The Role of Allergy in Phonation

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Summary: Background. Allergies are among the most common chronic conditions worldwide affecting 10%−30% of adult individuals and 40% of children. Phonation can be affected by different allergic conditions in various ways. The role of allergy in phonation has been under-researched and poorly understood and the respective literature is poor. Several studies have investigated the role of certain allergic diseases in phonation. In this review, we tried to include all allergic conditions that can affect voice production.

Methods. We conducted a bibliography review looking for allergic conditions that can affect phonation. Allergic asthma, allergic laryngitis, allergic rhinitis and sinusitis, oral allergy syndrome, and angioedema were included in our search.

Results. The literature on the impact of allergy in phonation remains poor and many key questions concerning basic information for epidemiology, pathophysiology, and larynx pathology in allergic patients with phonation problems still remain unanswered.

Conclusions. The role of allergy in voice production remains underinvestigated and many basic questions still remain open. Further research is needed to improve our understanding for these very common conditions.

Key Words: Asthma−Laryngitis−Rhinosinusitis−Oral allergy syndrome−Angioedema.

INTRODUCTION

Allergies are among the most common chronic conditions worldwide. Approximately 10%−30% of adult individuals in the industrialized world and 40% of children are affected by some sort of allergic condition,[1] and this number seems to be increasing.[2]

Phonation is a complicated function that incorporates the upper and lower respiratory tract as well as part of the digestive system. The larynx and its vocal cords are responsible for transforming the aerodynamic forces generated by the elastic recoil of the lungs and diaphragm, and active contraction of chest and abdominal muscles into acoustic energy. The upper respiratory tract and the articulators then further modify the sound spectrum and produce speech sounds.

Allergic respiratory disease can affect vocalization in many different ways depending on the organs that are affected. Although voice disorders have been commonly associated with respiratory allergy,[3] several other allergic conditions can affect phonation in various ways. During the last decade, clinical researchers have proposed the single unified airway model according to which the respiratory system is characterized by a system of organ linkages with anatomical similarities and common pathophysiological mechanisms that mediate hyper-reactivity and inflammatory responses.[4−6] In this sense, the upper and lower respiratory tract as well as the middle ear share a histologically similar epithelium that spreads from the ciliated epithelium of the nares and the membranous tissue matrices of the nasal, oral, pharyngeal, and laryngeal cavities to the respiratory bronchioles and alveoli of the lungs. A mediator response in one organ can trigger similar responses along the rest of the respiratory tract and pathologies originating in one part of this unified airway often concurrently affect other parts.[6−9] It is well established that changes in any of the organs comprising the single unified airway can induce variably spread inflammatory response in both the upper and lower respiratory tract.[10−12]

Unfortunately, very little published data exist on the voice disorders in allergic patients and the available evidence for allergic reactions of the larynx is poor.

The purpose of our study was to review the impact of allergic diseases in voice production and the way phonation is affected by these very common conditions. We tried to include in one review all the allergic diseases that can affect voicing. In this regard, allergic asthma, allergic laryngitis, allergic rhinitis and rhinosinusitis, oral allergy syndrome (OAS), and angioedema were included for review. Clinical data for the epidemiology, the mechanisms of voice changes, clinical manifestations and pathologic findings related to allergic diseases, and their impact on phonation are presented in this review.

METHODS

We performed a literature search in the following databases: PubMed, EMBASE, and Cochrane Library. The combinations of keywords in our search were "allergic asthma [AND] voice," "allergic laryngitis [AND] voice," "allergic rhinitis [AND] voice," "allergic rhinosinusitis [AND] voice," "oral allergy [AND] voice," "pollen allergy [AND] voice," "angioedema [AND] voice." Articles, letters, summaries, and dissertations published in English from 1980 to June 2017 were included in our search. Additional information was gathered from references cited in the identified publications. Particular emphasis was given to original articles and, on a secondary basis, to books and reviews. Only studies reporting appropriate information on our study design were included for review. After reviewing all the titles of related articles, a total number of 243 studies were identified. From these studies, 125 studies, finally, were found to give enough and appropriate information concerning the scope of our study. Unfortunately, very few

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articles were found to be of high level quality and the majority of these studies referred to allergic asthma and allergic rhinitis (rhinosinusitis) while OAS and angioedema are even less investigated and the lack of information for these two conditions is bigger. In this regard, the voice problems in allergic patients, under-researched as it is, is underscored and the need for further investigation of this important topic may trigger other investigators to pursue to fill the existing gap of information.

RESULTS

Asthma and phonation

Asthma is a chronic inflammatory disease of the lower respiratory tract, affecting all age groups and both genders. It is characterized by recurrent attacks of breathlessness, chest tightness, cough, and whizzing, which vary in severity and frequency from person to person. It affects 5% of the adult population, but its peak incidence occurs in young children, where asthma is probably underdiagnosed. The prevalence of asthma is increasing worldwide.[13]

Three factors contribute to the attacks of breathlessness: bronchial smooth muscle spasm, bronchial wall inflammation and edema, and increased mucus production. Asthma management includes both the prevention of the attacks by avoiding triggers such as allergens and various irritants, and the symptomatic therapy by use of inhaled short- and long-acting beta agonists, corticosteroids, and antileukotriene agents. Corticosteroids are the cornerstone on asthma management as they are the most potent anti-inflammatory agents currently available. Inhaled corticosteroids (ICS) are preferred to orally administered agents as they are associated with significantly fewer side effects. Dysphonia is the most common and the most annoying side effect of ICS affecting both patients' treatment compliance and their quality of life. The problem remains despite the development of new ICS molecules and new, more sophisticated delivery systems.[14]

Mechanisms of phonation changes in asthma

It is not yet clear how asthma affects variables of voice. In theory, there are three ways in which asthma can interfere with the mechanism of phonation. First, the inflammatory mucosal changes of the upper respiratory tract may be affecting the superficial layers of the vocal cords, thus altering their vibrating characteristics. Second, reduction of air flow and available air pressure is another way voice can be affected. Third, dysphonia can be a result of the action of antiasthmatic medication many people suffering from asthma have to use, especially ICS.

Force vital capacity and forced expiratory volume in 1 second are reduced in asthmatic patients. A reduced forced expiratory volume in 1 second to force vital capacity ratio indicates an airway obstruction. The airway obstruction associated with an asthma attack results in a reduction in vital capacity and airflow. This reduction translates to subglottic air pressure and therefore reduced amplitude of vocal fold vibration. Weak lung function has been associated with altered phonatory function and reduced maximum phonation time (MPT). It is likely that asthma affects the patient's ability to maintain a sufficient subglottic air pressure during phonation.

Inflammation of the airway also increases the mass of the vocal folds that results in a reduction in the fundamental frequency (F_0) and harmonics-to-noise ratio. Increased mucus secretion results in mucus pooling at the laryngeal area resulting in "wet" voice.[15] Forceful coughing during asthma attacks can also traumatize the vocal fold mucosa. Dysphonia in asthma can be attributed to mucosal changes due to the obstructive respiratory disease on one hand and mucus abnormalities and regularly accompanying chronic sinusitis on the other hand.[16]

Singers often complain of performance-related vocalization problems caused by increased bronchial reactivity. This can be considered equivalent to exercise or cold-induced asthma.[17] Airway reactivity-induced asthma in singers is caused by hyperventilation during singing and this is what is considered to trigger the asthmatic attack. The performer notices shortness of breath or voice changes such as vocal fatigue, decreased range of phonation, and impaired volume control. In these cases, bronchodilators seem to improve the singer's performance. Addressing airway reactivity-induced asthma in singers usually helps singers to restore their singing capacity by optimizing their respiratory function. Cohn et al studied 20 asthmatic singers with no noticeable impairment on their speaking voice. Treating these individuals for asthma produced measurable improvement on their singing voice.[18]

Mild asthma and underdiagnosed allergies may be the cause of voice disorders in many professional voice users with no other apparent cause for their voice pathology. Patients with mild asthma who have minimal or even no abnormalities on spirometry can present with voice complaints during speaking or singing. These individuals may represent an exercise-induced asthma-like group that responds to conventional bronchodilators and other asthma therapy.

Dysphonia and other vocal symptoms continue to be the main local side effect of ICS, despite the development of new ICS molecules and new, more sophisticated delivery systems. Many factors have been found to be related to dysphonia in ICS users[19] (Table 1).

The frequency of dysphonia has been reported in 8%–58% of asthmatic patients treated with ICS.[20] Several studies

TABLE 1.
Factors Related to Dysphonia Appearance in ICS Users[19]

1	Active compound of ICS
2	Type of ICS (active drug or prodrug)
3	Potency of ICS
4	Dosage and frequency of ICS use
5	Patient's compliance and right use of product delivery device
6	The size of the delivered particles
7	The velocity of the delivered particles
8	The type of the delivery system (DPI, MDI)
9	The use of spacer

Abbreviations: DPI, dry-powder inhaler; ICS, inhaled corticosteroids; MDI, metered-dose inhaler.

suggest that this can be attributed to myopathic bowing of the vocal folds.[21] Dysphonia in ICS users can also be secondary to oropharyngeal candidiasis, a well-known side effect of ICS. Asthmatic dysphonia is very often misdiagnosed as laryngopharyngeal reflux (LPR) disease.

LPR can mimic or coexist with asthma, and asthmatic dysphonia very often is misdiagnosed as LPR disease. If not correctly diagnosed, it can lead to overtreatment with corticosteroids with consequent risk of side effects. LPR and asthma are very common diseases in the general population and LPR is a frequent condition in asthma patients.[22]

The coexistence of LPR and asthma can have an additive effect on larynx performance as both pathologic conditions can have negative effect in voice production and, working in combination, can put larynx at risk. Unfortunately, there are no data in the bibliography concerning the symbiosis of these very common disorders and their impact in voicing.

Clinical data for asthma impact on phonation

The effect of asthma on phonatory variables is not clear. Nearly half of the patients with asthma complain of permanent voice disorders.[16]

Asthma-related vocal symptoms are principally viewed as secondary to the main symptoms of the disease. However, preliminary results have suggested that there may be a direct causal effect of an allergen exposure to dysphonia. This may be the case at least in allergic asthma.[3]

Functional sequelae of vocal fold changes observed in asthmatic patients include reduced amplitude of vibration and reduced propagation of the mucosal wave.[23] Asnaashari et al in a controlled study of 34 patients with asthma found that asthma as a lower airway disease can impair phonation.[24]

The results of Dworkin et al paper indicate that the allergen provocation to the larynx may lead to increased viscous secretions in the larynx, vocal fold edema and erythema, coughing, increased throat clearing, and hoarseness in people with perennial dust mite allergy.[25]

Hamdan et al showed that there is a statistically significant difference in the prevalence of dysphonia between subjects with asthma and without asthma. The overall grade of dysphonia was significantly higher in asthmatics compared to controls, and the degree of asthenia and straining was significantly higher in asthmatics with borderline significant difference with respect to roughness.[26]

A study of 20 asthmatic singers, with no noticeable impairment of speaking voice, had a measurable improvement of singing voice when treated for asthma.[27] Undiagnosed allergies and mild asthma may be implicated in undiagnosed voice problems in voice users.

Park and Choi, comparing participants with asthma and without asthma, showed that those with asthma who had taken asthma medication recently had a higher adjusted odds ratio for dysphonia. Vocal nodules, laryngeal polyps, and laryngitis were not associated with asthma.[28]

Computerized speech analysis has detected cycle-to-cycle irregularities as described by increased jitter and shimmer as well as reduced MPT in asthmatic patients who describe dysphonia-like symptoms.[20] Dogan et al investigated voice quality in 40 mild to moderate adult asthmatic patients using acoustic analysis. It turned out that asthmatic patients had significantly higher voice handicap index (VHI) scorings, reduced MPT, and increased amplitude perturbation (shimmer) when compared to normal controls.[29]

The reduced peak flow readings associated with asthma seem to be responsible for subjectively and objectively diagnosed voice disorders, although there is no published evidence that the degree of airway obstruction is correlated to the degree of vocal impairment. A study that included 80 children with asthma concluded that almost half of them had voice and/or articulation disorders.[30]

We have to keep in mind that many cases of vocal cord dysfunction (VCD), a functional disorder, is often misdiagnosed as asthma, and that VCD can complicate coexisting asthma. Reports have suggested that up to 30% of patients with asthma may have coexisting VCD. Concomitant VCD and asthma are seen in a high degree of patients (up to 50%).[31] VCD masquerading as bronchial asthma is a diagnostic challenge as it is based on laryngoscopy to detect abnormal vocal cord movements without any other pathologic finding. Dynamic volume computed tomography of the larynx has been proposed as a noninvasive method for the diagnosis of VCD.[32]

Laryngeal pathology in asthmatic patients

Laryngoscopic signs of laryngeal irritation, such as edema or erythema over the arytenoids, may be absent in asthmatic patients. Any mucus, if present, is usually thick and sticky. This mucus can dampen the vibration of the vocal fold mucosa. In asthmatic patients with dysphonia, the laryngoscopic findings that are usually present are hyperemia and plaque-like changes.[22]

Allergic laryngitis and phonation

The term laryngitis is used to describe the inflammation of the mucosa and other tissues of the larynx. This inflammation can be the result of different causes and can be classified either as acute or as chronic depending on the duration of symptoms.

Whether ingested and inhaled allergens can be the cause of laryngeal symptoms in allergic patients remain a matter of debate among clinical researchers for the past 50 years. There is still little consensus in the literature relative to whether or not allergic laryngitis is a true clinical entity. This is partly because of the limited research that has been done on allergic laryngitis, our poor understanding over this clinical entity, and the poor existing data to support such a clinical diagnosis. However, accumulating epidemiological and experimental evidence suggest that there may be a causal association between allergy and vocal pathologies in some patients and that allergy may be the trigger and causative mechanism responsible for the laryngeal inflammation and symptomatology.[5,33,34]

The underlined allergic reaction in allergic laryngitis can be an immediate or delayed hypersensitivity to inhaled or digested allergens.

Due to limited literature data, the prevalence of allergic laryngitis remains unknown. This is partly because the disease is

TABLE 2.
Symptoms and Findings Supporting the Diagnosis of Laryngeal Allergy[6]

1	History of test positive allergic disease
2	Chronic throat clearing or dry hacking cough
3	Itching of the larynx
4	Transient vocal fold edema
5	Tenacious, thick, viscid endolaryngeal mucus strands
6	Globus sensations
7	Abnormally pale, glistening, and edematous arytenoid mucosa
8	Unremarkable pulmonary function test, chest x-ray, and sinus images
9	Absence of contaminating laryngopharyngeal reflux or gastroesophageal reflux symptoms or treatment history
10	Acute or delayed dysphonia, odynophagia, or both, secondary to repetitive exposure to an inhaled, ingested, or topical antigen

usually considered part of a more complex allergic disease of the respiratory system. In this regard, it is probably unrecognized, underdiagnosed, and probably underreported. One study has estimated its yearly incidence in 3.47 per 1000.[35]

According to some researchers, to support the possible diagnosis of laryngeal allergy, several clinical symptoms and/or clinical examination studies have to be present[6] (Table 2).

Allergy testing can be of benefit in detecting those patients that are atopic and can prove a valuable diagnostic test, but it is not on its own sufficient to diagnose allergic laryngitis. It may be hard to differentiate between allergic laryngitis and LPR since both clinical entities share similar symptoms and findings.

Clinical data for the impact of allergic laryngitis on phonation

Allergic laryngitis is still an under-researched and poorly understood entity. Many aspects of the disease are poorly understood due to limited existing data. The amount of data associating allergic laryngitis with voice disorders is also limited.

Epidemiological data from a large population-based study shows that the presence of allergic rhinitis appears to increase the risk of laryngitis as it is positively associated with dysphonia and the presence of vocal nodules, suggesting a relationship between these two conditions. These researchers proposed that frequent throat clearing and chronic upper airway inflammation may play a role in the pathogenesis.[36] Patients with voice disorders have higher incidence of allergy and patients with high allergen exposure are more likely to have vocal symptoms than those with low allergen exposure. More specifically, Randhawa et al have shown that the incidence of undiagnosed vocal dysfunction is higher in patients with more air-borne allergies as determined by the raised VHI score than those with fewer or no such allergies, and patients with higher allergen exposure are more likely to have vocal symptoms than those with lower allergen exposure.[37] Simberg et al compared 49 students with allergic rhinitis symptoms on immunotherapy for 3 years with 54 control patients with no known allergic disease, and they found that patients with allergic rhinitis had an increased number of vocal complaints compared with their normal counterparts. These complaints improved with increasing duration of immunotherapy treatment.[38] Lauriello et al endoscopically examined 76 patients with vocal complaints. They found that 76% of patients in their sample had a history of allergy. There was a statistically significant association of allergy and dysphonia among female patients. They concluded that there is a clinically important association between allergy and dysphonia, primarily noted among women. They also proposed that workup of allergy is indicated in patients presenting with dysphonia.[39]

Koç et al found that VHI scores and the s/z ratio were significantly higher in individuals with allergies versus age-matched nonallergic controls, and they described the s/z ratio as an index of laryngeal disorder.[34]

In another study, VHI scores were examined in allergic and nonallergic patients during birch season. Results demonstrated that allergic patients exhibited significantly higher VHI scores than the nonallergic individuals.[40]

Turley et al demonstrated that individuals with both allergic rhinitis and nonallergic rhinitis (NAR) had higher incidences of dysphonia than nonallergic study counterparts, and this was attributed to chronic, reactive throat clearing, and coughing behaviors in the former subgroup.[41]

Experimental data from a recently published study support the association of allergy with certain laryngeal inflammatory changes. More specifically, Belafsky et al investigated the effects of iron soot and house dust mite allergen on the larynx and the trachea of guinea pigs studying the mean eosinophil profile on the epithelium and submucosal layers of the glottis, subglottis, and trachea. Significant eosinophilia was noted with the soot and house dust mite allergen combination.[42] These results support previous research findings that indicated notable adverse effects of inhaled irritants in several segments of the unified airway, resulting specifically in characteristic laryngeal inflammation.

A large cohort that tested individuals not previously diagnosed with an allergic disorder revealed that half of the individuals with larynx related complaints, such as history of intermittent dysphonia, had positive test results to at least one inhalant allergen. The odds ratio of having a positive test for allergies was statistically similar among patients evaluated for rhinitis and chronic sinusitis. Dust mite antigen sensitivity was by far the most common finding.[43] The association of vocal pathologies and laryngeal provocation reactions with dust mite allergy has been extensively evaluated.[5,25,33]

A double-blind study of laryngeal challenge by Roth et al assessed the changes in objective measures of vocal function. They exposed five participants with no airway reactivity to methacholine challenge to either an inhaled saline placebo or an active allergic suspension using a randomly ordered crossover model. They measured phonatory threshold pressure after each condition and demonstrated a significant increase in phonatory threshold pressure following antigen inhalation. Based

on the findings of their experiment, the authors argued that they were able to suggest a causal relationship between allergen inhalation and worsening of objective vocal function in individuals without concurrent asthma.[44]

Dust mite sensitization is the most common sensitization in patients with allergic laryngitis. Patients with chronic laryngeal symptoms and positive allergy testing were most often sensitized to dust mite (63%) and least often sensitized to molds (1.3%).[43]

Laryngeal pathology in patients with allergic laryngitis

According to laryngoscopic findings of two researcher groups, vocal fold edema may be an important sign of laryngeal allergy. Vocal fold edema was present in all (100%) of their "allergic laryngitis" patient group. It is clear that, when vocal fold edema is present with patterns of vocal abuse and misuse, we should consider inhalant environmental allergens like house dust or dust mites as a potential cause.[10] This provides a possible mechanism for the development of allergy-related dysphonia.

Jackson-Menaldi et al[45] and Sala et al[46] stated that patients with allergy frequently had thick secretions, hoarseness, and laryngeal edema/erythema. These findings were not specific enough to reveal a direct relationship between allergy and laryngeal findings.

The most common endoscopic findings in allergic laryngitis are vocal fold edema and erythema/hyperemia of the laryngeal mucosa, but these findings are nonspecific for allergic laryngitis as they are also common in LPR and may not be reliable to support the diagnosis of allergic laryngitis.

It has been demonstrated by direct laryngeal provocation studies that sticky viscous endolaryngeal mucous is the only reliable finding consistently associated with allergy and potential allergic tissue reactivity. The sticky, viscid mucus in the endolarynx was statistically predictive of allergy presence ($P < 0.012$) and should be viewed as a sign of a potential allergic reaction contributing to the patient's laryngeal symptoms.[5,25,33,47]

Eren et al demonstrated that there was no association between allergic sensitization and the presence of LPR, nor was there any significant difference in laryngeal appearance between allergy-positive and LPR-positive individuals.[47]

Allergic rhinitis and phonation

The term rhinosinusitis is preferred by many investigators to the separate terms "rhinitis" and "sinusitis." This is because the nose and sinus mucosa are continuous, rhinitis and sinusitis frequently occur together, rhinitis commonly leads to sinusitis, and nasal symptoms are common with sinusitis.[40] However, the term allergic rhinitis is still in use in clinical practice and throughout the literature, while the current trend is to use the term rhinosinusitis only for sinusitis.

For the scope of this review, allergic rhinitis and allergic rhinosinusitis will be presented as different clinical entities, although in everyday practice, it is very difficult to distinguish allergic rhinitis from allergic sinusitis.

Allergic rhinitis, also known as hay fever, is a type I allergic inflammatory disease of the nasal mucosa which occurs as an overacting response of the immune system to various allergens in the air. Allergic rhinitis is characterized by paroxysmal repetitive sneezing, watery rhinorrhea, and nasal blockage. In allergic rhinitis, the fluid from the nose is usually clear. Allergic rhinitis is classified into seasonal allergic rhinitis (SAR) or hay fever and perennial allergic rhinitis, which occurs year-round. Of the total cases of allergic rhinitis, it is estimated that 20% of cases are SAR, 40% of cases are perennial rhinitis, and 40% of cases are mixed.

Allergic rhinitis is common, affecting 10%–30% of children and adults in the United States and other industrialized countries.[48] It may be less common in some parts of the world, although even developing countries report significant rates.[49]

Mechanisms of voice changes in allergic rhinitis

The nose and nasopharynx belong to the supraglottic vocal tract and are the main resonating organs responsible for vocal quality and perceived characteristics of speech sounds.[38]

Allergic rhinitis and nasal polyposis narrow the nasal passage, resulting in changes in the resonance of the voice. The altered resonance is a result of reduced amount of air directed through the nasal cavity because of the narrowing. This is called hyponasality and can be observed both subjectively and objectively.[40]

Nasal obstruction causes two different types of nasality problems called rhinolalia clausa anterior and posterior. Rhinolalia clausa anterior is the anterior obstruction and it causes echoed sound in nose. Rhinolalia clausa posterior is the posterior obstruction that causes phonemes /b/ and /d/ to be perceived as /m/ and /n/, respectively. SAR had some features from both types of rhinolalia.

Nasal symptoms in allergic rhinitis have been extensively studied; comparatively very little information has been published on the effects of allergic rhinitis on voice and speech. This is because voice changes are fairly mild, and this explains the fact that very little attention has been dedicated to this symptom.

Several mechanisms are responsible for voice problems in allergic rhinitis:

1. The mucus hypersecretion of the nasal glands that causes postnasal drainage and as consequence production of cough, throat clearing, and dysphonia. Jackson-Menaldi et al[45] and Sala et al[46] stated that patients with allergy frequently had thick secretions, hoarseness, and laryngeal edema/erythema.
2. The rhinolaryngeal reflexes. Sympathetic and parasympathetic fibers demonstrated in the vocalis muscle secondary to allergic rhinitis may contribute to the presence of dysphonia.[41]
3. The specific receptors sensitive to negative pressure in the nasal cavity and in the pharynx may increase the muscular activity of the posterior cricoarytenoid muscle.[39]
4. The serous otitis media diagnosed in nearly 66% of children affected by allergic rhinitis may induce vocal abuse.[30]
5. Up to half of the children with a speech or voice disorder have allergic rhinitis and/or asthma. Both of these

conditions result in the inflammation and swelling of the airways. As the nasal tissues become inflamed, they affect the voice. This often results in improper articulation.
6. Allergies may also result in irritated and traumatized vocal cords, due to frequent cough and/or clearing of the throat from increased nasal drainage.
7. Children with severe nasal congestion quite often breathe through the mouth, and this frequently leads to the habit of having a perpetually open mouth and protruding tongue. This greatly affects the quality of speech and articulation

Clinical data related to voice changes in allergic rhinitis

Little information has been published on the effects of allergic rhinitis on voice and speech.

Millqvist et al confirmed the experience of voice changes in allergic rhinitis due to birch pollen. These changes were found in the physical and functional domains, manifested by hoarseness. Analyzing the VHI responses of vocal records in patients with SAR they concluded that some patients had voice changes which can be confirmed objectively. They also found a significant difference in the mean VHI values and the mean s/z ratio between patients with allergic rhinitis and healthy controls, indicating a relationship between allergy and dysphonia. The voice changes were fairly mild.[40]

Baker et al found voice disorders in 44.75% of a population of 80 allergic rhinitis cases. They investigated vocal quality, articulation, and audiological characteristics in children and young adults with diagnosed allergies. The findings of the study suggest that bronchial asthma and allergic rhinitis are related to disorders of voice quality and that allergic rhinitis is associated with misarticulations and diminished hearing. The presence of speech sound omissions in patients with allergic rhinitis above the age of 8 years may predict the presence or previous history of fluctuating hearing loss.[30] Koç et al, studying 30 patients with perennial allergic rhinitis, showed that the mean VHI score was significantly higher in the allergic rhinitis group than in controls although there was no significant difference on the mean MPT values, fundamental frequency (F_0 values), and stroboscopic assessment. A significant difference in the mean VHI values and the mean s/z ratio between patients with allergic rhinitis and healthy controls indicates a relationship between allergy and dysphonia.[34]

Singers with voice problems are more likely to have allergic rhinitis, and patients with allergic rhinitis who needed allergen immunotherapy were more likely to have dysphonia.[38]

Develioglu et al found that vocal changes triggered by allergic rhinitis were improved by medical treatment. Both the Total Nasal Symptom Score (TNSS) and the VHI-10 scores decreased significantly after treatment. After treatment, the acoustic analysis parameters also improved significantly and were similar to those of the control group. MPT also increased significantly.[50] Simberg et al found that college students with allergic rhinitis had symptoms such as throat clearing, hoarseness, vocal fatigue, voice breaks, globus pharyngeus, or difficulty being heard.[38]

Ohlsson et al investigated voice function in patients with birch pollen allergy. Voice recordings were made both during pollen season and nonpollen season in 30 patients and 30 controls. The samples were analyzed and the results showed that the patients reported more voice symptoms than controls during both seasons.[51] Turley et al investigated the prevalence of dysphonia among patients with allergic rhinitis and NAR and patients with no rhinitis symptoms (controls). Patients with rhinitis (allergic rhinitis or NAR) had a higher prevalence of dysphonia than controls. The patients with worse rhinitis symptoms had worse voice-related quality of life and more severe chronic laryngeal symptoms.[41]

Verguts et al demonstrated rapid induction of laryngeal complaints in allergic singers by nasal allergen provocation and during the pollen season. There was no subject-reported or investigator-measured change in voice quality.[52]

Uyar et al, evaluating the possible changes on voice caused by SAR, found a statistically significant difference in the mean VHI score between patients with allergic rhinitis and controls. They concluded that SAR has an adverse effect on vocal quality, when measured subjectively.[53]

Kim et al also concluded that VHI was significantly higher in patients with allergic rhinitis than that of control group. Shimmer (the amplitude variation of the sound wave) and the speaking fundamental frequency value were higher and MPT was shorter in the group of allergic patients than in the control group. Based on findings of their study, they concluded that patients with allergic rhinitis have considerable voice problems. Most of them have hypernasality, which may be a compensatory mechanism for the nasal obstruction they experience.[54]

From a clinical point of view, there are strong epidemiological data about the relationship between allergic rhinitis and asthma,[10,12] while treatment of allergic rhinitis has been shown helpful in controlling asthma and preventing its progression.[55]

In 1971, Boone, who first described the s/z ratio, also hypothesized that individuals with no laryngeal pathology should be able to prolong the voiceless /s/ and the voiced /z/ phonemes for approximately the similar duration of time, and therefore the s/z ratio is expected to be 1. After that report, it was estimated that patients with laryngeal pathologies would have difficulty prolonging the voiced sound /z/ for the same length of time as the voiceless /s/ in many studies. The s/z has been used as a marker for laryngeal pathology, with a cutoff of 1−1.2. Boone concluded that the s/z ratio was significantly higher in the allergic rhinitis group than in the control group; however, the mean value is within normal limits according to the previously described values. Boone's finding suggested that patients with allergic rhinitis had laryngeal pathology, so they had difficulty in prolonging the sound /z/, although the mean s/z ratio was within the normal limits.[56]

Nasal pathology in allergic rhinitis patients

Physical examination in patients with allergic rhinitis may be either normal or with nonspecific findings, such as edema, erythema, or thick mucus labeled as functional dysphonia.[56]

Koç et al compared stroboscopic views of subjects in an allergic rhinitis group and those in a control group. Several parameters were assessed, such as closure level, vocal fold edges, supraglottic involvement, amplitude, mucosal wave, nonvibrating portion, and closure phase. The differences he observed were not significant.[34]

Kosztyła-Hojna et al evaluated voice pathology in patients with allergic rhinitis. Organic laryngeal pathology was found in 75% patients with coexisting allergic rhinitis in the form of Reinke edema, chronic hypertrophic laryngitis, laryngeal polyp, and vocal nodules. It caused serious voice disorder (dysphonia), which was confirmed by an objective spectrographic method. Overt organic laryngeal pathology was not recognized in 15% of the subjects. In these cases, rhinophonia was found as a consequence of nasal passage narrowing.[57]

Allergic rhinosinusitis and phonation

Sinusitis is almost always preceded by rhinitis and rarely occurs without concurrent rhinitis that is why the term rhinosinusitis tends to replace the term sinusitis. Rhinosinusitis is defined as an inflammation of the mucous membrane that lines the paranasal sinuses. Rhinosinusitis is a common condition in everyday practice. It affects between 10% and 30% of people each year in the United States and Europe.[58,59] Sinusitis can be of allergic or infectious origin and can be classified in acute, subacute and chronic rhinosinusitis. Common signs and symptoms include thick nasal mucus, postnasal drip, stuffed nose, and facial pain. Other signs and symptoms may include fever, headaches, poor sense of smell, sore throat, and cough. The cough is often worse at night. Serious complications are rare.

There are no data focusing on the implication of allergic sinusitis on phonation, and all existing data refer to sinusitis in combination with allergic rhinitis.

Medical research has supported the close relationship between allergic rhinitis and sinusitis. In a retrospective study on sinus abnormalities in 1120 patients (from 2 to 87 years of age), thickening of the sinus mucosa was more commonly found in sinusitis patients during July, August, September, and December; months in which pollen, mold, and viral epidemics are prominent. Eosinophilic-type CRSwNP is generally considered a variant at high risk of recurrence after surgery and significant associations were found in the elderly group between CRSwNP recurrence and allergy, asthma, and acetyl salicylic acid intolerance.[60]

Congestion of the nasal membranes may even block the Eustachian tube, resulting in a feeling of blockage in the ear or fluid in the middle ear. Additionally, nasal airway congestion causes the individual to breathe through the mouth.

Oral allergy syndrome

A standardized definition of OAS does not exist so far, as many aspects of OAS remain unknown or poorly understood.[61]

OAS is a special contact allergy affecting the oral cavity (oral mucosa, lips, tongue) and throat subsequent to the consumption of specific amino acids in food usually fruits, nuts, and vegetables. OAS usually occurs in atopic individuals who usually suffer from rhinitis, bronchial asthma, or both. The prevalence of OAS is difficult to estimate and data in the literature significantly vary from 8% to 70%, since the crossed-reactivity patterns show geographical and climatic differences depending on the exposure to inhaled and ingested allergens.[62] Some studies have noted that OAS is more frequent in female population.[63]

OAS usually provokes minor local reactions but it can be the cause of serious systematic reactions, like food-induced anaphylaxis manifested as difficulty in breathing, appearance of a rash, or hypotension. Unlike simple food allergy, OAS requires prior sensitization to a cross-reacting inhalant allergen rather than direct sensitization to a specific food protein.[64]

Pathophysiology of OAS is complicated with a multitude complexity of cross-reactivities between IgE antibodies specific to pollen and antigen in food.

The allergic reaction in OAS normally occurs immediately as soon as the responsible food is in contact with the oral mucosa. The symptoms often start after a few minutes, maximum 1 hour, affecting almost exclusively the anatomical regions that enter in contact with the food, which is the oropharynx. OAS symptoms usually are localized in the oral cavity and can be manifested by itching and a burning sensation of the lips, mouth, ear, and throat or by the appearance of perioral erythema and generalized urticaria. Sometimes symptoms from surrounding to oral cavity organs (larynx, eyes, nose, ears, and skin) can accompany the oral symptoms. The patient may develop swelling of the lips, tongue, and uvula, occasionally a sense of suffocation, and rarely anaphylaxis. Symptoms usually last for a few minutes to half an hour.

In clinical practice, OAS may be difficult to be recognized leading usually to misdiagnosis and mistreatment plans.

Effect of oral allergy on voice

There are no data in the literature concerning the input of OAS in voice production. Generally, voice problems in OAS can be considered as secondary in importance compared to other more annoying and, sometimes, more serious symptoms like swelling of the lips, tongue, and uvula, a sense of suffocation, and rarely anaphylaxis. Voice can be affected in OAS either directly because of the laryngopharyngeal edema or indirectly in the cases that OAS is accompanied by allergic rhinitis manifested with nasal congestion or nasal discharge that changes the voice resonance. Swelling of the lips, tongue, and uvula can alter the articulation and also the voice resonance affecting the quality of voice. In more serious cases where systematic reactions occur, laryngeal involvement can lead to direct voice changes due to laryngeal edema.

Angioedema and phonation

Angioedema is the swelling of deep dermis, subcutaneous, or submucosal tissue due to vascular leakage. Acute episodes often involve the lips, eyes, and face; however, angioedema may affect other parts of body, including respiratory and gastrointestinal mucosa. Laryngeal swelling can be life-threatening.

Angioedema can be acute or chronic, and each episode may last a few hours to a few days. The frequency and severity of the clinical symptoms are highly variable from patient to patient and even from episode to episode in the same patient.[65]

Angioedema is a highly heterogeneous group of conditions and it can stand alone or in combination with urticaria. According to the new international work group recommendation angioedema without urticaria can be characterized either as acquired or as hereditary.[66] In the case that angioedema is associated with urticaria, the classification of urticaria is followed (ie, acute vs chronic or induced vs spontaneous).

Angioedema may affect many organs or systems. Swelling of the skin and urogenital area (eg, eyelids or lips, tongue, hands, feet, scrotum, etc) is common in peripheral angioedema and is often associated with local burning sensation and pain without pronounced itchiness or local erythema. In the case of coexisting urticaria, pronounced itching accompanies the erythema. Other symptoms include abdominal pain (sometimes can be the only presenting symptom), throat tightness, voice changes, and breathing trouble, which indicates airway involvement and which potentially can be life-threatening.

Effect of angioedema on voice

There are no data in the literature concerning the input of angioedema in voice production. Voice changes are not the dominant symptom in angioedema, but when present, mean involvement of the larynx requires special attention since laryngeal swelling can be life-threatening. The voice problems in the case of angioedema is of minor importance compared to other dominant symptoms like skin swelling, itchiness and burning erythema, or systemic anaphylaxis accompanied by dyspnea.

Findings from the larynx

Laryngoscopy is needed for direct visualization of the vocal folds, uvula, and tongue swelling, and to assess laryngeal or vocal cord involvement. Laryngeal swelling can be life-threatening.

CONCLUSIONS

Although voice problems seem to be a very common symptom in allergic diseases like allergic asthma, allergic laryngitis, allergic rhinosinusitis, OAS, and angioedema, many information regarding the mechanism/s that allergy affects voice production are lacking. Lack of information also exists concerning the voice-related epidemiology and pathology in allergic diseases. The role of allergy in voice production remains underinvestigated, and this is the main reason why many basic questions still remain unanswered. Further large-scale prospective investigations are needed to improve our understanding on epidemiology and pathology as well as on the mechanisms of voice problems in allergic diseases. This need is more obvious for OAS and angioedema, two very common diseases, for which information for their impact on phonation are lacking.

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