

Audiological findings in pediatric perineal allergic rhinitis (house dust mite allergy) patients

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Abstract Allergic rhinitis is the type 1 hypersensitivity reaction of the nasal mucosa and its primary mediator is Ig E. It is most frequently observed in children and adolescents. Our purpose in this study is to investigate the impact of allergy on hearing functions in children with perineal allergic rhinitis (house dust mite allergy). 50 perineal allergic rhinitis (house dust mite allergy) patients (33 male, 17 female patients, aged between 6 and 15, average age 10.4) and 20 control patients (12 male, 8 female, aged between 6 and 15, average age 11.2) underwent high frequency pure tone audiometry, acoustic reflex, otacoustic emission (OAE) and auditory brainstem potentials to assess their auditory functions. No statistically significant difference was detected between the study group and the control group with respect to their hearing thresholds (250–16,000 Hz). No statistically significant difference was detected as a result of the comparison between the study group and control group in terms of their signal–noise ratios at Distortion Product OAE in all frequencies (996–8,004 Hz). No statistically significant difference was detected between the study group and the control group in terms of the 1st, 3rd and 5th wave latencies and 1–3, 3–5 and 1–5 inter-peak values. This study is the first study

where the audiological functions of the pediatric perineal allergic rhinitis (house dust mite allergy) patients were assessed. No significant difference was detected between the group of pediatric perineal allergic rhinitis (house dust mite allergy) patients and the control group with respect to their audiological functions.

Keywords Allergic rhinitis · Audiological · Pediatric · Otacoustic emission · Auditory brainstem potentials

Introduction

Allergic rhinitis (AR) is the type 1 hypersensitivity reaction of the nasal mucosa and it begins to manifest itself typically after the 2nd year of life. AR is characterized by the symptoms of itchy nose, blocked nose, sneezing, aqueous nasal discharge and its diagnosis is made based on the history and physical examination [1]. AR affects 10–30 % of adults; however, its incidence in the childhood period is between 10 and 40 % [2]. It is most frequently observed in children and adolescents [3].

AR involves both the inner ear and the middle ear in children. It is known that AR affects the middle ear in relation with its nasal involvement. In children, the incidence of otitis media and AR ranges between 5 and 80 % (23 % on average) [4]. The presence of an allergic airway is expected to affect the middle ear; it creates an allergic inflammatory response here. Finally, in otitis media cases, all cells and mediators are also related to the allergic inflammation of the middle ear fluid [5].

Recent studies demonstrated that the inner ear created more immune response as compared to the brain [6]. Many studies were conducted on the immunological function of

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the inner ear and it was shown that it had a role to play in both cellular and humoral immunity. It was demonstrated that the immunological activity in the inner ear results from endolymphatic sac (ES) [7]. The ES secretes Ig G, M and A; furthermore, the existence of mast cells and macrophages was detected in the peri saccular connective tissue [7]. Additionally, it was demonstrated that there was an increase in the number of immune complexes in circulation with the Meniere's disease [8]. The studies conducted also demonstrated evidence of local antibody production in the perilymphatic zone [9]. When cochlea meets antigen, it creates a locally stimulated response. This in turn shows the existence of congenital immune response in cochlea [10].

Since AR is a disease on the immunological base and it was demonstrated that it affected the middle ear during the childhood period, we aimed to investigate its effect on the inner ear which plays a role in humoral and cellular immunity. The otologic and audiological symptoms of patients in the pediatric age group diagnosed with AR were compared.

Materials and methods

An approval was received for the study from the Ethical Board for Clinical Studies dated 25.11.2011 and number 944. 50 patients who presented to the Pediatric Diseases Outpatient Clinic between the dates January 2012–July 2012, who were diagnosed with AR and 20 healthy volunteers in the same age group, were included in the study. The AR diagnosis was made according to the symptoms and Prick tests of the patients. All allergic rhinitis patients involved within our study had been diagnosed with perineal allergic rhinitis previously. They were not included in our study for seasonal allergic rhinitis patients. According to the results of the Prick test, the sensitivity of perineal allergic rhinitis (PAR) patients to the allergen is as follows. The participants of the study were informed on the study and their informed consent forms were received.

All the patients who took part in the study went through a full otorhinolaryngological examination at Bezmialem Vakif University, School of Medicine, Department of Otorhinolaryngology. Following the examinations, the patients who were eligible went through audiological tests. The patients whose history involved exposure to noise, use of ototoxic medicines, metabolic problems, neurological problems or other otorhinolaryngological problems were excluded from the study. The only pathological problem of all the patients in the study group was PAR (house dust mite allergy).

The study group consisted of 50 patients (33 male, 17 female, aged between 6 and 15, average age 10.4). None of the patients in the study group had hearing loss complaints.

Normal hearing sensitivity was defined as a hearing threshold of <25 dBHL at each frequency tested within the range 250–16,000 kHz [11]. Type A response was considered normal in impedance audiometry [12].

The control group consisted of 20 healthy individuals (12 male, 8 female, aged between 6 and 15, average age 11.2). 20 healthy volunteers were included in the control group. The criteria which the healthy volunteers are included in terms of allergic rhinitis diagnosis are:

1. Not being detected sensitivity against allergen in Prick test: Prick test was applied to all healthy volunteers accepted for the study for this purpose, and no sensitivity was detected against the controlled allergens (*D. farinae*, *D. pteronyssinus*, mold mix, epidermal mix, tree mix, grass mix, weed mix).
2. Not having allergic rhinitis symptoms: none of the healthy volunteers accepted in the study has allergic rhinitis symptoms such as itchy nose, blocked nose, sneezing, aqueous nasal discharge, etc.
3. Not having allergic rhinitis findings at nasal examination: None of the healthy volunteers accepted in the study had any allergic nasal findings in their nasal examinations such as breath, edematous and inflamed mucosa, hypertrophic view, serous secretion, etc.

The participants in the control group had no systemic disease or AR. The healthy volunteers also went through a full otorhinolaryngological examination. Those who were identified to have hearing loss, neurological pathology, exposed to acoustic trauma, had metabolic problems, had history of ototoxic medicines during the audiological test were excluded from the study.

Audiological tests

The audiological tests were conducted in a soundproof room that had a maximum level of noise allowed for the limits determined as per the American National Standards Institute (1977) and International Standards Organization (ISO). The hearing threshold tests were conducted using Inter acoustics AC 40 and TDH 39 earphones (Madsen, Electronic, Taastrup, Denmark) and TDA 200 earphones for high frequency audio.

GSI Tympanstar was used for tympanometry and acoustic reflex tests. A 226 Hz probe was used for tympanometry (pressure ranged between +200 and −400 daPa).

A GSI Audera was used for OAE measurements. Judging by the DPOAEs, the emissions were considered to be present if the signal–noise ratio at every frequency was above 6 dB.

For ABR, the Viasys Healthcare Synergy was used. The ABR measurements were taken while all patients were in supine position with their eyes closed. Silver–silver

chloride electrodes were used. The measurement parameters for recording were selected as follows: the filter bandwidth was set at 100–3,000 Hz, a click was used as stimulus, the stimulus ratio was set at 21.1/s with a duration of 100 μ s; at least 1,000 clicks were used for every recording; if the wave was suboptimal, it was raised to 2,000 (it was repeated at every intensity level in order to assure reproducibility of results); the waves were recorded for every ear respectively for a volume of 80 dB nHL.

The electrodes were placed on the cleaned skin. The 1st, 3rd and 5th waves and 1–3, 3–5 and 1–5 inter-peak latencies were evaluated.

Statistical analysis

Data were analysed using Statistical Package for the Social Sciences version 13.0 software for Windows (SPSS Inc, Chicago, Illinois, USA). All quantitative variables were estimated using measures of central location (i.e., mean and median) and measures of dispersion [i.e., standard deviation (SD)]. Data normality was checked using the Kolmogorov–Smirnov tests of normality. For normally distributed data, means were compared using independent samples *t* test for two groups. A *p* value of <0.05 was accepted as statistically significant.

Results

According to the results of the prick test, the sensitivity of perineal allergic rhinitis patients to the allergen is as follows; *D. farinae* (65.6 %), *D. pteronyssinus* (67.4 %), mold mix (10.7 %), epidermal mix (7.9 %), tree mix (5.7 %), grass mix (4.5 %), weed mix (4.2 %) (Fig. 1).

Table 1 shows the hearing thresholds of the study and control groups (between 250 and 16,000 kHz). No patients in the study group showed hearing loss. No statistically

significant difference was detected as a result of the comparison of airway thresholds between the study and control groups between the frequencies of 250 and 16,000 kHz.

The tympanogram was type A in all patients included in the study. The mean tympanometric values were 47.4 ± 98.2 daPa in Group perineal allergic rhinitis (house dust mite allergy), whereas it was 34.2 ± 46.6 daPa in the control group. There was no statistically significant difference between two groups (*p* = 0.286). Acoustic reflex thresholds at 500Hz, 1,000Hz and 2,000 Hz for the patients in perineal allergic rhinitis (house dust mite allergy) and the control group were evaluated. No statistically significant difference was detected between two groups at 500Hz, 1,000Hz and 2,000 Hz (Table 2).

Table 3 shows the average values of the signal–noise ratios for DPOAE at 996–8,004 Hz.

No statistically significant difference was detected between the study group and control group in terms of their signal–noise ratios in all frequencies at DPOAE.

Table 4 shows the 1st, 3rd and 5th wave latencies and 1–3, 3–5 and 1–5 inter-peak values of the study group and control group at ABR. No statistically significant difference was detected between the study group and the control group in terms of the 1st, 3rd and 5th wave latencies and 1–3, 3–5 and 1–5 inter-peak values.

Discussion

AR is a chronic disease with a rather high rate of incidence and it is observed during childhood period at a rate of 10–40 % [13]. It is considered that the ES in the inner ear acts as a target organ during allergic reactions and this situation accounts for a possible mechanism for the inner ear changes observed in AR [14–17].

Our study is the first study conducted on patients with perineal allergic rhinitis (house dust mite allergy) at

Fig. 1 Results of the prick test

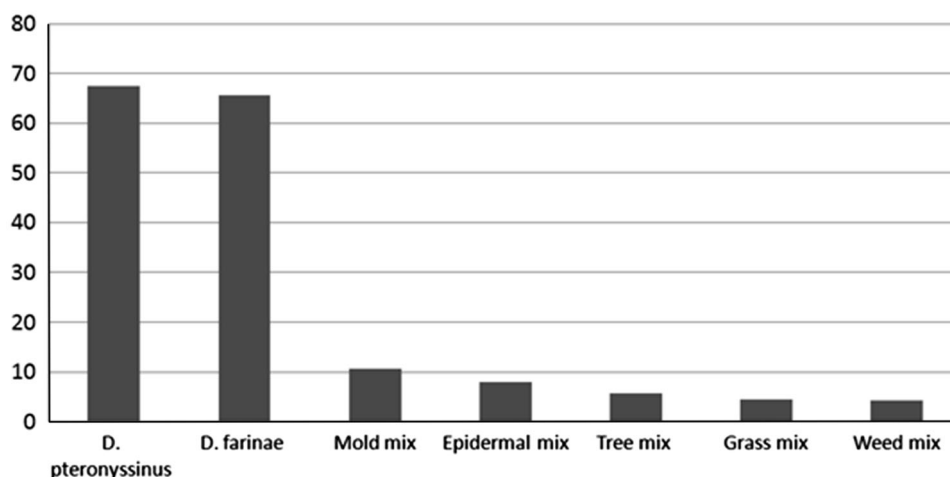


Table 1 Hearing thresholds: study and control groups

Frequency (Hz)	Study group (Mean $\pm$ SD)	Control group (Mean $\pm$ SD)	Mean difference (95 % CI)	<i>p</i>
250	15.8 $\pm$ 5.6	14.7 $\pm$ 5.4	1.1 (−3.5–1.4)	0.410 [¥]
500	12.4 $\pm$ 7.0	11.0 $\pm$ 5.5	1.4 (−4.4–1.7)	0.382 [¥]
1,000	11.6 $\pm$ 5.9	9.3 $\pm$ 5.3	2.3 (−4.8–0.3)	0.087 [¥]
2,000	9 $\pm$ 6.7	6.8 $\pm$ 5.8	2.2 (−5.1–0–8)	0.160 [¥]
4,000	8.5 $\pm$ 6.4	7 $\pm$ 8.7	1.5 (−4.5–1.6)	0.353 [¥]
8,000	11.4 $\pm$ 8.2	10.6 $\pm$ 12.6	0.8 (−4.9–3.3)	0.696 [¥]
10,000	6 $\pm$ 9.1	6.8 $\pm$ 16	0.8 (−3.9–5.7)	0.721 [¥]
12,500	7.6 $\pm$ 11.2	8.1 $\pm$ 15.8	0.5 (−5.0–5.9)	0.864 [¥]
14,000	4.5 $\pm$ 9.7	4.7 $\pm$ 16.2	0.2 (−4.8–5.3)	0.925 [¥]
16,000	4.1 $\pm$ 8.3	4.1 $\pm$ 14.1	0.01 (−4.3–4.3)	0.994 [¥]

[¥] No significance level obtained

* Independent samples *t* test (*p* < 0.05)

Table 2 Acoustic reflex thresholds: study and control groups

Frequency (Hz)	Study group (Mean $\pm$ SD)	Control group (Mean $\pm$ SD)	Mean difference (95 % CI)	<i>p</i>
500	93.6 $\pm$ 10.3	94.8 $\pm$ 7.3	−1.2 (−4.3–1.9)	0.444 [¥]
1,000	93.2 $\pm$ 9.7	94.1 $\pm$ 8.8	−0.8 (−3.9–2.2)	0.580 [¥]
2,000	95.5 $\pm$ 7.7	94.7 $\pm$ 8.2	−0.7 (−1.8–3.2)	0.596 [¥]

[¥] No significance level obtained

* Independent samples *t* test (*p* < 0.05)

Table 3 DPOAE results: study and control groups

Frequency (Hz)	Study group (Mean $\pm$ SD)	Control group (Mean $\pm$ SD)	<i>p</i>
996	13.9 $\pm$ 7.5	18.2 $\pm$ 8.6	0.023 [¥]
1,515	21.5 $\pm$ 7.3	24.4 $\pm$ 8.2	0.096 [¥]
2,004	21.2 $\pm$ 7.8	24.7 $\pm$ 7.4	0.050 [¥]
2,637	23.1 $\pm$ 7.7	25.6 $\pm$ 5.3	0.145 [¥]
3,035	25.3 $\pm$ 8.2	26.3 $\pm$ 7.0	0.585 [¥]
3,996	27.8 $\pm$ 8.9	29.8 $\pm$ 7.9	0.317 [¥]
4,594	26.1 $\pm$ 10.3	29.7 $\pm$ 7.3	0.115 [¥]
5,273	25.7 $\pm$ 9.1	29.4 $\pm$ 7.6	0.085 [¥]
6,059	22.8 $\pm$ 22.8	22.7 $\pm$ 9.0	0.985 [¥]
6,961	14.7 $\pm$ 7.2	16.1 $\pm$ 7.3	0.464 [¥]
8,004	12.0 $\pm$ 6.2	13.7 $\pm$ 5.4	0.305 [¥]

[¥] No significance level obtained

* Independent samples *t* test (*p* < 0.05)

pediatric age. A limited number of studies exist in the literature on the audiological symptoms of AR. Singh et al. found hearing loss and abnormal OAE responses with high prevalence in the AR patients as compared to the control group. They ascribed this to the fact that ES is able to develop its own antigenic and anti-body response. However, hearing loss may be due to the antigen and local antibody response of ES as shown for adults while it may also be due to the inflammatory mediators and toxins accumulated in the middle ear as a result of repeated acute and serous otitis media passing through the round and oval windows affecting the inner ear in children. As a result,

inflammatory mediators and toxic products may affect the functions of the hairy cells [18].

In another study that was conducted, it was detected that the AR patients heard better than those in the control group at 8,000 Hz and it was expressed that this was due to the physiological role played by the histamine in the cochlea and that the increased histamine release during AR enhanced cochlear functions providing such an improvement [19].

In our study, no statistically significant difference was detected between the perineal allergic rhinitis (house dust mite allergy) group and the control group with respect to

Table 4 ABR parameters: study and control groups

Parameter	Study group (Mean $\pm$ SD)	Control group (Mean $\pm$ SD)	<i>p</i>
Wave I latency	1.6 $\pm$ 0.1	1.6 $\pm$ 0.1	0.514 [¥]
Wave II latency	3.7 $\pm$ 0.2	3.7 $\pm$ 0.1	0.959 [¥]
Wave III latency	5.7 $\pm$ 0.2	5.7 $\pm$ 0.1	0.307 [¥]
Wave I–III interp. lat.	2.0 $\pm$ 0.2	2.0 $\pm$ 0.2	0.656 [¥]
Wave III–V interp. lat.	1.9 $\pm$ 0.2	1.9 $\pm$ 0.2	0.685 [¥]
Wave I–V interp. lat.	4.0 $\pm$ 0.2	4.0 $\pm$ 0.3	0.539 [¥]

[¥] No significance level obtained

* Independent samples *t* test (*p* < 0.05)

their pure tone hearing thresholds (250–16,000 Hz). There are no other studies in the literature investigating the pure tone thresholds in pediatric age groups. It is required that additional studies are conducted in relation to this topic.

There are no studies published in the literature where DPOAE was applied on pediatric patients with perineal allergic rhinitis (house dust mite allergy). In our study, normal DPOAE measurements were detected in all the 50 AR. These results indicate that perineal allergic rhinitis (house dust mite allergy) does not cause dysfunction in the outer hair cells at the pediatric age.

There are no studies published in the literature where ABR was applied on pediatric patients with perineal allergic rhinitis (house dust mite allergy). In our study, no statistically significant difference was observed between two examinations with respect to both latency and inter-peak values. These findings indicate that the patients with perineal allergic rhinitis (house dust mite allergy) do not have cochlear involvement.

The inner ear is an immunologically active structure and it has cellular and humoral immunity. The white blood cells enter the cochlea by means of the spiral modular vein [20]. The cochlea has congenital immune response. Because when cochlea meets antigen, it can create a locally stimulated response [10].

An immune response is created as lipopolysaccharides and other viral or bacterial antigens enter the inner ear, resulting in local inflammation [10].

The ES has the capability to process antigens and to create its own local antibodies [9, 21]. A surgical injury of the ES reduces antigen and antibody response [21].

There are various mechanisms that are at play in relation to the effect of allergic reactions on the inner ear [22].

1. Mechanism (antigenic stimulation of the ES and mast cell degranulation): ES is the target for allergic reactions. ES has the capability of both processing antigens and generating its own local antibody response thanks to its high vascular sub-epithelial space and fenestrated blood vessel. The peripheral and fenestrated vessels of the ES allow entrance of antigens and stimulate the mast cell degranulation in the peri saccular connective tissue. As a result, inflammatory mediators and metabolic toxic products

are secreted and they affect the functions of the hairy cells.

2. Mechanism (immune complex accumulation): for example, the food antigens, which are accumulated along the fenestrated vessels in ES, cause inflammation. The adhesion of immune complexes on the cell membrane facilitates phagocytosis and tissue damage occurs as a result of secreted enzymes. Increases in immune complexes in the serum were described for Meniere's disease and AR [8, 23]. This mechanism is considered to account for the inexplicable sensory-neural hearing loss that develops along with the Wegener granulomatosis (IC mediator disease).
3. Mechanism (viral antigen–allergic interaction): a third possible mechanism is a viral antigen–allergic interaction. An upper respiratory infection at pediatric period results in antigenic stimulation at the Waldeyer's ring as a predisposition. The next targets are the T cells in the ES. As a result of this antigenic stimulation, a chronic low-grade inflammation occurs. This is not enough at the beginning to cause hearing loss; however, it begins to cause a slight, yet real disruption in the fulfillment of the function of ES. This dysfunction progresses along with the increase in the age [24]. The viruses may enhance allergic symptoms. They do this by raising histamine secretion. The viruses damage the epithelial surface. Thus, the entrance of antigens is enhanced and the histamine response of the target organ is also increased. It has been demonstrated that this is more frequent in people with a long-term and severe allergy and in people with a history of upper respiratory tract infection among those with no allergies [25]. Judging by this information, the viral upper respiratory tract infections experienced in childhood period, namely, antigenic–allergic interaction creates an inflammatory response in the ES, which may cause the recurrence of such infections at later ages and consequently hearing loss.

The studies conducted demonstrated that the ES was not equipped with immune competent cells in undifferentiated or young mice [26]. However, it was detected that the ES was equipped with immune competent cells in adult mice and human samples, cellular and humoral immune

response was created with lymphocytes being available [7, 27]. Since ES is activated with antigenic stimulation, it can be concluded that this stimulation and activation may not be adequate at pediatric period and, therefore, the perineal allergic rhinitis (house dust mite allergy) may not affect auditory functions in pediatric age groups.

The increase in the number of activations that occur in time in older ages (for example, by means of the direct exposition of the pathogenesis presented by the lymphatic tissue in Waldeyer's ring) may trigger the immune response by the ES, thus hearing loss may result from chronic inflammation.

Yan et al. [24] demonstrated in the ES the T cell zone in the Waldeyer's ring in the nasopharynx. The systemically sensitized rodents produce antigen-specific reaction in the ES and peri-lymphatic vessels as a result of the antigen stimulation that occurs in the Waldeyer's ring with hemocyanins via the intranasal pathway. This finding supports the view that viral or allergic agents trigger a specific immune reaction in the ES during the time they remain in the nasopharynx. In the childhood period, especially in cases of AR, viral infections abound and this situation suggests that it may enable the formation of antigen-specific reaction in the peri-lymphatic vessels of the ES, thus triggering local inflammatory response. We are of the view that this process may become chronic as the person gets older, thus hearing loss may develop.

Conclusion

This study is the first one where the hearing functions of the pediatric perineal allergic rhinitis (house dust mite allergy) patients were assessed. No significant difference was detected between the pediatric perineal allergic rhinitis (house dust mite allergy) patients and the control group in terms of their hearing functions. Prospective studies are needed for this field.

Conflict of interest The authors state that this is an original work that has not been published or submitted to another journal. We did not receive any financial support, and no conflict of interest.

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