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Audiological manifestations in patients of upper airway allergy

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ABSTRACT

Background: The pathophysiology of involvement of inner ear in patients of upper airway allergy is poorly understood. The endolymphatic sac may be the likely seat of involvement in these patients as it can process antigens and produce its own local immune response. The aim of study was to assess the audiological profile of these patients.
Methods: 53 patients of upper airway allergy (33 females and 20 males with mean age 25.77 years) and 20 control subjects (9 females and 11 males with mean age of 35.65 years) underwent haematological and audiological assessment.
Results: The study group had sensorineural hearing loss at 4000 and 8000 Hz frequencies. Abnormal distortion product otoacoustic emissions (DPOAEs) were noted in the study group as compared with the controls. On auditory brain stem response testing, no statistically significant difference was noted in the absolute latencies of waves I, III and V between study and control groups. Also no statistically significant difference was noted in the wave I-III and wave I-V inter peak latencies between the two groups.
Conclusions: We found higher prevalence of high frequency sensorineural hearing loss and abnormalities of DPOAEs in patients having upper airway allergy. The likely seat of damage appears to be the inner ear as evidenced by abnormalities of DPOAEs. However the exact pathophysiology of inner ear damage in patients of upper airway allergy is poorly understood and needs further research.

Keywords: Allergic rhinitis, Upper airway allergy, Pure tone audiometry, Otoacoustic emissions, Auditory brain stem response, Hearing loss

INTRODUCTION

Upper airway allergy is one of the most common ailments seen amongst people visiting outpatient unit of otorhinolaryngology. These patients manifest a variety of symptoms pertaining to head and neck region. The scientific basis of involvement of inner ear in patients of upper airway allergy is not clear. The endolymphatic sac has a unique property of processing antigens and producing its own local immune response.[1] The endolymphatic-sac along with its duct is one of the target organs of upper airway allergy.[2] Sufficient literature is not available on this subject thereby the need of this study was felt. Correlation between upper airway allergy and consequent audiological abnormalities may help in planning the management of these patients with appropriate therapies, thus possibly resulting in better clinical outcome in such patients.

The objectives of the study were to study the prevalence of audiological abnormalities in patients with upper airway allergy, to study the incidence of sensorineural hearing loss in these patients and to determine the likely seat of pathophysiology in the hearing pathway affected in these patients.

METHODS

53 patients of upper airway allergy attending the ENT outdoor department of Dayanand Medical College and Hospital, Ludhiana, Punjab, from January 2012 to December 2012 were included in the study. 20 controls were selected from relatives and friends accompanying the study group patients. This group of controls had similar environmental exposure as of the patient group but were not suffering from upper-airway allergy or any other systemic disease. Both study and control subjects were subjected to the relevant audiological and haematological investigations and a thorough general physical and ear, nose, throat examination.

Inclusion criteria

Patients with diagnosis of upper airway allergy were selected for the study. This diagnosis was based on thorough ear, nose, throat and systemic examination with exhaustive history taking.

Exclusion cirteria

Any history of hearing loss, prolonged exposure to abnormally loud noise**,** ototoxic medication, neurological or metabolic or endocrinological disorders, presence of any obvious external or middle ear pathology.

Both study and control group subjects underwent haematological investigations in the form of absolute eosinophil count (AEC) and immunoglobulin E titres (IgE).

The audiological assessment was performed in the departmental speech and hearing unit which conforms to the American National Standards Institute and International Organisation for Standardization standards for maximum permissible noise-level. This included pure tone audiometry (using a diagnostic audiometer ARPHI make, model year 2001), tympanometry (using a siemens SD-30 tympanometer), otoacoustic emission testing (OAE) and auditory brainstem response (ABR) both using Neurosoft 2005, developed by neuro-audio technologies.

Pure tone average hearing threshold was calculated for each patient at 250, 500, 1000, 2000, 4000 and 8000 Hz. Normal hearing sensitivity was defined as hearing threshold of less than 25 dBHL at each frequency tested within the range of 0.25 to 8 KHz. For tympanometry a 226 Hz pure tone was used with pressure of (+) 200 to (-) 300 daPa.

For OAE, distortion product otoacoustic emissions (DPOAE) were studied. The graph of DPOEAs as a function of primary frequencies is known as distortion product (DP) gram. When measuring the DP-gram, the stimulus consisted of two primaries i.e., f_1, f_2 (in Hz) with f_2 ranging from 1000 to 8000 Hertz. The ratio of primary frequencies was f_2/f_1- 1.22 with L_1 and L_2 set to 65 and 55 dB SPL respectively. The parameter considered in DPOAE testing was a signal to noise ratio of more than 6 dB in 3 consecutive test frequencies.

Auditory evoked potentials were measured in all subjects in supine position with eyes closed by using Neurosoft 2005 apparatus, developed by neuro-audio technologies. TDH-39 earphones were used to present stimuli. The filter band-width was adjusted to 100-3000 Hz. The clicks acted as stimuli. The stimulus rate was 17.1 per second and the duration was 100 microsecond/click. A minimum of 1024 clicks was presented at each recording, increased to 2048 when the waves were suboptimal. Responses were repeated at each intensity level to ensure reproducibility. Wave forms were recorded at the sound intensity of 70-90 dB nHL in both ears separately. The parameters studied were: absolute latencies of waves I, III and V, and the inter-peak latencies of waves I–III and I–V.

Statistical analysis

All quantitative variables were estimated using measures of central location (i.e., mean and median) and measures of dispersion (i.e., standard deviation). Data normality was checked using the Kolmogorov Smirnov tests of normality. For normally distributed data, means were compared using Student's t-test for two groups. ABR inter-peak latencies of waves I-III and I-V were studied and observations of the study versus control group were compared using unpaired t-test. For skewed data, the Mann-Whitney test was applied. A p value of less than 0.05 was considered statistically significant.

RESULTS

The study group consisted of 53 patients with 33 (62.26%) females and 20 (37.74%) males. In the control group, out of 20 subjects, 9 (45%) were females and 11 (55%) were males. The mean age of the study group was 25.77 years (range 12-58). In the control group the mean age was 35.65 (range 19-55).

The mean AEC in study group was 0.42×10^9/l ranging from 0.04 to 1.9×10^9/l, whereas in control group it was 0.26×10^9/l ranging from 0.1 to 0.6×10^9/l. Although, the mean absolute eosinophil count was double in case of the study group as compared to control group, the difference was not statistically significant (p value=0.088).

The mean IgE levels in the study group was 690.37 IU/ml, ranging from 6 to 4941 IU/ml. Whereas, in control group it was 516.37 IU/ml ranging from 22 to 2500 IU/ml. However, the difference was not statistically significant (p value=0.338).

The mean compliance (Table 1) in the right ear for study group was 0.80 cubic centimetre (cc)±0.56 SD. In the

control group the mean compliance of right ear was 0.61 cc±0.357 SD. The difference between the two groups was not statistically significant. Similarly, for left ear for study group, the mean compliance was 0.84 cc±0.635 SD. In the control group the mean compliance of left ear was 0.56 cc±0.314 SD. Here also, the difference between the two groups was not statistically significant.

Table 1: Mean compliance on tympanometry in study and control groups.

Group	Right ear				Left ear			
	N	Mean (cc)	SD	Range	N	Mean (cc)	SD	Range
Study	53	0.80	0.560	0.18-3.34	53	0.84	0.635	0.06-3.28
Control	20	0.61	0.357	0.02-1.23	20	0.56	0.314	0-1.28
P value	0.173				0.143			

Table 2: Mean hearing thresholds of right and left ears of the study and control groups for frequencies ranging from 250-8000 Hz.

Frequency (Hz)	Ear	Study group		Control group		P value
		Mean (dB HL)	SD	Mean (dB HL)	SD	
250	Right	10.9	4.81	14.75	5.25	0.003
	Left	16.53	7.13	19.25	4.06	0.147
500	Right	12.87	4.42	15.75	5.68	0.042
	Left	17.17	6.54	17.75	5.73	0.698
1000	Right	15.38	5.08	17.00	6.16	0.435
	Left	18.11	6.06	18.25	5.2	0.656
2000	Right	17.74	5.68	17.00	6.16	0.609
	Left	20.62	5.99	18.25	5.2	0.165
4000	Right	34.25	4.09	17.50	4.13	<0.001
	Left	34.43	4.00	20.25	4.99	<0.001
8000	Right	37.92	5.32	21.75	4.67	<0.001
	Left	38.21	5.29	23.00	3.40	<0.001

In pure tone audiometry (Table 2), there was statistically significant difference in mean thresholds between study and control groups, for both ears, at 4000 Hz and 8000 Hz. At these frequencies the hearing threshold was poorer in study group as compared to the control group. Interpretation is that statistically significant levels of sensorineural hearing loss exists in the study group as compared to the control group at frequencies of 4 kHz and 8 kHz.

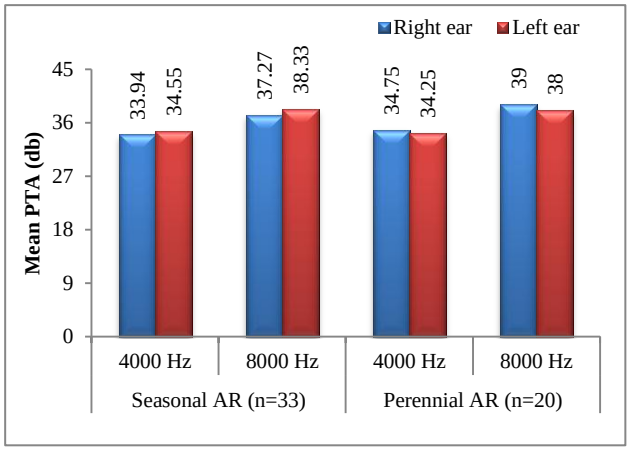

Figure 1: Mean pure tone average of seasonal and perennial allergic rhinitis patients at 4 kHz and 8 kHz.

In this study, 33 patients (62.26%) had seasonal allergic rhinitis and 20 patients (37.74%) had perennial allergic rhinitis. On comparing pure tone averages at 4000 and 8000 Hz frequencies, no statistically significant difference was noted between seasonal and perennial allergic rhinitis patients (Figure 1).

Table 3 shows mean±SD DPOAE signal to noise ratio value in study and control groups from 988 to 8000 Hz. The mean signal to noise ratio (in dB) among the study group varied from -3.15±5.079 dB to 4.04±9.35 dB and ranged from -20.5 to 32.4 dB. The mean signal to noise ratio (in dB) among the control group varied from 1.97±13.00 dB to 28.88±64.904 dB and ranged from -18.2 to 302.0 dB. There was a significant difference in mean averages of signal noise ratio between study and control groups. This difference was statistically significant at most of the frequencies.

Table 4 shows the ABR parameters of inter peak latency between wave I-III (in milli seconds) in study and control group. In the study group, the mean inter peak latency at 70 to 90 dB nHL varied from 2.18±0.54 msec to 2.37±0.60 msec. In control group, the mean inter peak latency at 70-90 dB nHL varied from 2.04±0.54 msec to 2.31±0.33 msec. The difference between two groups was not statistically significant.

Table 3: DPOAE results.

Frequency (Hz)	Ear	Signal to nose ratio (dB)						P value
		Study group (n=53)			Control group (n=20)			
		Mean	SD	Range	Mean	SD	Range	
988	Right	-1.85	6.047	-11.3-12.5	7.10	6.328	-5.1-17.1	<0.001
	Left	-3.15	5.079	-9.8-9.2	6.00	10.290	-7.7-27	<0.001
1441	Right	0.45	4.25	-6-8.9	14.7	10.96	4.2-26.5	<0.001
	Left	-2.05	8.972	-20.5-11.4	4.13	0.828	1.9-6.8	0.086
2222	Right	-1.37	5.612	-18.7-8.7	3.69	10.082	-15.9-12.7	0.013
	Left	-1.4	7.947	-12.6-13.7	1.97	13.008	-18.2-16.1	0.375
2963	Right	-0.08	8.184	-13.7-17.2	3.76	14.049	-18.2-19	0.126
	Left	-1.51	6.907	-16.9-14.1	10.15	5.829	4.7-18	<0.001
4444	Right	0.67	10.326	-14.8-32.4	16.48	9.872	4.6-27.2	<0.001
	Left	0.65	9.41	-16.9-30.2	8.4	9.229	-3.3-27	0.001
5714	Right	4.04	9.353	-7.5-26.5	13.2	8.776	3.5-26.5	0.001
	Left	0.92	9.589	-20.2-16.3	8.34	4.909	-0.5-15	<0.001
8000	Right	3.07	9.483	-26.2-21	14.6	15.721	-7.7-32.4	0.010
	Left	2.62	8.646	-16.5-24.4	28.88	64.904	4.2-302	<0.001

Table 4: ABR parameter wave I-III inter-peak latency.

Intensity (dB nHL)	Ear	Wave latency (m sec)						P value
		Study group (N=53)			Control group (N=20)			
		Mean	SD	Range	Mean	SD	Range	
70	Right	2.28	0.492	1.28-3.15	2.04	0.546	1.3-3.28	0.092
	Left	2.24	0.496	0.82-3.2	2.19	0.510	1.365-3.2	0.480
80	Right	2.30	0.936	1.23-7.93	2.17	0.503	1.28-3	0.752
	Left	2.27	0.491	0.85-3.25	2.16	0.546	1.33-3.3	0.357
90	Right	2.37	0.6	1.25-5.5	2.31	0.339	1.75-2.9	0.785
	Left	2.18	0.546	0.65-3.4	2.29	0.607	1-3.4	0.528

Table 5: ABR parameter wave I-V inter-peak latency.

Intensity (dB nHL)	Ear	Inter peak latency (m sec)						P value
		Study group (n=53)			Control group (n=20)			
		Mean	SD	Range	Mean	SD	Range	
70	Right	12.06	55.417	0.01-289.19	3.58	8.429	0.02-38.49	0.520
	Left	1.66	2.174	0.01-8.98	7.27	16.517	0.03-60.92	0.271
80	Right	2.28	3.687	0-19.35	25.35	109.477	0.07-490.45	0.166
	Left	1.33	1.330	0.02-5.3	1.33	1.178	0.1-4.2	0.790
90	Right	4.48	13.218	0.03-90.84	7.08	17.683	0.03-58.63	0.621
	Left	1.96	2.889	0-14.65	2.36	3.509	0-12.14	0.843

Table 5 shows ABR parameter of inter peak latency wave I-V (in msec) for study and control group. In the study group, the mean inter peak I-V latency at 70 to 90 dB nHL varied from 1.33±1.33 msec to 12.06±55.417 msec. Comparatively in the control group the mean inter peak latency (wave I-V) varied from 1.33±1.178 msec to 25.35±109.4 msec. The difference between the study and control group was not statistically significant. The absolute latencies of wave I, III and V also showed no statistically significant difference between study and control groups in this study.

DISCUSSION

In this study, 53 patients of upper airway allergy attending the otolaryngology outpatient clinic of Dayanand Medical College and Hospital, Ludhiana and 20 controls were subjected to relevant audiological and haematological investigations. This was preceded by through general physical and ear, nose, throat examination. None of the study or control group subjects with pre-existing otological complaints were included, so, the study and control group patients were asymptomatic

as far as hearing was concerned. In this study, the mean pure tone thresholds were significantly poorer at 4000 and 8000 Hz frequencies in the study group. So, it can be interpreted that patients with upper airway allergy had sensory neural hearing loss at these frequencies as compared to the controls. Similar observations were made in study by Singh et al.[3] They found that all the study group patients had sensorineural hearing loss that was worse in the higher frequencies. In contrast, in a recent study by Nursoy et al, no patient of the study group and the control group had any hearing loss between frequency range of 250-16000 Hz.[4] No statistically significant difference was detected as a result of the comparison of auditory thresholds between the study and control groups between the frequencies 250 and 16000 Hz.

We found no statistically significant difference in the compliance on tympanometry between patients of upper airway allergy and controls. We were unable to find any study in the literature comparing compliance in the patients of upper airway allergy with controls.

In this study, we were able to demonstrate abnormal DPOAEs in the study group patients. There was statistically significant difference in the signal to noise ratios in study and control groups at most of the frequencies. These results indicate inner ear damage in patients with upper airway allergy. Singh et al found abnormal transient evoked otoacoustic emissions in all and abnormal DPOAE in 27 out of 30 (90%) patients in their study, thus indicating involvement of outer hair cell dysfunction of cochlea.[3] However, Nursoy et al found no statistically significant difference between the study group and the control group in terms of their signal noise ratios in all frequencies of DPOAE.[4]

In this study, we found no significant difference in wave I-III as well as wave I-V interpeak latencies between study and control groups in ABR testing. There was also no significant difference in absolute latencies of wave I, III and V between the two groups. Our findings are similar to the study by Nursoy et al.[4] However, our findings are in contrast to the study by Singh et al.[3] Here authors found that all the patients in the study group had statistically significant prolonged wave I latency and shortened wave I-III and wave I-V inter peak latencies as compared with controls.

The conventional concept was that the inner ear existed as an "immune-privileged" site along with the brain, protected from immunological reactions, partly due to the existence of "blood-brain" and "blood-labyrinthine" barriers respectively. However, the inner ear shows a greater tendency to be immune-responsive than the brain. Harris et al found that antigen presented to the inner ear evoked an immune response equal to immunization via a parenteral route while exceeding the response elicited by immunization through the middle ear.[5] The endolymphatic sac (ELS) plays a significant role in the inner ear immune response. The sac contains a resident population of lymphocytes and it has been shown that the immune response within the ear may be significantly reduced and cochlear damage minimised with the destruction of the endolymphatic sac or duct.[6,7] The role of the endolymphatic sac is not completely clear however, as the normal cochlea does not contain lymphocytes, and lymphocytes present in the cochlea in the immune response do not originate within the ELS. The lymphocytes responding to antigenic stimulation in the inner ear enter from the systemic circulation, apparently via the spiral modiolar vein.

The inner ear immune response protects the cochlear structures from insults such as viral labyrinthitis and other infections. The delicate nature of the inner ear tissues makes them quite vulnerable to this inflammatory response however. Darmstadt et al showed that cochlear damage from viral labyrinthitis is reduced by immunosuppressive therapy.[8]

All four types of immune reactions described by Gell et al have been hypothesized to contribute to inner ear disease. Inhalant allergy and anaphylaxis fall into type I category of immune response. The type I immune response has been hypothesized as a cause of disruption of ionic transport within the inner ear due to histamine induced vasodilation, resulting in endolymphatic hydrops. Other hypotheses of the role of type I sensitivity in inner ear disease have been put forth, but none have been proved with any degree of certainty. Evidence is growing that type II immunity is a cause of inner ear disease. Using western-blot analysis, a bovine inner ear protein of molecular weight 68 kDa was recognized in sera from patients with presumed autoimmune SNHL.[9] Type III immune reactions are the result of the deposition of intermediate-sized immune complexes in the microcirculation. The deposition of these biologically active immune complexes induces vascular injury with subsequent injury to the labyrinthine structures. Consistent with this theory has been the demonstration of deposition of immunoglobulin around an apparently occluded blood vessel as shown by immunofluorescence of the ELS in patients with Meniere's disease.[10] Derebery et al analysed sera from 30 patients with Meniere's disease.[11] Ninety five percent of these patients demonstrated elevated levels of circulating immune complexes as compared with only 20% of controls. Evidence supporting the role of type IV reactions in inner ear disease is largely from laboratory testing. Cellular immune responses to inner ear antigens have been demonstrated in Meniere's disease and Cogan's syndrome.[12,13]

Lasisi had suggested some peculiar predisposition to inner ear pathology in patients of nasal allergies.[14] The endolymphatic sac has been proposed as a target organ responsible for inner ear symptom in allergic subjects in a study conducted by him. Similarly, Singh had observed that allergic rhinitis patients had a higher prevalence of

hearing loss and otoacoustic emission abnormalities than controls.[3] It was proposed that endolymphatic sac can process antigens and produce its own local antibody response. The resulting inflammatory mediators and toxic products may interfere with hair cell function.

CONCLUSION

We could demonstrate higher prevalence of high frequency sensorineural hearing loss and abnormalities of OAEs in patients having allergic rhinitis. These abnormalities were detected even though none of the patients had complaints of hearing loss. The likely seat of damage appears to be the inner ear as evidenced by abnormalities of DPOAEs. However the exact pathophysiology of inner ear damage in patients of upper airway allergy is poorly understood and needs further research.

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