mmHg. Glaucoma was diagnosed as presence of one of the following criteria: typical glaucomatous optic nerve head damage (e.g., thinning or notching of the neuroretinal rim) or glaucomatous visual field defects. Visual field testing was performed using the central 30-2 program of the Humphrey 740 automated perimeter (Humphrey Systems, Dublin, CA)[7].

Presbyacusis patients were selected from the patients who presented at the ENT clinic with complaints of hearing loss. An otoscopic investigation was carried out prior to testing. It was ensured that the test results were not influenced by conditions such as wax or occlusion/obstruction/collapse of the external auditory canal. Then, audiometry, TEOAE, and tympanometry were performed in all cases. Pure-tone audiometry was performed by the same examiner in all participants with the Interacoustics Clinical Audiometer AC 40 (Interacoustics, Assen, Denmark). Pure-tone hearing threshold levels (HTLs) were measured in decibels (dB) using air and bone conduction audiometry. Pure-tone HTLs were measured at 0.5, 1, 2, and 4 kHz for each ear. The pure-tone audiogram hearing levels were classified into 6 groups as follows: 0-20 dB, normal hearing; 21-40 dB, mild hearing loss; 41-60 dB, moderate hearing loss; 61-80 dB, moderate to severe hearing loss; 81-100 dB, severe hearing loss; and >100 dB, profound hearing loss.

Tympanometry was performed using a MAICO MI 44 Analyzer. Tympanometry results were classified as a type A, B, or C tympanogram.

TEOAE testing and analysis were accomplished utilizing the MAICO ERO SCAN Analyzer (Maico, ERO Scan Analyzer, GmbH Salzufer, 13/14, 10587, Berlin GE). Disposable ear tips were used to cover the probes and seal the ear canals snugly during testing. When a test was completed, the results displayed on the screen as "PASS" when there was TEOAE response, and "REFER" when there was no response to a stimulus. When a "REFER" result was obtained, the screening test was repeated twice to confirm the result.

Statistical Analysis Data were analyzed by using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL) for Windows version 14.0. The Chi-square test and independent-samples T test were used to examine the association between variables. A P-value less than 0.05 was considered statistically significant.

RESULTS

Overall, 60 subjects were enrolled in this prospective case-control study, which included 30 patients with PES (study group)[16 (47%) men, 14 (53%) women] and 30 patients with presbyacusis (control group) [16 (47%) women, 14 (53%) men]. Both groups were similar in gender ($t=0.38$, $P=0.700>0.05$). The mean patient age was 66.50±9.26 (range 50-87) years. The mean patient age of study group was 71.83±6.56 years; the women were aged 73.50±6.87 (range 50-87) years, and the men were aged 70.37±6.13 (range 50-85) years. In the control group, the mean patient age was 61.12±8.51 years; the women were aged 61.07±10.22 (range 50-77) years and the men were aged 61.25±7.06 (range 50-79) years. There was no difference between the 2 groups ($t=1.31$, $P=0.199>0.05$). A statistically significant difference was found between Snellen visual acuity and fundoscopic examinations ($P<0.05$).

Glaucoma was present in one eye of 7 (23%) or both eyes of 23 (77%) patients in study group, but did not exist in the patients of control group. A significant difference was found between the 2 groups ($P<0.05$). Open angle glaucoma was detected in 25 (83%) patients in study group, but was not determined in the patients of control group. A statistically significant difference was found between the 2 groups ($\chi^2=27.80$, $P=0.001<0.005$). There were no statistical differences between the 2 groups in terms of angle closure glaucoma ($P>0.05$).

In study group, 13 patients (43%) had normal hearing levels, while 17 (57%) patients had hearing loss at various levels: 13 (43%) patients had mild hearing loss; 2 (7%) patients, moderate hearing loss; 1 (3%) patient, moderate to severe hearing loss; and 1 (3%) patient, severe hearing loss. In control group, the distribution of hearing levels was 12 (40%) patients, mild hearing loss; 11 (37%) patients, moderate hearing loss; 4 (13%) patients, moderate to severe hearing loss; 2 (7%) patients, severe hearing loss; and 1 (3%) patient,

Table 1 Distribution of hearing levels of bilateral and unilateral PES (+) and PES (-) patients *n*(%)

Hearing level	Unilateral PES (+)	Bilateral PES (+)	PES (-)	Total
Normal hearing (0-20 dB)	4 (7)	9 (15)	0 (0)	13 (22)
Mild hearing loss (21-40 dB)	5 (8)	10 (17)	10 (17)	25 (42)
Moderate hearing loss (41-60 dB)	0 (0)	2 (3)	11 (18)	13 (22)
Moderate to severe hearing loss (61-80 dB)	0 (0)	1 (2)	4 (7)	5 (8)
Severe hearing loss (81-100 dB)	0 (0)	0 (0)	2 (3)	2 (3)
Profound hearing loss (>100 dB)	0 (0)	1 (2)	1 (2)	2 (3)
Total	9 (15)	23 (38)	28 (47)	60 (100)

Table 2 Mean pure-tone hearing thresholds of PES and presbyacusis patients (AC: Air conduction, BC: Bone conduction) $\bar{x}\pm s$

Frequency (kHz)			PES group HTLs in dB	Presbycusis group HTLs in dB	*P* value
0.5 kHz	Right ear	BC (dB)	22.00±16.37	29.83±13.67	$P=0.0049$, $t=2.01$
		AC (dB)	27.50±23.55	39.16±20.04	$P=0.043$, $t=2.06$
	Left ear	BC (dB)	18.50±15.20	27.83±15.62	$P=0.023$, $t=2.34$
		AC (dB)	23.00±21.35	34.16±21.29	$P=0.048$, $t=1.96$
1 kHz	Right ear	BC (dB)	19.66±15.53	29.00±17.19	$P=0.031$, $t=2.20$
		AC (dB)	25.66±23.40	39.33±15.35	$P=0.010$, $t=2.67$
	Left ear	BC (dB)	20.00±16.45	30.61±15.41	$P=0.012$, $t=2.59$
		AC (dB)	25.66±22.15	39.00±19.71	$P=0.017$, $t=2.46$
2 kHz	Right ear	BC (dB)	25.16±17.97	39.33±13.11	$P=0.001$, $t=3.48$
		AC (dB)	30.66±23.40	46.83±14.41	$P=0.002$, $t=3.22$
	Left ear	BC (dB)	24.16±17.37	37.00±15.89	$P=0.004$, $t=2.98$
		AC (dB)	31.00±24.08	44.16±19.52	$P=0.024$, $t=2.32$
4 kHz	Right ear	BC (dB)	37.16±23.69	47.33±17.35	$P=0.063$, $t=1.89$
		AC (dB)	42.83±22.99	57.83±18.46	$P=0.007$, $t=2.78$
	Left ear	BC (dB)	36.16±21.92	44.83±16.68	$P=0.090$, $t=1.72$
		AC (dB)	45.00±23.67	53.16±19.45	$P=0.150$, $t=1.46$

dB: Decibels; HTLs: Hearing thresholds; kHz: kilohertz; SD: Standard deviation.

profound hearing loss. Distribution of the hearing levels was significantly different between the two groups ($P<0.01$).

In study group, 7 patients (23%) presented unilateral and 23 (77%) patients presented bilateral PES. 28(93%) patients' eye examinations were normal. 2(7%) patients presented unilateral PES in control group. There was a statistically significant difference between the 2 groups in terms of pseudoexfoliation($P<0.05$).

Hearing levels of unilateral PES (+), bilateral PES (+) and PES (-) patients were compared in Table 1.

Pure-tone HTLs were identical for both air and bone conduction audiometry in all patients. Audiometry results were recorded for both ears of 60 patients. Mean HTLs at each of the examined frequencies were compared directly between PES and presbyacusis patients. Clinically significant differences were found when comparing mean pure-tone HTLs between the 2 ears of PES and presbyacusis patients. However, there were no statistically and clinically significant differences between 2 ears pure-tone HTLs in high frequency (4kHz, $P>0.05$). Presbyacusis patients displayed significantly higher mean audiometric HTLs compared with PES patients at frequencies of 0.5, 1 and 2 kH, but not at frequency of 4 kHz (Table 2, Figure 1, 2).

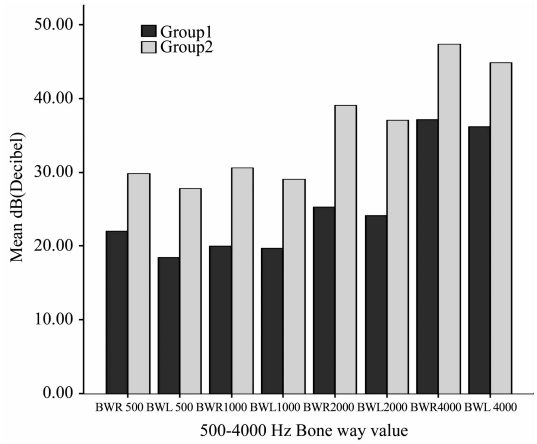

Figure 1 Mean hearing thresholds for bone conduction (BC): During the measurement of BC hearing for each frequency in the detection mean threshold distribution of the groups. BWR: Bone way right ear; BWL: Bone way left ear.

All patients' tympanometric evaluations were obtained by a type A tympanogram.

In TEOAE screening, 15(25%) patients bilaterally passed; 31 (52%) patients were bilaterally referred, 10(17%) patients were left ear referred,and 4(7%) patients were right ear referred. The TEOAE results of all patients are shown in Table 3.

Table 3 Distribution of TEOAE screening results of bilateral and unilateral PES (+) and PES (-) patients *n*(%)

TEOAE screening results	Unilateral PES (+)	Bilateral PES (+)	PES (-)	Total
Bilateral pass	3 (5)	10 (17)	2 (3)	15 (25)
Bilateral referred	3 (5)	5 (8)	23 (38)	31 (52)
Left ear referred	2 (3)	6 (10)	2 (3)	10 (17)
Right ear referred	1 (2)	2 (3)	1 (2)	4 (7)
Total	9 (15)	23 (38)	28 (47)	60(100)

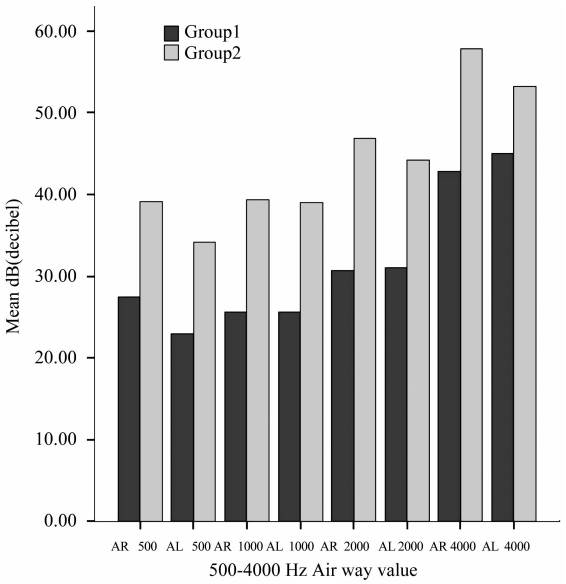

Figure 2 Mean hearing thresholds for air conduction (AC): During the measurement of AC hearing for each frequency in the detection mean threshold distribution of the groups. AWR: Air way right ear; AWL: Air way left ear.

DISCUSSION

This study is to find out whether an association exists between presbyacusis and PES and to determine if presbyacusis is a predictive clinical parameter for early diagnosis of PES. According to our findings, the detection rate of PES was low in patients with presbyacusis, as only 2 (7%) patients presented with unilateral PES in the presbyacusis group's patients. There was a statistically significant difference between the 2 groups in terms of pseudoexfoliation. The results of the present study show that presbyacusis is not a predictive clinical parameter for early diagnosis of PES.

PES occurs worldwide, but its prevalence varies among different age groups, races, and geographical locations. PES onset is rarely found before age 50 and usually is noted after age 70[8]. The highest prevalence (20%-70%) has been reported in elderly people, and it is estimated that PESG affects 10%-20% of all individuals above 60 [3]. Moreover, prevalence varies in different countries, with the highest rate of about 46.9% in Greece [9], 31.3% in Iceland [10], and 5.5% in France [11]. PES disease is common in Sivas, Turkey, but a study of the prevalence of PES has not been performed there.

PES and presbyacusis are age-related diseases that share common predisposing factors such as dietary factors affecting free radical production[7,12]. This implies that there may be similarities in the pathologic and biochemical findings of these conditions. Both of the ocular anterior segment structures were affected by the PES and the tectorial and basilar membranes in the inner ear structures embryologically originate from the neural ectoderm [13]. Therefore, fibrils of PES material that accumulate on the lens, pupillary margin, and other anterior segment structures can also accumulate on the tectorial and basilar membranes and stria vascularis in the inner ear[13,14]. Therefore, sensorineural hearing loss in PES is due to deposition of pseudoexfoliation material on the organs of Corti, thus causing dysfunction in hearing mechanoreceptors. In addition, the inner ear and eyes are involved in some similar enzymatic activity. For example, carbonic anhydrase enzyme is found in the inner ear as well as in the eyes, in the ciliary body non-pigmented and pigmented epithelium and retinal pigment epithelium. Seidman[12] showed that treatment with antioxidants or dietary restriction can attenuate age-related hearing loss. Koliakos *et al*[15] found that significantly increased 8-Isoprostaglandin F2 and decreased ascorbic acid in the aqueous of patients with PES, which provided evidence of a role for free radical-induced oxidative damage in the pathobiology of PES.

Sensorineural hearing loss associated with PES has been shown in several studies[13,14,16]. Two known causes of sensorineural hearing loss are the loss of auditory hair cells following exposure to environmental stresses and ischemia. Sensorineural hearing loss could be due to the presence of exfoliation fibrils in the vessel walls that can impair the blood supply to the inner ear and cause cochlear ischemia. We know that the cochlear base is more sensitive to the ischemia. Therefore, in PES patients, hearing loss is more pronounced at high frequencies. Seth and Dayal[17] first described an association between glaucoma and inner ear disease in 1889. After that, a number of reports have suggested such an association. However, in some other studies, the relationship between hearing loss and glaucoma and PES could not be determined. Turacli *et al*[13] demonstrated a higher prevalence of sensorineural hearing loss in PES patients. Sensorineural hearing loss was detected in the majority of PES patients by Yazdani *et al*[6]. Shapiro *et al*[18] did not find an association between glaucoma and hearing loss in 67 glaucoma patients. Geribeyoğlu *et al*[5] evaluated 54 patients divided into 3 groups (PES, PESG, and control) and did not find an association with hearing loss in any group. Sensorineural

hearing loss was detected in 17 PES patients and 30 presbyacusis patients in our study. Distribution of the hearing levels was significantly different between study group and control group ($P<0.01$). However, PES patients' hearing levels were found to be better than those of the presbyacusis patients in this study. Papadopoulos *et al*[7] demonstrated that in PES patients, mean HTLs were significantly increased at 4 and 8 kHz. Detorakis *et al*[19] found that mean HTLs were significantly increased in PES patients for 3 and 8 kHz. However, in our study, presbyacusis patients' mean HTLs were significantly higher than those of PES patients at 0.5, 1, and 2 kHz, and both groups' sensorineural hearing levels were high at 4 kHz. In addition, there was no significant difference between the 2 patient groups at 4 kHz ($P>0.005$).

PES is a systemic disorder, and ocular exfoliation-like deposits were discovered in various visceral organs such as heart, lung, liver, gall bladder, kidney, skin, and cerebral meninges[5,6,13]. Cahill *et al*[14] suggested that PES does not only affect ocular anterior segment structures, but may also be a systemic disease. Sixty-nine patients with PES were evaluated in this study, and the researchers found that a large proportion of them had sensorineural hearing loss in comparison to age-matched controls, regardless of whether this was associated with glaucoma. Papadopoulos *et al*[7] demonstrated that the relationship between PES and sensorineural hearing loss supports the theory that this ocular disease may be a manifestation of a systemic condition, which also causes inner ear disorders. Shaban *et al*[16] found ocular PES in 41 PES patients during routine ophthalmic examinations. Their study suggested that ocular PES, which is considered a systemic disease, could also affect other organs as well as the eye.

Erberk *et al*[20] also demonstrated a higher prevalence of sensorineural hearing loss in PES patients, but these differentiations were not demonstrated with otoacoustic emissions. Transient evoked otoacoustic emissions TEOAE were present in 42 patients with PES and in 32 healthy subjects, which was not statistically significant ($P>0.05$). Erberk *et al*[20] aimed to assess whether outer hair cell function in patients with PES was affected or not. Their results confirmed the presence of sensorineural hearing loss in PES patients. However, they failed to show a difference in outer hair cell functions of this group. Our TEOAE screening results are shown in Table 4. All patients underwent TEOAE screening; 13 patients passed and 19 patients were referred in the PES (+) patients, while 2 patients passed and 26 patients were referred in the PES (-) patients. The relatively small number of patients may be considered as a limitation of our study. For this reason, we could not draw any definite conclusions from our statistical results for the TEOAE.

Tympanometric peak values were found to be significantly lower in PES patients compared with presbyacusis patients[19]. The reduced tympanometric peak value in PES patients implies impairment in the elastic properties of the middle ear in PES. This differentiation was not found in our study because we examined tympanometric peak values in all patients and found type A timpanograms.

PES is the most common identifiable cause of open angle glaucoma worldwide. Exfoliation syndrome plays an etiologic role in open angle glaucoma, angle-closure glaucoma, cataracts, and retinal vein occlusion. The early diagnosis of ocular PES is very important for the ophthalmologist, since PES causes chronic open angle glaucoma, angle-closure glaucoma, and increased lens opacification that increases the risk of intraoperative and postoperative complications in cataract surgery[7].

CONCLUSION

In this study, we examined mean audiometric thresholds, tympanometric peak values, and TEOAE in patients with PES and presbyacusis patients.

We investigated if presbyacusis predicted clinical symptoms were in PES patients. If PES is not diagnosed at an early stage, it increases the incidence of complications of treatment. There are 2 common features of these diseases: those that are seen in elderly patients and ocular anterior segment structures affected by the PES and the tectorial and basilar membranes in the inner ear structures that have embryologically originated from the neural ectoderm.

We have put forward a hypothesis for the early diagnosis of PES, noting that patients diagnosed with presbyacusis should have an eye examination performed as a routine clinical benefit. We also asked, "Should the ophthalmologic examination be performed in presbyacusis patients for early diagnosis of pseudoexfoliation syndrome?" PES was found in 7% (2 patients) of our presbyacusis patients. This finding is statistically significant ($P<0.05$). However, PES was detected in a low proportion of patients with presbyacusis in our study. For this reason presbyacusis is not a predictive clinical parameter for early diagnosis of PES in our opinion.

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老年性耳聋患者应否进行眼科检查以早期诊断假性剥脱综合征?

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摘要

目的:探讨老年性耳聋是否为早期诊断假性剥脱综合征(pseudoexfoliation syndrome,PES)的临床预测参数。

方法:这是一项前瞻性病例对照研究。单眼或双眼 PES 患者组成研究组,另有 30 例老年性耳聋患者。测量 0.5,1,2 和 4kHz 纯音听阈水平。同时记录鼓室测压高峰值和瞬态诱发耳声发射测试结果。所有受试者进行了详细的眼科检查。

结果:PES 组与老年性耳聋的听力水平分布不同。轻度听力丧失(21~40 分贝)第 2 组高于第 1 组。对 PES 和老年性耳聋患者各检查频率之平均听力阈值进行直接比较。比较 PES 和老年性耳聋患者的平均纯音听阈可发现两耳之间存在显著性差异。然而高频率(4kHz)时,两耳之间无统计学意义。

结论:所有在耳鼻喉科诊断为老年性耳聋的患者不应该进行眼科检查。在临床实践中,此种检查是时间和金钱的巨大浪费。

关键词:老年性聋;假性剥脱综合征;瞬态诱发耳声发射;早期诊断