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MAIN ARTICLE

Association of age-related macular degeneration with age-related hearing loss

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Abstract

Objective: To assess the association between age-related macular degeneration and age-related hearing loss in Turkish subjects aged 50 years or older.

Study design and setting: Prospective, case–control study within a tertiary university hospital.

Subjects and methods: Fifty subjects with age-related macular degeneration and 43 healthy subjects underwent ophthalmological and otolaryngological examination. Statistical analyses were conducted for the poorer eye and ear, comparing age-related hearing loss and pure tone average in the macular degeneration group versus controls.

Results: Median pure tone average was significantly poorer in the macular degeneration group (35 dBHL) compared with controls (23 dBHL). In the macular degeneration group, hearing loss was significantly greater in dry type (43 dBHL) than wet type (32 dBHL) cases. There was a significant difference between the prevalence of varying degrees of hearing loss in the macular degeneration versus control groups, being respectively: mild, 50 and 35 per cent; moderate, 20 and 5 per cent; and severe, 6 and 0 per cent. There was a weak, but significant correlation between each patient's visual acuity and pure tone average results ($r_s = -0.37$, $p < 0.001$).

Conclusion: Age-related hearing loss is more common in patients with age-related macular degeneration. Such patients should be questioned regarding hearing difficulty, and referred to an otolaryngologist if appropriate.

Key words: Age-related Macular Degeneration; Presbycusis; Vision Loss

Introduction

Age-related hearing loss is a common health problem affecting approximately 35–45 per cent of adults older than 50 years.[1] It is the third most common chronic disease in the US geriatric population, after hypertension and arthritis. Age-related hearing loss is a complex disorder influenced by genetic, environmental and lifestyle factors.[2] It is generally thought to result from age-related degeneration of the cochlea, arising from cumulative extrinsic and intrinsic damage. This cochlear degeneration is most pronounced in the basal cochlear coil, and is characterised by degeneration of the organ of Corti, ganglion cell loss, strial atrophy and basilar membrane stiffness.[3] Pathological mechanisms contributing to presbycusis include hypoxia and ischaemia, reactive oxygen species formation and oxidative stress, apoptotic and necrotic death of hair cells and spiral ganglion cells, and inherited and acquired mutations of mitochondrial DNA.[4] Patients report that sounds often seem less clear and lower in volume, which contributes to difficulty in hearing and understanding speech and greatly decreases the patient's health-related quality of life.[5,6]

Age-related macular degeneration is the most common cause of visual loss among people over the age of 60 years, and affects millions of people every year. This condition affects the central regions of the retina and choroid, resulting in central visual loss. This causes difficulty in reading, driving and performing other activities requiring fine, detailed vision, decreasing the patient's health-related quality of life.[7–9] There are two major clinical presentations of age-related macular degeneration: the non-exudative, atrophic or dry type, characterised by degeneration of choriocapillaris, retinal pigment epithelium and neurosensory retina; and the wet, exudative or neovascular type, characterised by development of serous retinal pigment epithelium detachment and/or new choroidal vessels, which can lead to bleeding, exudation and eventual scar formation.[10] The risk factors for age-related macular degeneration include ethnicity, gender, hypertension, genetics, smoking, diet and sunlight exposure. The pathophysiology of age-related macular degeneration is complex. In addition to genetic predisposition, at least four other pathogenetic processes contribute to the disease: lipofuscinogenesis

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(linked to oxidative stress), drusogenesis, local inflammation and neovascularisation.[11]

In the 1999 US National Health Interview Survey, 18 per cent of US adults aged 70 years or older reported visual impairment, 33 per cent reported hearing impairment, and 9 per cent reported both visual and hearing impairment.[12] In another study, of 65–99-year-old individuals being evaluated for aged care services at a geriatric assessment centre, visual impairment was found in 30.2 per cent, moderate to severe hearing loss in 50.5 per cent, and combined sensory impairment in 22.5 per cent (of individuals taking both tests).[13]

In population-based cohort studies, hearing loss has been shown to be associated with both age-related macular degeneration and cataract development.[14–16]

The present study assessed the association between age-related macular degeneration and age-related hearing loss in a cohort of Turkish subjects aged 50 years or older.

Subjects and methods

This prospective, case–control study included 50 subjects with age-related macular degeneration and 43 healthy controls.

The study protocol adhered to the tenets of the Declaration of Helsinki, and was approved by the ethics committee of the Selcuk University Meram Medical Faculty. All subjects gave informed consent to inclusion in the study.

The study group comprised patients followed for age-related macular degeneration at the Selcuk University Hospitals ophthalmology department retina service. The control group consisted of individuals who had visited the Selcuk University ophthalmology department for routine examination or eyeglasses prescription.

All subjects underwent a complete ophthalmological examination performed by one of the study's senior ophthalmologists (BTO), including visual acuity testing (using a Snellen chart), slit-lamp biomicroscopy, intraocular pressure measurement (using Goldmann applanation tonometry), dilated fundus examination (with a 90 diopter lens), fundus photography and optical coherence tomography.

Age-related macular degeneration was classified according to the system proposed by the International Age-Related Maculopathy Epidemiologic Study Group.[17]

Subjects with previous ear disorders and/or ocular diseases (other than age-related macular degeneration) that decreased visual acuity (e.g. corneal opacities, cataract, diabetic retinopathy, other macular pathologies and glaucoma) were not included in the study. Subjects with mild nuclear sclerosis were not excluded.

The study and control groups were similar as regards co-associated systemic vascular diseases such as hypertension and uncomplicated diabetes mellitus.

Otolaryngological examination was performed by one of the study's senior otolaryngologists (MKB). Hearing evaluation was conducted by a clinical audiologist. Audiometric examination was performed with the subject seated in a sound-proofed room, using a standard audiometer (OB822; Madsen Electronics, Copenhagen, Denmark) calibrated according to conventional standards (American National Standards Institute). Hearing thresholds were determined for each ear at 250, 500, 1000, 2000, 4000 and 6000 Hz.

Definitions

Visual impairment was defined using the following visual acuity thresholds: mild, 20/40 to 20/80; moderate, 20/80 to 20/200; and severe, less than 20/200. In patients with unilateral age-related macular degeneration, the diseased eye was utilised for statistical analysis. When both the patient's eyes were involved, the poorer eye was used for statistical analysis.

Pure tone air conduction thresholds were obtained for each ear at the frequencies noted above. Hearing loss was defined as a pure tone average (PTA) of higher than 25 dBHL in either ear, calculated at 500, 1000, 2000 and 4000 Hz. Mild hearing loss was defined as poorer than 25 dBHL but better than 45dB HL, moderate hearing loss as poorer than 45 dBHL but better than 65 dBHL, and severe hearing loss as poorer than 65 dBHL. Hearing loss for the higher frequencies was defined as a PTA of higher than 40dBHL for 4000 and 6000 Hz.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences software (SPSS Inc, Chicago, Illinois, USA). Analyses were conducted for the poorer eye and ear. The percentage of hearing loss in the study and control groups was compared using the chi-square test. Pure tone averages for the two groups were compared using the non-parametric Mann–Whitney U test, with the correlation between visual acuity and PTA level calculated using the Spearman test. The age-related macular degeneration patients were subclassified as dry type or wet type, and these subgroups were statistically analysed to evaluate any differences in visual acuity and PTA. The study and control groups' higher frequency PTAs were compared. A p value of less than 0.05 was considered statistically significant.

Results

The age-related macular degeneration group had a mean age ± standard deviation (SD) of 69.34 ± 8.6 years (range 53–93 years); 46 per cent of these patients were female and 54 per cent male (Table I). The control group had a mean age ± SD of 66.88 ± 4.4 years (range 58–76 years); 41.9 per cent of these subjects were female and 58.1 per cent male. There were no significant differences in gender or age between the two groups ($p > 0.05$). The mean age of men and women in the whole study population was similar, with no statistically significant difference ($p = 0.2$).

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TABLE I
DATA FOR STUDY AND CONTROL GROUPS

Parameter	Study grp	Control grp	*p*
Age (mean ± SD; y)	69.34 ± 8.6	66.88 ± 4.4	>0.05
Median VA	20/200	20/20	<0.001
Speech PTA (dBHL)			
– Median	35.5	23	<0.001
– Mean ± SD	38.24 ± 17.5	25.09 ± 10.83	
– Range	15–93	10–57	
HF PTA (dBHL)			
– Median	60	45	<0.001
– Mean ± SD	60.2 ± 17.1	42.7 ± 16.8	
– Range	25–95	10–80	

Grp = group; SD = standard deviation; y = years; VA = visual acuity; speech PTA = pure tone average for speech frequencies, HF PTA = PTA for higher frequencies

Based on fundus examination and optical coherence tomography findings, two patients with drusen and 14 with geographical atrophy were categorised as having dry type age-related macular degeneration, while 22 patients with choroidal neovascular membrane and 12 with macular scarring were categorised as having wet type degeneration.

The median presenting visual acuity in the poorer eye was 20/20 in the control group (range 10/20 to 20/20) and 20/200 in the study group (range 20/2000 to 16/20). In the study group, visual impairment was mild in 12 per cent, moderate in 36 per cent and severe in 46 per cent. Patients with dry type and wet type age-related macular degeneration showed no significant difference in visual acuity (median values 20/200 and 20/200, respectively; $p = 0.7$).

The median PTA in the study group was significantly higher than that of the control group ($p < 0.001$) (Table I). Furthermore, the median PTA of dry type age-related macular degeneration patients was significantly higher than that of wet type patients ($p = 0.027$) (Table II). Hearing loss in the study and control groups was respectively mild in 50 and 34.9 per cent, moderate in 20 and 4.7 per cent, and severe in 6 and 0 per cent ($p = 0.001$). In the study group, there was no significant difference in the prevalence of hearing loss in men (74 per cent) versus women (78.2 per cent) ($p = 0.2$).

At higher frequencies, the median PTA was significantly higher in the study group compared with the control group ($p < 0.001$) (Table I). There was no significant difference between the high frequency PTA values of dry versus wet type age-related macular degeneration patients ($p = 0.07$) (Table II). Higher frequency hearing loss was observed in 92.5 per cent of the study group and 60.5 per cent of the control group ($p < 0.001$). Thirty-five subjects (37.6 per cent) had combined visual and hearing impairment.

The correlation between visual acuity for the poorer eye and PTA for the poorer ear was significant, ($r_s = -0.37$, $p < 0.001$) (Figure 1). Using linear regression analysis, for each one-line reduction in best-corrected visual acuity (i.e. five letters), the PTA was shown to increase by 13.8 per cent ($p = 0.001$). The multivariate-adjusted odds ratio for hearing loss and age-related macular degeneration was 4.58 (95 per cent confidence interval (CI) 1.76–11.9) ($p = 0.002$); for hearing loss and age it was 1.13 (95 per cent CI 1.04–1.22) ($p = 0.003$). Gender was not found to be a risk factor for hearing loss ($p = 0.3$).

Discussion

Age-related combined visual and hearing impairment is an important health problem in older populations.[12,14] One study found that individuals reporting combined

TABLE II
DATA FOR WET AND DRY TYPE STUDY GROUP PATIENTS

Parameter	Wet type*	Dry type†	*p*
Age (mean ± SD; y)	69.62 ± 8.4	68.75 ± 9.28	>0.05
Median VA	20/200	20/200	0.7
Speech PTA (dBHL)			
– Median	32	43.5	0.027
– Mean ± SD	34.44 ± 14.7	46.3 ± 20.6	
– Range	15–87	18–93	
HF PTA (dBHL)			
– Median	60	67.5	0.07
– Mean ± SD	57.1 ± 17.8	66.9 ± 13.8	
– Range	25–95	40–95	

*$n = 34$; †$n = 16$. SD = standard deviation; y = years; VA = visual acuity; speech PTA = pure tone average for speech frequencies, HF PTA = PTA for higher frequencies

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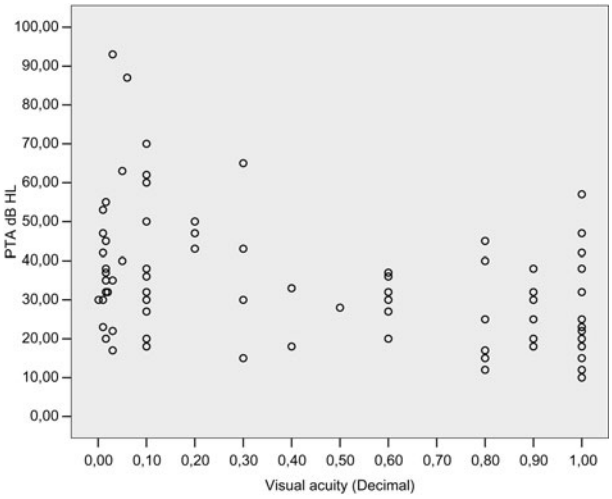

FIG. 1

Scatter plot graph showing correlation between pure tone average (PTA dB-HL) and visual acuity measurements (converted to a decimal scale).

visual and hearing loss were three times more likely to have difficulty walking, getting outside, moving into or out of a bed or chair, preparing meals, and managing medication.[12] They were also more likely to give a self-reported history of falling in the previous 12 months and to have experienced a broken hip, and were significantly less likely to participate in social activities.[12]

In the Epidemiology of Hearing Loss Study, the Beaver Dam Study Group reported associations between hearing loss and both age-related macular degeneration and cataract; these associations were confirmed by Chia *et al.*[14–16] Klein *et al.* found multivariate-adjusted odds ratios of 3.15 for hearing loss and late age-related macular degeneration (95 per cent CI 1.34–7.42) and 3.76 for hearing loss and pure neovascular age-related macular degeneration (95 per cent CI 1.24–11.38).[15] They could not find a significant relationship between early age-related macular degeneration and hearing loss (multivariate-adjusted odds ratio 1.12, 95 per cent CI 0.92–1.35). The combination of any type of cataract together with hearing loss was frequent, with a prevalence of 27.8 per cent in the overall population, which increased consistently with age.[16] Chia *et al.* found multivariate-adjusted odds ratios of 1.3 for cataract and hearing loss (95 per cent CI 1.0–1.7) and 1.6 for age-related macular degeneration and hearing loss (95 per cent CI 1.1–3.1).[14] They found a stronger association between early age-related macular degeneration and soft, indistinct drusen or reticular drusen. For each one-line reduction in best-corrected visual acuity, hearing loss prevalence was shown to increase by 18 per cent.[14] The discrepancies between these two studies' results may be partially explained by different study definitions.[14,15] Klein *et al.* defined hearing loss in the more impaired ear and did not exclude conductive hearing defects from their analysis; in contrast, Chia *et al.* defined hearing impairment as a PTA air conduction hearing threshold worse than 25 dBHL in the better ear.[14,15] By comparison, Singh *et al.* evaluated the association between hearing loss and visual loss related to various macular degenerations, and found hearing impairment in three patients within the maculopathy group (n = 10 patients) but no hearing loss in the control group patients.[18]

In the present study, hearing loss was defined as a PTA of greater than 25 dBHL in either ear, and statistical analyses were conducted for the poorer eye and ear, similar to the study design of Klein *et al.*[15] For each one-line reduction in best-corrected visual acuity, the PTA was shown to increase by 13.8 per cent; this was a statistically significant change ($p = 0.001$). The multivariate-adjusted odds ratio for hearing loss and age-related macular degeneration was 4.58 (95 per cent CI 1.76–11.9) ($p = 0.002$). Seventy-six per cent of the age-related macular degeneration patients had some degree of hearing impairment; this was substantially higher than the hearing loss prevalence found in control subjects of similar age and sex (39.6 per cent) ($p = 0.001$). Subjects with lower best-corrected visual acuities were more likely to have hearing impairment ($p < 0.001$).

Although this was a case–control study with a small number of subjects (compared with large, population-based cohort studies), we found that age-related macular degeneration was an important risk factor for the development of age-related hearing loss. Age-related macular degeneration and age-related hearing loss share common underlying chronological and biological ageing and/or disease processes, possibly due to common genetic, environmental and lifestyle factors (e.g. exposure to oxidative stress, atherosclerosis, high cholesterol levels, or a history of heavy drinking, smoking or occupational exposure to noise).[4,11,14,15] The ageing process appears to involve a loss of antioxidant defences. Impaired function of antioxidant enzymes has been postulated to lead to failure of cellular responses to the toxic effects of reactive oxygen species, with subsequent peroxidative cell injury. Free radicals and other reactive oxygen species are considered to be important causative factors in the development of both age-related macular degeneration and age-related hearing loss.

In the current study, both the age-related macular degeneration group and the control group were similar as regards hypertension and uncomplicated diabetes mellitus; however, other risk factors were not evaluated.

We could not compare hearing loss in patients with early versus late age-related macular degeneration, since only two patients had drusen while the rest of the subjects had late age-related macular degeneration. However, we did compare the PTA values of patients with wet versus dry type age-related macular degeneration, and found a higher median PTA in dry type patients (43.5 dBHL) compared with wet type patients

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(32 dBHL). The reason for this discrepancy is unknown and requires further study.

- **Age-related hearing loss and age-related macular degeneration are both common problems in older adults**
- **When combined, these impairments are associated with poorer health-related quality of life**
- **Age-related hearing loss is more common in subjects with age-related macular degeneration**
- **Patients with age-related macular degeneration should be questioned about their hearing and referred when necessary**

The relation between age-related macular degeneration and hearing loss in both the speech frequency range (500–4000 Hz) and at higher frequencies (4000 and 6000 Hz) was evaluated, as ageing is thought to affect higher frequency hearing first. Hearing loss was more pronounced at higher frequencies in both the study and control groups; however, high frequency hearing loss was much more prevalent in the study group compared with the control group ($p < 0.001$).

Conclusion

Age-related hearing loss is more common in patients with age-related macular degeneration. Therefore, such patients should be questioned about hearing difficulty, and if necessary should be referred to an otolaryngologist for evaluation and treatment of associated hearing loss.

Further epidemiological studies, with a large number of subjects, are needed to understand the relationship between visual and hearing impairment in older patients, and the combined adverse effect of these impairments on health-related quality of life.

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