

## ORIGINAL ARTICLE

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# Investigation of Hearing in Patients with Allergic Rhinitis

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## ABSTRACT

The aim of the current study is to investigate hearing function in patients with allergic rhinitis.

Fifty-eight patients with positive skin prick test (Group 1) (116 ears) and 31 subjects with negative skin prick test (62 ears) as group 2 were included. Pure tone audiometry at 250, 500, 1000, 2000, 4000 and 8000 Hz and immittance measures, including tympanometry and acoustic reflex tests, were performed in both groups.

There was statistically significant difference between pure-tone threshold of the group 1 and group 2 at 8000 Hz ( $p < 0.05$ ).

Based on our study, the patients with allergic rhinitis had better hearing than the control group at 8000 Hz.

**Key words:** Allergic Rhinitis; Audiometry; Hearing; Histamine; Inner Ear

## INTRODUCTION

Allergic rhinitis (AR) is a type-I hypersensitivity reaction of the nasal mucosa, primarily mediated by immunoglobulin E (IgE) that is regarded as a complex etiology, determined by genetic and environmental interactions. AR of prevalence involves between 9% and 42% in the general population.<sup>1</sup> The clinical symptoms of allergic rhinitis are nasal obstruction, watery rhinorrhea, sneezing and itching at the nose,

palate and nasopharyngeal region. The diagnosis is made based on the detailed history taking and symptoms of the patient.<sup>2</sup>

It is believed that allergy may affect the outer, the middle, or the inner ear.<sup>3</sup> Therefore, some authors have investigated the correlation between inner ear symptoms and allergy.<sup>4,5</sup>

Recent study showed that lower concentration of histamine was needed to physiological effects on the cochlea of the guinea pig. Histamine have been potential physiological functions mammalian cochlea<sup>6,7</sup> however, histaminergic innervation have not been described in the human cochlea.

However, there are very few studies regarding auditory evaluation in humans with known allergic

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rhinitis. The aim of the current prospective study is to evaluate of hearing in patients with allergic rhinitis.

## PATIENTS AND METHODS

### Patients

Patients with the prediagnosis of AR who had been followed-up with the allergy test in Kecioren Training and Research Hospital Otorhinolaryngology Clinic between January 2008 and December 2008 were included in the study. We conducted a case-control study with totally 89 subjects. The study group consisted of 58 patients (116 ears) with positive skin prick test (patient group). The control group had sixty two ears of 31 patients (62 ears) with negative skin prick test. Patients had mild, moderate-severe allergic symptoms. Both patient and control groups had no atopy. Patients did not have orofarengeal surgery history. Drug history was questioned in each patients, and some drugs were withdrawn before prick test. For the test, antihistamines had to have been withdrawn 10 days previously, H2 receptor blockers had to have been withdrawn 24 hours previously, and antidepressant drugs withdrawn 20 days previously. The diagnosis of allergic rhinitis was made according to the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology that included the presence of discolored rhinorrhea, sneezing, itching and/or nasal blockage, excessive tearing or conjunctival redness when exposed to allergens, in combination with positive skin test reactions to suspected allergens.<sup>8</sup>

### Skin Prick Testing

Patients withheld antihistamine medication for four days prior to skin prick testing. We performed following a standard protocol (Stallergens testing solution, France) using extracts including two storage mites, three moulds, one insect, three epithelia, three animal epithelia, fifteen pollen, six food extracts in addition to a positive (0.1% histamine solution) and negative controls (saline solution). The allergen extracts which are often met and routinely used in prick test were used in our study for prick test. Skin prick tests were read after 15 min, as positive if the mean wheal diameter was 3 mm greater than negative control<sup>9</sup>. At least one positive allergens made the prick test positive.

Diagnosis of AR was made on the basis of history, physical examination findings, nasal endoscopic

examination findings and the skin prick test results. Presence of sneezing, watery runny nose, nasal obstruction and nasal itching, presence of serous secretion in the nasal cavity, pale nasal mucosa, edematous, and pale or purple conchae, were interpreted in favour of AR.

The patients were examined in terms of skin findings and the presence of a rash, itching, urticaria and erythema was recorded. Coughing, dyspnea and wheezing were evaluated as respiratory symptoms. The skin prick test was not performed on patients who had been treated with the diagnosis of asthma, on those who had a suspicion of asthma, or on those who had been using beta-blockers. The skin prick test was performed on patients who were considered as having isolated AR. Patients who were detected to have dermatographism were excluded from the study.

### Audiometry

Pure-tone and speech audiometry were performed by using a diagnostic audiometer (Madsen Orbiter 922-2, Denmark) in a sound-treated cabin. TDH-39 standard headset was used for air conduction thresholds and speech tests. Radio ear B-71 vibrator was used in high frequency audiometry. Air conduction pure tone thresholds were measured at the frequency of 250, 500, 1000, 2000, 4000 and 8000 Hz. Bone conduction thresholds were measured at the frequency of 500, 1000, 2000 and 4000 Hz. Measurements were done using an ascending-descending technique, in 5 dB steps at all frequencies. If a patient made two or more responses to a set of 3 stimuli, she/he was deemed to have heard the sound.

Normal middle-ear function was defined as proper if the hearing threshold for both air and bone conduction was equal. Tympanometric measurements were done using a TDH-39 headset and Middle Ear Analyzer (TympStar GSI, Grason-Stadler Inc., Milford, USA). On immitance, all participants had a normal peak compliance, peak pressure, gradient and ear canal volume, and acoustic reflex.

### Excluding Criteria

We applied excluding criteria as follows: (1) use of ototoxic agents, (2) metabolic and systemic disease causing hearing loss, (3) otoscopic evidence of a perforated tympanic membrane or other middle-ear pathology, (4) a flat tympanogram or absence of acoustic reflexes at 1 kHz with contralateral stimu-

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lation, (5) an air-bone gap >5 dB at any frequency, (6) 40 years older for presbycusis, (7) noise exposure, (8) ear surgery, (9) Meniere's disease, (10) cranial trauma.

The statistical analyses were performed using SPSS 15.0 for Windows. Criterion for statistically significant difference was accepted for two-tailed *p* values of less than 0.05. For overall comparisons of the groups (i.e. allergic rhinitis patients and controls), Mann-Whitney U test were performed. The Independent Sample T Test was used to compare the ages of patients and controls. Chi-square testing was used to compare the number of hearing loss and the gender of patients and controls.

### RESULTS

The mean age of patient group was  $27.7 \pm 6$  years (range 18-40 years), 43 were female and 15 were male patients. The mean age of control group was  $27.4 \pm 5.7$  years (range 19-37 years), 19 were female and 12 were male subjects. Otoscopic examination was normal in all participants. There was no statistically significant difference between the ages and genders of the groups ( $p > 0.05$ ).

The pure tone audiometry descriptive results of both ear for each group are shown in table 1. Compared to groups the pure tone thresholds significantly differed at 8000 Hz ( $p=0.026$ ). There were no statistically significant differences between the right and the left ear thresholds at all frequencies in both groups. Pure tone thresholds results are shown in figure 1.

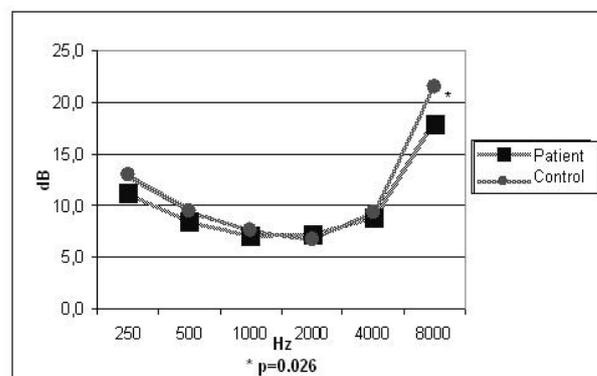


Figure 1. Hearing thresholds at pure tone audiometry results in patients' and controls' ears

Table 1. Pure tone audiometry results of patient and control group

Frequency (Hz)	Patient (Right ear)			Patient (Left ear)		
	Range (dB)	Mean (dB)	SD	Range (dB)	Mean (dB)	SD
250	0-20	11.0	5.2	0-25	11.6	5.6
500	0-20	8.3	3.9	0-20	8.6	4.7
1000	0-15	7.1	3.5	0-15	7.1	3.8
2000	0-20	7.3	4.9	0-20	7.2	4.7
4000	0-25	9.0	6.9	0-105	10.3	14.7
8000	0-50	17.4	11.2	0-65	18.3	12.2

Frequency (Hz)	Control (Right ear)			Control (Left ear)		
	Range (dB)	Mean (dB)	SD	Range (dB)	Mean (dB)	SD
250	5-25	12.6	5.9	0-30	13.4	7.5
500	0-20	9.4	5.1	0-25	9.7	6.3
1000	0-20	7.1	4.0	0-20	8.2	5.3
2000	0-15	5.8	4.5	0-30	7.7	7.3
4000	0-40	9.7	7.8	0-20	9.0	6.0
8000	0-45	23.5	11.0	5-50	19.4	11.2

**Table 2. Number of hearing loss in patient and control group**

	Patient	Control	P value (Chi 2)
PTA 1	10 (8.6%)	11 (17.7%)	0.089
PTA 2	0	3 (4.8%)	0.041
PTA 3	36 (31%)	32 (51.6%)	0.009

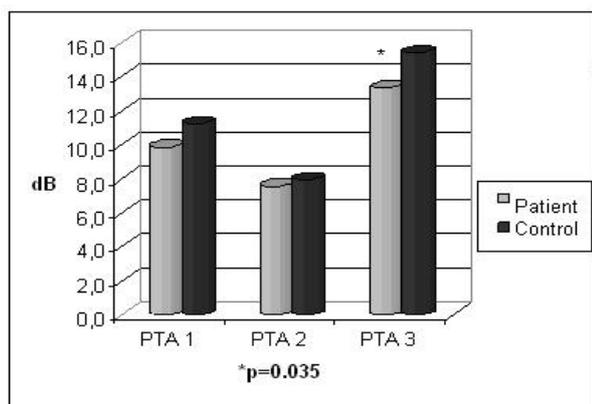
Pure tone averages (PTA) of air conduction thresholds at 250, and 500 Hz (PTA1), 500, 1000 and 2000 Hz (PTA2), 4000, and 8000 (PTA3), for each ear separately were measured. Compared to groups the pure tone averages were significantly different for PTA 3 ( $p=0.035$ ). Pure tone average (PTA) results are shown in figure 2. The PTA results over 15 dB was described as hearing loss. According to PTA, the number of patients with hearing loss is shown in table 2.

Speech discrimination scores were within normal limits in all patients and controls. Normal peak compliance, peak pressure, gradient, ear canal volume and acoustic reflexes were obtained by immittance measures in all patients and controls.

## DISCUSSION

Histamine is the main mediator in type 1 hypersensitivity reaction and allergic rhinitis. It demonstrates its effects via activation of receptor system. Histamine acts by binding to receptors on target cells, and different cell types express different receptors.

There are 4 main types of histamine receptors: histamine1 H1, H2, H3, and H4.<sup>10,11</sup> The H1 receptor



**Figure 2. Pure tone average thresholds for patient and control groups at 250, and 500 Hz (PTA1), 500, 1000 and 2000 Hz (PTA2), and 4000 and 8000 Hz (PTA3).**

causes contraction of smooth muscle, increases vascular permeability, and excites sensory nerve endings.<sup>12</sup>

Several experimental studies have suggested that histamine may play physiological role in the inner ear<sup>13-18</sup>. Azuma et al have found that the H1, H2, and H3 histamine receptors is expressed in the rat cochlea, spiral ganglion, nerve fibers, cochlear artery and cochlear vein.<sup>13</sup> Dagli et al showed the immunohistochemical localization of H1, H2, and H3 histamine receptors in the rabbit ES.<sup>14</sup>

The question arises why histamine had a protective effect on inner hair cells in their study, since it is assumed that histamine may act as an extracellular signal to stimulate neurotransmitter release from inner hair cells.<sup>15</sup> Azuma et al speculated that histamine at a low concentration may act as a neurotransmitter or neuromodulator in the cochlea by way of both H1 and H2 receptors, which are present in the modiolus of the cochlea. Minoda et al reported that the inhibitory effects of histamine are in supraphysiological concentrations, while the excitatory effects of histamine are in low concentrations in cochlea of the guinea pigs.<sup>16</sup>

Mast cells in the subepithelial connective tissue of the human ES has been found, and histamine released by mast cells seems to play a role in the physiologic functions of the inner ear.<sup>17</sup>

Xiaoyu Tan et al. reported that incubation of human coronary artery endothelial cells with histamine lead to increased expression of COX-2 with resultant enhancement in the production of PGE2 and PGI2. The activity of PGE2 is mediated by four Eprostanoid receptors (EP1-4).<sup>19</sup>

Most research suggested that several types of PGs during allergic reaction in human and experimental animals were produced.<sup>20-22</sup> Ryusuke Hori et al. showed both EP4 expression in the cochlea and cochlear protection against noise trauma as a result of the local application of an EP4 agonist.<sup>23</sup>

In our prospective study we found that the patients with allergic rhinitis had considerably better hearing at 8000 Hz then the control group, in contrast Lasisi<sup>4</sup> demonstrated in a retrospective study that there were hearing loss in patients with allergic rhinitis.

We speculated that histamine may have protective effect on hearing by vasodilatation in cochlear artery and vein.

### CONCLUSION

To date, this study is the first prospective study that has been conducted to evaluate hearing in patients with allergic rhinitis. Based on our study, the patients with allergic rhinitis had better hearing at 8000 Hz the control group. In addition, our findings support that histamine might play a physiological role in the cochlea. A detailed evaluation of cochlear with OEA test should be done in the future studies that would provide more accurate information.

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