

ORIGINAL ARTICLE

Is dysphonia due to allergic laryngitis being misdiagnosed as laryngopharyngeal reflux?

PREMJIT S. RANDHAWA, SHAJI MANSURI & JOHN S. RUBIN

Department of Otolaryngology, Royal National Throat Nose and Ear Hospital, 330 Grays Inn Road, London, WC1X 8DA, UK

Abstract

Objectives. Voice problems affect up to 30% of the population at some time during their life, and in particular it affects those who use their voice professionally. Patients who commonly present with dysphonia are often found to have symptoms of both allergy and reflux. Clinical examination of the larynx often makes it difficult to differentiate between the main causative factors of dysphonia, as the clinical findings on nasendoscopy between reflux and allergy are similar. Laryngopharyngeal reflux (LPR), an entity of gastro-oesophageal reflux, is a common diagnosis made in the voice out-patient clinic. Few studies have been able to successfully correlate management of LPR and outcome of dysphonia. Allergy or more specifically allergic rhinitis is said to affect approximately 24% of the population, but few studies have investigated its role in dysphonia. **Design.** Prospective observational study. **Settings.** University teaching hospital otolaryngology department. **Participants.** Fifteen new patients with primary voice disorder were investigated for possible LPR and allergy from April 2007 to October 2007. All patients were tested using the validated reflux symptom index (RSI), reflux finding score (RFS) to diagnose LPR, and both skin prick tests (SPT) and nasal nitric oxide (NO) levels to diagnose the presence of allergy. **Main outcome measures.** Prevalence of symptoms of reflux and allergy in patients presenting with primary voice disorders, and also whether dysphonia thought to be caused by LPR could actually be due to allergy. **Results.** No positive correlation or statistical significance was found between reflux and allergy. From our sample 20% (three patients) were diagnosed with LPR and 67% (ten patients) with allergy. The three patients diagnosed with LPR also had concomitant allergy. **Conclusions.** In our patient cohort, three times as many patients demonstrated allergy compared with LPR. This has led us to question if some patients with allergic laryngitis are being misdiagnosed with LPR and thereby being over-treated with proton pump inhibitors (PPIs).

Key words: Allergic laryngitis, allergy, dysphonia, gastro-oesophageal reflux, laryngopharyngeal reflux

Introduction

Voice problems affect up to 30% of the population at some time during their life (1) and particularly affect those who use their voice professionally. If professional voice use is defined as use of the voice as a primary means of occupational communication (2), then approximately 25% of the work-force in Western Europe can be considered to fall within this group.

The production of voice requires the usage of the entire upper and lower airway (2). Voice is generated when air under pressure in the lower airway, the lungs, and the trachea is sent up to and through the vocal folds which are then set into action by

vibration thereby creating sound; this sound is then modified and damped by the mucous membranes and structures of the upper airway including the tongue, nose, and mouth.

The upper and lower airways are in many ways a continuum, each with the potential to be adversely acted upon both directly and indirectly by gastro-oesophageal reflux and by environmental and food allergens. The upper aerodigestive tract is particularly susceptible to both. This complex interrelationship between gastro-oesophageal, environmental and food allergy, and pulmonary disorders has become clearer in recent years (2).

Gastro-oesophageal reflux (GERD) and its laryngopharyngeal component (laryngopharyngeal reflux (LPR)) are common conditions. LPR differs from GERD in many ways, including its presentation. Heartburn and reflux, which are common symptoms in GERD, are not typically present in patients with LPR. Patients with LPR present with a variety of symptoms that include dysphonia, chronic throat clearing, excessive phlegm, globus pharyngeus, and throat discomfort. In a large series of ear, nose, and throat patients with LPR it was found that dysphonia (92%), not heartburn, was the most common symptom (3).

It has been stated that 50% of individuals with laryngeal and voice disorders suffer with LPR as the primary cause or as a significant aetiological co-factor (4). In our and others' clinical practices it is not uncommon for proton pump inhibitors (PPIs) to be prescribed and used for prolonged periods of time in patients with clinical symptoms and signs consistent with LPR.

The role of allergy/atopy in patients with dysphonia is now being explored in greater detail as this represents another group of disorders that can affect voice production. Allergic rhinitis is said to affect approximately 24% of the population across Europe (5). The associated inflammation or irritation of the pharynx and nasal mucosa affects voice production by increasing mucous production, nasal drainage, or congestion; and oedema of the respiratory mucosa will alter vocal tract resonance and inhibit phonation if excessive secretions reach the level of the vocal folds (6,7).

Clinical manifestations of LPR include arytenoid and interarytenoid oedema, Reinke's oedema, diffuse erythema, mucosal swelling without erythema, and granuloma of the vocal process of the arytenoids. The appearance of the larynx in allergy is not dissimilar to that seen in LPR (8).

As can be seen, a large amount of overlap may exist between symptoms and signs of LPR and allergy in the larynx, thus there is potential for one being mistaken for the other.

The effects of GERD and LPR on the larynx and the voice have been well documented (9,10). Research into the effects of allergy on the larynx and voice is less readily available. To date no study has examined the cross-effects of LPR and allergy on the larynx and voice.

This pilot study sets out to investigate the correlation between dysphonia, allergy, and LPR and to assess the possibility that dysphonia due to allergic laryngitis may be being misdiagnosed as laryngopharyngeal reflux, and thereby we may be over-treating for LPR.

Materials and methods

General

The study was conducted in the specialist voice clinic in our tertiary referral centre. Fifteen consecutive patients who were diagnosed with primary voice disorder or with a presenting complaint of a lump in the throat were recruited into the study. Exclusion criteria included patients under the age of 16, on medication for reflux or rhinitis, pregnancy, inability to give informed consent, inability to speak and understand the English language, or a central or peripheral neurological problem causing the voice or throat problem. Written consent was obtained from all patients.

Clinical assessment of reflux and allergy

All patients underwent routine clinical examination and standard evaluation for voice disorders and allergy at our institution. These included reflux finding score (RFS), reflux symptom index (RSI), skin prick test (SPT) and nitrous oxide (NO) measurements together with laryngeal examination with flexible nasendoscope. All patients were scoped by the primary investigator to exclude inter-observer bias. Clinical findings and appearance of the larynx were documented in the clinical notes, and the RFS data sheet was completed by the primary investigator.

Assessment of laryngopharyngeal reflux

Patients were given the validated reflux symptom index (RSI) (11,12), and the reflux finding score (RFS) (10) was filled in by the primary investigator. A diagnosis of LPR was made when both the RSI > 13 and the RFS > 10, based on the work done by Belafsky et al. (11,12).

Assessment of allergy

All patients underwent skin prick tests (SPT) to common allergens (house dust, dust mite, *aspergillus*, *cladosporium*, grass pollen, feathers, cat, silver birch, trees, and dog), which were subsequently graded based on Patterson's system for scoring skin tests (wheal diameter grade: 0: no reaction; 1+: <4 mm; 2+: 5–10 mm; 3+: 10–15 mm; 4+: >15 mm) (13). Patients subsequently underwent nitrous oxide measurement in the nose and upper airway to assess degree of airway inflammation (14).

Ethical considerations

No ethical approval was sought as all patients were subjected to routine investigation and examination in

our voice clinic. However, written consent was obtained to ensure that all patients were aware that the results from their investigation were to be used in a study.

Results

General

There was no variation in the sex of the patients in our study (male = 7; female = 8), with the mean age at presentation of 28.5 ± 10 years ($\pm$ SD). For the purpose of this study, LPR was defined as a positive score in both RSI and RFS (RSI > 13; RFS > 10). Allergy, on the other hand, was diagnosed when a positive result was obtained from both SPT and NO measurements. Table I gives a break-down of the number of positive results for each individual test.

Correlation between LPR and allergy

Altogether, ten (67%) patients were diagnosed with allergy based on the above criteria, and only three (20%) diagnosed with LPR. The three patients diagnosed with LPR also had a positive allergy finding. There were five patients with no positive finding of allergy or LPR. In the patients with allergy, seven of the ten patients exhibited a positive and significant reaction (4+ Petterson grade) to grass pollen. Table II gives a break-down of the findings of the SPT and Table III a break-down of the NO findings.

Discussion

Synopsis of findings

In this study, we audited allergy and reflux findings in a population of patients presenting with voice disorders. Due to the population size ($n=15$), no overarching conclusions can be drawn from the study.

However, a number of observations can be made. A large percentage of our population (67%), or three times as many patients, had positive findings for allergy compared to LPR, which does raise the question of over-diagnosis of LPR in patients

Table II. Skin prick test findings.

Allergen	Patterson grading				
	0	1+	2+	3+	4+
House dust	7	7	1	–	–
Dust mite	6	3	3	1	2
Cladosporium	14	1	–	–	–
Aspergillus	13	2	–	–	–
Grass pollen	5	1	1	1	7
Feathers	14	1	–	–	–
Cat	8	3	3	–	1
Silver birch	9	2	1	2	1
Trees	9	2	1	2	1
Dog	11	4	–	–	–

n = number of patients.

with dysphonia. Also, all patients diagnosed with LPR had positive allergy findings, which raises the question of the specificity of the reflux test, i.e. RFS. Whilst we used skin prick tests and elevation of nitric oxide as evidence of allergy in individual subjects, we recognize that allergy challenges were not specifically performed. That notwithstanding, we feel that the accordance of these two features does allow us to state that these subjects were positive for allergy.

The key issue from the standpoint of auditing our practice is that many patients are placed on PPIs due to clinical findings on laryngoscopy, and these may prove not to be reflux-related.

Clinical applicability of the study

The larynx lies at the junction of the upper and lower airway, immediately anterior and superior to the introitus of the oesophagus. Its chief role is to protect the lower airway from food and secretions. Intuitively its very location is likely to cause it to be at risk from the effects of both LPR and allergy. LPR has been shown to significantly and negatively influence patients' quality of life (15). The severity of voice problems on the voice handicap index (VHI) was found to be similar to that caused by vocal fold polyps (11).

Table I. Break-down of investigation results.

Investigation	Number of patients
Reflux finding score (RFS)	3
Reflux symptom index (RSI)	10
RFS and RSS	3
Skin prick test (SPT)	11
Nitrous oxide level (NO)	12
SPT and NO	10

Table III. Nitrous oxide measurements.

Measurement (parts per billion)	Right nostril (No. Patients)	Left nostril (No. Patients)
<100 ^a	–	–
100–400 ^b	–	–
400–900 ^c	3	3
>900 ^d	12	12

^a<100 = very low (primary ciliary dyskinesia).

^b100–400 = low (blockage/polyps/cystic fibrosis).

^c400–900 = normal.

^d>900 = high (inflammation).

Allergies are well known to impact upon the upper and lower airways, and the 'unified airway model' has been developed which considers the entire respiratory system, from the nose through the larynx and trachea to the distal bronchioles, as a single unit. (16). It has been argued that local and systemic influences can stimulate reactions throughout this system, with the patient becoming increasingly symptomatic as the severity of the airway disease worsens (17).

Comparisons with other studies

A number of prospective well designed studies have demonstrated contradicting findings in relation to the benefit of proton pump inhibitors (PPIs) for LPR (18,19). One speculation raised by a study is whether some of the patients labelled with reflux in fact had allergic laryngitis, thereby blunting the effects of a PPI.

Strengths of the study

This study adds further to the evidence in a clinically relevant debate that has yet to be fully resolved. Only new patients with primary voice disorders or a lump in the throat who were not on medication for reflux or rhinitis were included. Potentially confounding factors, like pregnancy and patients with central or peripheral neurological problem causing the voice or throat problem, were excluded. No study has previously used all four clinical investigations, i.e. RFS, RSI, SPT, and NO, to assess reflux and allergy in a group of patients.

Limitations of study

Limitations of this study are the size of the population and that no test was carried out for the possibility of food allergies although this may well contribute to voice symptoms. We recognize that the number of patients in this study is small thereby limiting any generalization of conclusions from this study. We do plan on the basis of our findings to undertake a larger study.

Conclusions

This study investigates subjects with primary voice disorders and the correlation between allergy and LPR. The results suggest that three times as many patients demonstrated allergy compared with LPR. This has led us to question if some patients with allergic laryngitis are being misdiagnosed with LPR and thereby being over-treated with proton pump inhibitors (PPIs). The clinical applicability would be massive, as it would lead to a change in the trend of current practice. The authors accept, however, that the study sample is small, and a large study

comparing allergy and reflux and specifically testing for similarities and deficiencies of allergy findings and the RFS and RSI would be of considerable benefit.

Acknowledgements

This paper was presented at The Voice Foundation's 36th Annual Symposium: Care of the Professional Voice (Philadelphia, USA, 1 June 2008), and Choice for Voice (London; 10–12 July 2008).

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Roy N, Merrill RM, Thibeault S, Parsa RA, Gray SD, Smith EM. Prevalence of voice disorders in teachers and the general population. *J Speech Lang Hear Res.* 2004;47:281–93.
2. Rubin JS, Korovin G, Epstein R. Special considerations for the professional voice user. In: Rubin JS, Sataloff RT, Korovin GK, editors. *Diagnosis and treatment of voice disorders*, 3rd ed. San Diego, CA: Plural Publishers; 2006. p. 637–50.
3. Koufman JA, Wright SC. Laryngopharyngeal reflux and voice disorders. In: Rubin JS, Sataloff RT, Korovin GK, editors. *Diagnosis and treatment of voice disorders*, 3rd ed. San Diego CA: Plural Publishers; 2006. p. 419–30.
4. Koufman JA, Amin MR, Panetti M. Prevalence of reflux in 113 consecutive patients with laryngeal and voice disorders. *Otolaryngol Head Neck Surg.* 2000; 123:385–8.
5. Summary Report. Results of the patient voice allergy survey: Impact if allergic rhinitis in Europe. Available from: <http://www.efanet.org/> [Accessed July 2007].
6. Pennover D, Shefer A. Immunologic disorders of the larynx. In: Fried M, editor. *The larynx: a multidisciplinary approach*. Boston, Mass: Little, Brown and Company; 1988. p. 279–90.
7. Jackson-Menalow C, Dzul AI, Holland R. Allergies and vocal fold oedema: preliminary report. *J Voice.* 1999; 12:113–22.
8. Sala E, Hytonen M, Tupasela O, Estlander T. Occupational laryngitis with immediate allergic or immediate specific chemical hypersensitivity. *Clin Otolaryngol.* 1996; 21:42–8.
9. Farrokhi F, Vaezi MF. Laryngeal disorders in patients with gastroesophageal reflux disease. *Minerva Gastroenterol Dietol.* 2007;53:181–7.
10. Sereg-Bahar M, Jansa R, Hocevar-Boltezar I. Voice disorders and gastroesophageal reflux. *Logoped Phoniater Vocol.* 2005;30:120–4.
11. Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). *Laryngoscope.* 2001;111:1313–7.
12. Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). *J Voice.* 2002;16:274–7.
13. Tripathi A, Patterson R. Clinical interpretation of skin test results. *Immunol Allergy Clin North Am.* 2001; 21:291–300.
14. Scadding G. Nitric oxide in the airways. *Curr Opin Otolaryngol Head Neck Surg.* 2007;15:258–63.

15. Siupsinkiene N, Adamonis K, Toohill RJ. Quality of life in laryngopharyngeal reflux patients. *Laryngoscope*. 2007;117:480–4.
16. Krouse JH, Brown RW, Fineman SM, Han JK, Heller AJ, Joe S, et al. Asthma and the unified airway. *Otolaryngol Head Neck Surg*. 2007;136:S75–106.
17. Passalacqua G, Ciprandi G, Canonica GW. United airways diseases: therapeutic aspects. *Thorax*. 2000; 55:S26–7.
18. Reichel O, Keller J, Rasp G, Hagedorn H, Berghaus A. Efficacy of once-daily esomeprazole treatment in patients with laryngopharyngeal reflux evaluated by 24-hour pH monitoring. *Otolaryngol Head Neck Surg*. 2007;136:205–10.
19. Amin MR, Postma GN, Johnson P, Digges N, Koufman JA. Proton pump inhibitor resistance in the treatment of laryngopharyngeal reflux. *Otolaryngol Head Neck Surg*. 2001;125:374–8.