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Respiratory Allergy as a Contributory Factor in the Development of Vocal Fold Nodules

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Abstract

Introduction: Increasing evidence in the literature indicates that respiratory allergies are often a hidden contributory factor in vocal dysfunction. Although the precise allergic pathophysiological process within the vocal folds is not yet determined, modern understanding suggests that allergic changes in the lining of the larynx are an integral part of a systemic respiratory allergic reaction.

Goal: To determine whether there are differences in the acoustic voice parameters between the following groups of patients: 1) patients with allergies, 2) patients with nodules, 3) patients with allergies and nodules. To point out the possible pathophysiological mechanisms of phonation in the forementioned groups of patients, depending on the acoustic parameters and local signs in the larynx. To point out suggestions for treating dysphonia related to allergies and vocal fold nodules, based on the results.

Methods: The study included 60 patients divided into 3 groups of 20 patients of the same gender structure, aged from 18 to 55 years. All patients underwent allergy testing by using Prick test, indirect laryngoscopic examination and objective computer acoustic analysis of voice.

Results: Evaluation of voice quality between the groups has shown that the most sensitive parameters are the magnitude of noise energy in voice (NNE) and the maximum phonation intensity (Int max).

Conclusions: The presence of allergic vocal fold edema possibly reduces the "gap" between the vocal cords and the quantity of the noise in voice. Respiratory allergy as a comorbidity factor in a hyperkinetic voice disorder contributes to the increase of voice intensity, probably due to the lack of auditory control of voice. Allergy testing and acoustic voice analysis should be performed routinely in patients with vocal dysfunction.

Keywords

Respiratory allergies, Vocal folds, Vocal fold nodules

Introduction

Vocal fold nodules are benign, bilateral growths of different sizes, caused by the increased load on the vocal cords. They are usually located on the junction of the anterior and middle third of the vocal cords, where friction is most intense [1]. The result of a long-term mechanical friction of the vocal cords in these areas is thickening of the epithelium, followed by a development of an inflammatory reaction, which together stimulate proliferation of the connective tissue of the vocal cords and the creation of nodules [2]. The most common symptom associated with vocal fold nodules is dysphonia, which is a result of irregular vibration and inadequate occlusion of the vocal cords during phonation. Vocal professionals, namely people whose professions require an increased activity of the vocal apparatus, such as singers, teachers, lawyers, commentators and others, experience most problems with this disorder. In addition to vocal overload, there is an increasing body of evidence pointing at the importance of other contributory factors, including allergic reactions of mucosa [3].

According to Newacheck, respiratory allergies are the most common chronic condition of the adult population that affects 10-30% of the general population. Symptomatology is present for several months during the year in more than half of the patients [4] and is one of the major causes of disability worldwide, affecting people regardless of age, gender, ethnicity and socioeconomic status. The most common inhalant allergens that cause allergic reactions are: pollens (grasses, weeds, trees), dust mites, animal products (cats, dogs, rodents), fungal spores, cockroaches and others [5]. It is unknown what causes the hypersensitivity of the immune system of respiratory mucosa and why T-lymphocytes stimulate plasma cells to produce specific IgE antibodies. In the respiratory mucosa of patients with allergies IgE antibodies accumulate around mast cells, causing their degranulation and release of histamine and other mediators responsible for the symptoms of allergy [6].

The relationship between respiratory allergy and vocal dysfunction is often placed into question and the literature generally paid little attention to the subject. Allergic laryngitis is an entity that is still under-researched [4]. One reason for this is that the allergic pathophysiological process that takes place within the vocal cords still cannot be accurately determined. Other reasons are practical and technical limitations, due to the lack of specific allergy related voice symptoms and specific laryngoscopic findings [7]. The exception is anaphylactic reaction that draws attention to the connection between allergy and larynx. However, there is a growing body of evidence that indicates existence of other allergic reactions of the larynx [8]. It is considered that respiratory allergies are a frequent, although usually hidden, factor in comorbidity of vocal dysfunction [6].

Healthy phonation requires adequate breath support and

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control [9], generation of regular and periodic vibrations of the vocal cords and adequate resonant modulation of supraglottic and subglottic structures. Respiratory allergies may affect the voice and appearance of dysphonia in many ways. Nasal congestion can lead to the disorder of resonant characteristics of the nasal cavity and the pharynx, and increased secretion of the upper and lower airways can cover and irritate the vocal cords and affect the generating function of the larynx. The reduction in lung function (activator) can affect the respiratory support in voice production and motility of respiratory muscles which may have significant consequences on the singing voice. Cough also irritates the mucosa of the larynx [10]. Current understandings indicate that the allergic changes in the mucosa of the larynx are an integral part of the systemic allergic reaction of the respiratory tract [7].

Whereas allergic mechanisms are still not sufficiently determined by immunological and histological analysis, they may cause the primary edema of the vocal cords [6]. The first double-blinded, placebo-controlled study which excluded the impact of nasal allergy by oral inhalation of allergens, and the impact of lower respiratory tract allergy by normal pulmonary function tests, confirmed the increase of subglottic pressure together with the elevated concentration of antigens. Increase in subglottic pressure is an indicator of tissue changes in the larynx. Simberg demonstrated that patients with vocal dysfunction have a higher incidence of respiratory allergies and that patients with allergies have a higher incidence of vocal symptoms [4]. In addition to nasal symptoms, the four most common symptoms in patients with respiratory allergies, according to data from 14 studies in the Roth's review, are: throat clearing, chronic cough, feeling of a "lump" in throat and hoarseness. According to the same author, this is accompanied by the following local signs in the larynx: diffuse laryngeal edema, vocal fold edema, excessive thick viscous mucus, vocal fold and arytenoids erythema. However, these findings may be present in other diseases of the larynx, such as laryngopharyngeal reflux disease [7]. Even videostroboscopic evaluation is not specific [11]. Inhalant allergy is not often recognised with the appearance of dysphonia, either by the patients or by the physicians [6].

Goals

- To determine whether there are differences in the acoustic voice parameters between the following groups of patients: 1) patients with allergies, 2) patients with nodules, 3) patients with allergies and nodules.
- To point out the possible pathophysiological mechanisms of phonation in the forementioned groups of patients, depending on the acoustic parameters and local signs in the larynx.
- To point out suggestions for treating dysphonia related to allergies and vocal fold nodules, based on the results.

Respondents and methodology

The study was conducted as a retrospective study at the Department of Otorhinolaryngology at the Faculty of Medicine Novi Sad. It included 60 respondents who were divided into 3 groups of 20 patients of the same gender structure, aged 18 to 55 years. Data were obtained from allergic and phoniatric records. Allergy testing to standard inhalation allergens was conducted by Prick test. The presence of nodules on the vocal cords was determined by indirect laryngoscopy.

Group I - patients with respiratory allergies.

Group II - patients with vocal fold nodules.

Group III - patients with respiratory allergies and vocal fold nodules.

The acoustic parameters of the voice of the respondents were obtained using an objective computer acoustic analysis of voice. 14 acoustic parameters were determined for each respondent, i.e. a total of 640 acoustic parameters. Sample of voice (extended phonation of vowel A lasting at least 3 s, the most successful one of the three attempts) is provided in a room isolated from the noise in a comfortable sitting position with normal height and intensity of the speaking voice. The voice was recorded at a distance of 5 cm from the mouth using a microphone (model *Behringer ultravoice* XM 8500) with a mixer (*Eurorack* UB 520 *ultra low-noise design 5 - input 2 bus mixer*). The most stable segment of the voice sample was analyzed using *TIGER DRS* computer system with software version *Dr. Speech (4) Vocal Assessment* which provides analysis of various parameters of voice. Among them, the numerical values of the following parameters were determined:

- **Mean F0** (Hz) - the mean fundamental frequency of the speaking voice;

- **SD F0** - standard deviation F0;

- **Max and Min F0** (Hz) - the maximum and minimum F0 of the speaking voice;

- **Max and Min Int** (dB) - the maximum and minimum intensity of the speaking voice;

- **Jitter** (%) - a parameter that indicates the variability of frequency at short intervals;

- **Shimmer** (%) - a parameter that indicates the variability of amplitude at short intervals;

- **HNR** (dB) - *harmonic to noise ratio* - a parameter that represents the ratio of harmonic and noisy elements of voice;

- **SNR** (dB) - *signal to noise ratio* - a parameter that shows the ratio of audible and noisy components of voice and

- **NNE** (dB) - *normalized noise energy* - noise energy magnitude in the voice

Through comparison of the actual voice with the normal and pathological voices from the database (2937 normal and 902 pathological voices) three categories of pathological voices were determined: HOARSE voice - degree of hoarseness, HARSH voice - degree of roughness, BREATHY voice - degree of breathiness. All three parameters are given in four intensity levels: 0 - the state of a healthy voice, 1 - slight deviation, 2 - moderate deviation and 3 - severe deviation.

The statistical analysis used the methods of descriptive statistics (mean, standard deviation), and the parametric Student t-test. Non-parametric values were analyzed by Kruskal Wallis test.

None of the patients were treated for respiratory allergy nor voice disorder prior to this study.

Results

The results are presented in tables with emphasized statistical significances.

Acoustic analysis of gender-independent parameters between the three groups of patients

A statistically significant difference was found in the parameter NNE when comparing all three groups of patients. Comparing patients with allergies and patients with nodules, there was a significantly higher value of the parameter NNE in patients with nodules. Higher value of this parameter in patients with nodules was also found in comparison to patients that have both allergies and nodules. Acoustic analysis of patients with nodules and patients with allergies and nodules showed a significantly lower value of the parameter NNE in patients with allergies and nodules (Table 1).

Acoustic analysis of gender-dependent parameters between the three groups of patients

Since the groups had only a few male respondents, the analysis of gender-dependent acoustic parameters (Mean F0, Minimum F0, Maximum F0, SD F0, Minimum and Maximum intensity) was made only for females. Acoustic analysis of patients with allergies and

Table 1: Acoustic analysis of gender-independent acoustic parameters.

Gender-independent parameters	Comparison of patient groups	Groups	N	$\overline{X}$	SD	Minimum	Maximum	t	p
Jitter	allergies with nodules	allergies	20	0.2535	0.12959	0.12	0.57	1.497	0.143
		nodules	20	0.4860	0.68245	0.12	3.27		
		total	40	0.3698	0.49894	0.12	3.27		
	allergies with allergies and nodules	allergies	20	0.2535	0.12959	0.12	0.57	0.768	0.447
		allergies and nodules	20	0.2855	0.13399	0.15	0.62		
		total	40	0.2695	0.13111	0.12	0.62		
	nodules with allergies and nodules	nodules	20	0.4860	0.68245	0.12	3.27	1.289	0.205
		allergies and nodules	20	0.2855	0.13399	0.15	0.62		
		total	40	0.3858	0.49594	0.12	3.27		
Shimmer	allergies with nodules	allergies	20	27.940	246.453	0.34	9.70	0.162	0.872
		nodules	20	26.130	435.741	0.07	15.97		
		total	40	27.035	349.536	0.07	15.97		
	allergies with allergies and nodules	allergies	20	27.940	246.453	0.34	9.70	0.526	0.602
		allergies and nodules	20	23.630	271.254	0.11	8.73		
		total	40	25.785	256.735	0.11	9.70		
	nodules with allergies and nodules	nodules	20	26.130	435.741	0.07	15.97	0.218	0.829
		allergies and nodules	20	23.630	271.254	0.11	8.73		
		total	40	24.880	358.479	0.07	15.97		
NNE	**allergies with nodules**	**allergies**	**20**	**-129.370**	**452.776**	**-19.26**	**-5.75**	**4.848**	**0.000**
		nodules	**20**	**-59.570**	**457.743**	**-14.00**	**5.77**		
		total	**40**	**-94.470**	**571.732**	**-19.26**	**5.77**		
	allergies with allergies and nodules	**allergies**	**20**	**-129.370**	**452.776**	**-19.26**	**-5.75**	**2.478**	**0.000**
		allergies and nodules	**20**	**-95.240**	**417.710**	**-16.99**	**-3.45**		
		total	**40**	**-112.305**	**463.408**	**-19.26**	**-3.45**		
	nodules with allergies and nodules	**nodules**	**20**	**-59.570**	**457.743**	**-14.00**	**5.77**	**2.574**	**0.014**
		allergies and nodules	**20**	**-95.240**	**417.710**	**-16.99**	**-3.45**		
		total	**40**	**-77.405**	**468.729**	**-16.99**	**5.77**		
HNR	allergies with nodules	allergies	20	210.355	468.941	12.37	28.84	0.980	0.333
		nodules	20	195.258	492.738	11.17	27.04		
		total	40	203.000	480.420	11.17	28.84		
	allergies with allergies and nodules	allergies	20	210.355	468.941	12.37	28.84	0.980	0.333
		allergies and nodules	20	206.565	492.265	10.89	30.44		
		total	40	208.460	474.929	10.89	30.44		
	nodules with allergies and nodules	nodules	20	195.258	492.738	11.17	27.04	0.717	0.478
		allergies and nodules	20	206.565	492.265	10.89	30.44		
		total	40	201.056	489.333	10.89	30.44		

patients with nodules showed no statistically significant differences. Comparing patients with allergies and patients with both allergies and nodules, there was significantly higher values of the parameters Int min and Int max in patients with allergy and nodules. Higher value of the parameter Int max was found also in patients with allergies and nodules compared to patients with only nodules (Table 2).

Acoustic analysis of pathological types of voice between the three groups of patients

Comparation of patients with allergies and patients with nodules showed a statistically significant presence of the parameters HOARSE (Kruskal Wallis Test $\chi^2 = 4.238$; $p < 0.05$) and BREATHY (Kruskal Wallis Test $\chi^2 = 11.773$; $p < 0.01$) in patients with nodules (Table 3). Analysis of pathological types of voice in patients with allergies and patients with allergies and nodules showed no statistically significant difference in the values of the parameters HOARSE (Kruskal Wallis Test $\chi^2 = 0.201$; $p > 0.05$), HARSH (Kruskal Wallis Test $\chi^2 = 0.167$; $p > 0.05$) and BREATHY (Kruskal Wallis Test $\chi^2 = 3.301$; $p > 0.05$). No statistically significant difference in the values of the parameters HOARSE (Kruskal Wallis Test $\chi^2 = 2.424$, $p > 0.05$), HARSH (Kruskal Wallis Test $\chi^2 = 0.328$, $p < 0.05$) and BREATHY (Kruskal Wallis Test $\chi^2 = 2.001$, $p > 0.05$) was found when comparing the group with nodules and the group with both allergies and nodules.

Discussion

A small number of studies have dealt with acoustic voice analysis in patients with allergies, and an even smaller number with allergies as a comorbid factor in the development of vocal disorders. Self-assessment of voice in relation to allergies is usually performed using VHI (*Voice Handicap Index*) score, which estimates the negative impact of vocal symptoms on the quality of life. According to the available literature subjective acoustic analysis of voice by auditory perception was used in allergic conditions by some authors, but there were no significant differences compared to healthy voices [7,4,12].

Objective acoustic analysis of voice, aimed to detect possible disturbances of phonation in allergic conditions analyzing the acoustic parameters of vocal cords vibration disorders and other pathophysiological disorders of phonation, has been often used in research, but without spectacular results. In this study the analysis of the fundamental frequency of the speaking voice (Min F0) of female patients showed slightly lower values (allergies - 208 Hz, nodules - 212 Hz, allergies + nodules - 210 Hz) in comparison to normal voice (average of 220 Hz [13]). Jackson-Menaldi found lower F0 values in patients with allergies (169 Hz) [11]. Analysis of numerous numerical acoustic parameters according to the available literature gave significant results in individual cases. Bauer found no significant differences between respondents with allergies and respondents with healthy voices in any of the acoustic parameters, except in the maximum phonation time that reflects the state of respiratory support [12]. In this study through comparing patients with allergies and patients with nodules we found a significant difference (p = 0.000) in terms of the acoustic parameter of magnitude of noise energy (NNE), because this parameter in patients with allergies is within normal limits -12.93 (the normal is -10, given by software), while in patients with nodules this parameter is abnormal (-5.95). Comparing patients with allergies and patients with allergies and nodules, a significant difference was also found (p = 0.000), as this parameter is also abnormal (-9.52) in patients with allergies and nodules. Our

Table 2: Acoustic analysis of gender-dependent acoustic parameters

Gender-dependent parameters	Comparison of patient groups	Groups	N	$\overline{X}$	SD	Minimum	Maximum	t	p
Mean F0	allergies with allergies and nodules	allergies	17	208.2876	24.13549	166.56	256.48	0.239	0.812
		allergies and nodules	17	210.4412	28.15797	152.00	276.00		
		total	34	209.3644	25.84670	152.00	276.00		
	nodules with allergies and nodules	nodules	17	212.8824	31.11447	174.00	275.00	0.240	0.812
		allergies and nodules	17	210.4412	28.15797	152.00	276.00		
		total	34	211.6618	29.24627	152.00	276.00		
SD F0	allergies with allergies and nodules	allergies	17	2.0247	0.92430	0.82	4.18	1.300	0.203
		allergies and nodules	17	1.6841	0.55893	1.03	3.19		
		total	34	1.8544	0.77173	0.82	4.18		
	nodules with allergies and nodules	nodules	17	2.1724	1.18256	1.13	6.30	1.539	0.134
		allergies and nodules	17	1.6841	0.55893	1.03	3.19		
		total	34	1.9282	0.94388	1.03	6.30		
Max F0	allergies with allergies and nodules	allergies	17	213.1259	23.09094	171.60	259.41	0.235	0.816
		allergies and nodules	17	215.2300	28.75481	155.00	284.00		
		total	34	214.1779	25.70115	155.00	284.00		
	nodules with allergies and nodules	nodules	17	218.5882	30.80191	180.00	279.00	0.329	0.745
		allergies and nodules	17	215.2300	28.75481	155.00	284.00		
		total	34	216.9091	29.39048	155.00	284.00		
Min F0	allergies with allergies and nodules	allergies	17	203.7629	23.88461	161.54	250.57	0.268	0.790
		allergies and nodules	17	206.1347	27.54950	149.00	270.00		
		total	34	204.9488	25.41713	149.00	270.00		
	nodules with allergies and nodules	nodules	17	206.6471	31.17078	165.00	270.00	0.051	0.960
		allergies and nodules	17	206.1347	27.54950	149.00	270.00		
		total	34	206.3909	28.96796	149.00	270.00		
Int min	**allergies with allergies and nodules**	**allergies**	**17**	**66.76**	**5.858**	**54**	**74**	**3.813**	**0.001**
		allergies and nodules	**17**	**75.82**	**7.852**	**52**	**85**		
		total	**34**	**71.29**	**8.226**	**52**	**85**		
	nodules with allergies and nodules	nodules	17	70.00	9.760	45	78	1.917	0.064
		allergies and nodules	17	75.82	7.852	52	85		
		total	34	72.91	9.209	45	85		
Int max	**allergies with allergies and nodules**	**allergies**	**17**	**72.59**	**3.411**	**66**	**77**	**3.878**	**0.000**
		allergies and nodules	**17**	**79.24**	**6.190**	**61**	**89**		
		total	**34**	**75.91**	**5.966**	**61**	**89**		
	nodules with allergies and nodules	**nodules**	**17**	**74.18**	**4.475**	**63**	**78**	**2.731**	**0.010**
		allergies and nodules	**17**	**79.24**	**6.190**	**61**	**89**		
		total	**34**	**76.71**	**5.906**	**61**	**89**		

Table 3: Acoustic analysis of pathological types of voice.

Pathological types of voice	Intensity level	Group	
		allergies	nodules
		n	n
HOARSE	**absent**	**8**	**2**
	slight	**10**	**14**
	moderate	**2**	**3**
	severe	**0**	**1**
	total	**20**	**20**
HARSH	absent	16	16
	slight	2	0
	moderate	1	2
	severe	1	2
	total	20	20
BREATHY	**absent**	**12**	**1**
	slight	**0**	**2**
	moderate	**5**	**6**
	severe	**3**	**11**
	total	**20**	**20**

findings are similar to the findings of Jackson-Menaldi that found the average values of NNE in patients with allergies -10.69, i.e. near to normal [11]. The fact that patients with allergies and nodules have a lower noise magnitude of the voice compared to patients having only nodules seems controversial, because of the expected cumulative effect of the two comorbid factors. However, if we take into account the fact that the noise in the voice with vocal fold nodules is caused by an hourglass-shaped gap, it is possible that the edema of the vocal cords, if it is caused by allergies, reduces the occurrence of the noise in voice. The significant presence of the pathological type of BREATHY voice in patients with nodules in relation to patients with allergies confirms the fact that the noise is caused by an hourglass-shaped gap. When comparing the group called allergies and nodules with the group called allergies, as well as with the group called nodules, there is no significant increase of the parameter BREATHY. From all this, it can be indicated that the gap and the BREATHY category are the highest in the group with only nodules.

Analysis of the intensity of a speaking voice showed that there is a significant increase of minimum and maximum values of the intensity in patients with allergies and nodules compared to the patients with only allergies. Jackson Menaldi found a reduced range of voice in patients with allergies in terms of its height and intensity [11]. Through comparison of patients with allergies and nodules and patients with only nodules, a significantly higher maximum intensity of the speaking voice was found in patients with both allergies and nodules (allergies 72.59 dB, nodules 74.18 dB, allergies + nodules 79.24 dB). Normal values of the intensity of voice are 70-75 dB [14]. There seems to be a possible impact of allergies on the voice intensity. Although it is known that there is an increased voice intensity in patients with nodules, there are two possible reasons for a contributing effect of allergies on the intensity of voice: 1) it is possible that the edema of the vocal cords increases amplitudes of vibration; 2) it is possible that the edema of the Eustachian tube contributes to the lack of auditory control of one's own voice. This has been confirmed by other authors as well [6].

The negative impact of allergies on vocal function is not called into question in vocal professionals with allergies. They often complain about the changes in the quality of their voice during allergic episodes. [7] However, experience has shown that many patients do not take symptoms of respiratory allergies seriously and often associate them only with nasal manifestations. They often take a long time before they decide to see a doctor. A physician treating a patient with vocal symptoms must bear in mind that hidden respiratory allergies can be the cause of vocal disorders [6].

Objective computer acoustic analysis of voice was the main methodological tool in this research. Perhaps the most important limitation of the study is lacking of more diverse metodology to determine changes not only in voice quality but also in the mucosa of larynx.

Conclusions

1) The acoustic analysis of voice in patients with allergies showed that the most sensitive parameters are the magnitude of noise energy (NNE) and the intensity of voice.

2) On the basis of acoustic analysis of voice an allergy is a possible contributing factor in occurrence of edema of the vocal cords.

3) The presence of an allergy as a comorbidity factor in a hyperkinetic voice disorder contributes to the increase of voice intensity, probably due to the lack of auditory control of voice.

4) Allergy testing and acoustic voice analysis should be carried out routinely in all patients with a vocal dysfunction.

5) Treatment of respiratory allergies is an important element in the treatment of voice disorders.

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