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THE EFFECT OF LARYNGOPHARYNGEAL REFLUX ON ACOUSTIC PARAMETERS IN FUNCTIONAL DYSPHONIA PATIENTS

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Abstract

Laryngopharyngeal reflux (LPR) is a very common disorder and it's objective effects over voice are controversial. In this study, to find out objective measures, the effects of LPR on acoustic parameters in functional dysphonia (FD) patients was investigated.

129 patients, aged between 14 and 88 years of which 71 were females and 58 were males. 81 patients had functional dysphonia (mean age 46), and 48 patients (mean age 51) had functional dysphonia as well as LPR. All data were obtained at the time of the initial examination. The laryngeal changes related with LPR were evaluated according to the Reflux Finding Score. Furthermore, acoustic analysis [Jitter, shimmer, Disphonia Severity Index (DSH), Noise to Harmonics ratio (NHR) and (F0)], auditive analysis [Roughness, breathiness, and hoarseness], voice range profile and voice intensity were selected as parameters for investigation in this study.
Firstly, results show that the impact of LPR is significantly lower for male patients than for female patients. Secondly, maxdB was significantly higher for LPR patients. It decreases significantly with age for non-LPR patients and this decrease with age is even stronger for LPR patients. The percentage of jitter and schimmer increased significantly with age. Furthermore, DSH is significantly lower for males than it is for females. For all other dependent variables, age, LPR, and gender did not play a significantly role. Thus, for FD patients with LPR condition, we highly recommend that LPR treatment should be part of the treatment plan.

Introduction

Functional dysphonia is characterised by an abnormal quality of voice in the absence of an identifiable lesion. In cases where neither an anatomic nor an organic cause can be found to be the cause of dysphonia, it is considered to be a functional voice disorder . In recent years, many otolaryngologists have acknowledged the existence and potential importance of LPR in patients with otolaryngologic complaints, although the association between acid reflux and laryngeal abnormalities has been recognized for more than four decades. The most recent evidence indicates that LPR represents a complex spectrum of abnormalities, and it is important for physicians to understand the latest concepts in the relevant basic science and clinical care of patients with LPR. Symptoms and signs related to reflux have been identified in 4% to 10% of all patients seen by otolaryngologists, and it is probable that these estimates are low. Among patients with laryngeal and voice disorders, LPR appears to be associated strongly with, or be a significant etiologic cofactor in, about half of these patients. (1)

Hoarseness is an impairment of the voice, in which the basic sound produced by the glottis has more the character of a rustle or murmur than a tone. (2) Functional voice disorders account for at least 10% of the cases of dysphonia referred to multidisciplinary voice clinics (3). Many factors may contribute to the development of a functional voice disorders one of which may be laryngopharyngeal reflux (LPR). LPR is the backflow of stomach contents above the upper esophageal sphincter, into the pharynx, larynx, and upper aerodigestive system (4). So, the most common signs of LPR are posterior laryngeal edema and erythema, obliteration of the laryngeal ventricles, and interarytenoid hypertrophy. In up to 92% of cases, the most common organic symptoms of LPR are roughness/hoarseness (5) but LPR is also associated with the development of functional voice disorders like muscle tension dysphonia (6).

Proton pomp inhibitors (PPI)' s are universally accepted medications in the treatment of LPR(7,8). Our hypothesis is that that functional dysphonia with LPR may change/worsen some acoustic parameters of voice compared patients with functional dysphonia without LPR (9) .

Material and method

129 patients, aged between 14 and 88, 71 females and 58 males, are included to this study. 81 patients with functional dysphonia (mean age was 46), and 48 patients (mean age wa 51) with functional dysphonia and also LPR. We think that the diagnosis of "functional"/nonorganic dysphonia" is best using a stroboscope. The diagnosis of functional dysphonia and also LPR was established by videolaryngoscopy or stroboscopy using a 90º rigid scope. All data were obtained before any kind of therapy, at the time of the initial examination.
RSI and the RFS are generally accepted scales for the diagnosis of LPR. There are numerous papers in the literature using RSI and RFS as a diagnostic tool (10) .

In this study the laryngeal changes related with LPR were evaluated according to Reflux Finding Score (11). Patient consent was obtained for this study. This study was performed according to the principles of WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects.

Acoustic analysis

Jitter, shimmer, DSH and NHR were analyzed on a sustained (a:) using the Multi Dimensional Voice Program (MDVP) with the Computerized Speech Lab CSL 4400 (Kay Elemetrics Ltd., Lincoln Park, NJ, USA). F0 was registered by having the patients count from 20 to 40 (12).

Auditive analysis

Roughness, breathiness, and hoarseness were estimated by the attending physician with the patients reading a passage from the text as recommended by Nawka et al. (13). These parameters are estimated as 0 = normal or absent deviance, 1 = slight deviance, 2 = moderate deviance, 3 = severe deviance.
These examinations were performed as recommended by the Union of European Phoniatricians (UEP) (14).

Statistical analysis

The following multiple general least squares model is developed to assess the effect of LPR on various outcomes such as R, B, H, mpt, F0, mindB, maxdB, %jitter, %schimmer, DSH and NHR. . In particular, the model is designed so that it allows how the effect of LPR varies with the gender and age of the patients:

$$Y = \alpha + \beta_1 LPR + \beta_2 Age + \beta_3 Male + \delta_1 LPR.Age + \delta_2 LPR.Male$$

Where Y is the vector of dependent variables that include R, B, H, mpt, F0, mindB, maxdB, %jitter, %schimmer, DSH and NHR. LPR is a dummy variable that assumes the value of 1 if the patient is diagnosed with LPR. Age is the age of the patient. Male dummy variable takes the value 1 for male patients, and 0 for female patients. The following two variables are interaction variables to capture the interaction of LPR with Age and Male variables, respectively.

Given the structure of the model, the coefficient of LPR will capture the impact of LPR for female patients, and the coefficient of the interaction variable LPR.Male will capture how the the impact of LPR is different for males relative to female patients. The coefficient of Age shows how the dependent variable values change as the age of the patient increases by 1, and the coefficient of Male variable shows how the dependent variable values vary for male patients in comparison to females. Lastly, the interaction variable, LPR. Age captures if the impact of age is different for LPR patients. Also paired samples t test is used for the statistical analysis.

Results

The results of the regressions are given in table 1. The regression results suggest the following:

1. F0 is significantly lower for males.
2. mindB is higher for males. It also increases with age significantly. The impact of LPR is significantly lower for male patients than for female patients.
3. maxdB is significantly higher for LPR patients, but it it decreases significantly with age for non-LPR patients and this decrease with age is even stronger for LPR patients.
4. The percentage of jitter increases significantly with age.
5. %schimmer increases significantly with age.
6. DSH is significantly lower for males.

Last but not least, for all other dependent variables, age, LPR, and gender did not play a significant role.

Discussion

Laryngeal abnormalities in LPR may be caused by direct injury or by a secondary mechanism. Direct injury is due to contact of acid and pepsin with laryngeal mucosa, resulting in mucosal damage. Alternatively, irritation of the distal esophagus by acid may cause a reflex mediated by the vagus nerve, resulting in chronic cough and throat clearing, which may produce traumatic injury to the laryngeal mucosa.(1) Common symptoms and signs of reflux laryngitis include morning hoarseness, prolonged voice warm-up time (greater than 20 to 30 minutes), halitosis, excessive phlegm, frequent throat clearing, xerostomia, coated tongue, globus sensation, throat tickle, dysphagia, regurgitation of gastric contents, chronic sore throat, possibly geographic tongue, nocturnal cough, chronic or recurrent cough, difficulty breathing; especially at night, aspiration, occasionally pneumonia, laryngospasm, poorly controlled asthma, recurrent airway problems in infants, and occasionally dyspepsia or pyrosis. LPR has also been associated with sudden infant death syndrome. Traditionally, the diagnosis of LPR was missed because symptoms associated classically with GERD such as dyspepsia and pyrosis are frequently absent because patients with LPR either do not develop esophagitis, or do not respond to acid reflux with typical symptoms such as heartburn. (1) Mostly, LPR patients often suffer from dysphonia.

Jitter is a measure of cycle to cycle variability in the period of acoustic signal and detects irregularity of frequency of cycles in the acoustic signal. Shimmer is a measure of cycle to cycle variation in the amplitude of the acoustic signal and is a measure of how much intensity of phonation is perturbed from cycle to cycle (15) . Jitter and shimmer are referred to as perturbation measures (16). They measure short term irregularities in the acoustic signal and are considered to reflect instability of vocal cord vibration. The perceptual correlate of increased levels of jitter and shimmer is harshness (16).

LPR incidence in patients with chronic hoarseness is significantly higher than the LPR incidence in healthy individuals (17,18) . LPR had a large, negative influence on the patients voice quality (19). LPR should not be overlooked in the treatment of dysphonic patients (18,19).

The prevalance of reflux in patients with voice disorders may be as high as 50% (20) . Progressively impaired voice quality may be the primary complaint of posterior irritative laryngitis without soreness or other symptoms (15) . Generally as accepted, the voice can be assested objectively with a software such as using the Multi Dimensional Voice Program (MDVP) or subjectivelly using the RBH scale.(12,13) There are studies demonstrating deteriorated voice quality and restricted phonation capabilities in the LPR patients (4,13,18,21).

Oguz et al. reported in their study that the frequency perturbation measures eg. jitter and shimmer were higher in LPR patients (4).

Voice and voice quality are part of a person's identity and our judgements of others may be influenced by these characteristics. Thus vocal problems can precipitate negative psychological, emotional and social consequences for affected individuals (22) . The greatest impact of LPR is likely to be in the area of social functioning, although emotional and psychological well being and role performance might also be significantly affected. Four key symptom complaints were identified that affected LPR patients: voice problem, chronic cough, throat clearing, and swallowing difficulties, primarily in the context of social and occupational environments. LPR symptoms appear to lead to substantial psychological, e motional and social problems (22).

Cesari et al. led to the hypothesis of a possible correlation between duration of the reflux and dysfunction of the arytenoid muscles, upon which chronic vocal fatigue, with consequent laryngeal compensatory stress, depends (23) . Belafsky et al. reported similar findings supporting this hypothesis. They stated that MTD may be an indication of underlying glottal insufficiency. In the face of an organic voice disorder hyperkinetic laryngeal behaviors may be used to achieve glottal closure. Such compensatory laryngeal behaviors may mask the correct underlying diagnosis. Abnormal MTPs are common in persons with underlying glottal insufficiency. Clinicians should be aware that compensatory hyperkinetic laryngeal behaviors may mask an underlying organic condition (24).

Intrinsic laryngeal muscle investigations, especially those of the interarytenoid (IA) muscle, have determined IA muscle anatomy and histochemical and immunohistochemical classification of extrafusal and intrafusal (muscle spindle) fibers. Extrafusal fibers were oxidative type I and glycolytic types IIA and IIX. Intrafusal fibers of muscle spindles were identified by the presence of tonic and neonatal myosin. The results demonstrate that the IA muscle has a phenotype similar to that of limb skeletal muscle. Myosin coexpression, the absence of intrafusal fibers, and fiber type grouping were unusual features found previously in the thyroarytenoid and posterior cricoarytenoid muscles, but they were not present in the IA muscle. These findings lead to the conclusion that the IA muscle has functional significance beyond its assumed importance in maintaining vocal fold position during phonation. The presence of spindles demonstrates differences in motor control as compared to the thyroarytenoid and posterior cricoarytenoid muscles. Further, extrafusal fiber characteristics implicate IA muscle involvement in muscle tension dysphonia and adductor spasmodic dysphonia (25).

Willems-Bloemer et al. reported in their article that patients with LPR related dysphonia showed a significant improvement in their subjective score on dysphonia with the treatment of PPI, lansoprazole 30 mg once daily for 6 weeks (26) .

Often patients with FD are also highly likely to suffer from LPR. It is well-known that LPR seriously affects voice quality in patients. LPR's effects on voice quality is for the most part caused by posterior laryngitis developed in relation to LPR and by disruptions of mucosal wave consequently. Additionally, LPR may lead to malfunctioning interaritenoid muscles and gaps may develop in this region. Consequently, compensatory muscle spasms will deteriorate laryngeal dynamics and it will lead to further reductions in voice quality.

We believe that in cases of FD with LPR, reductions in voice quality will be felt more strongly. In our study, we found that in FD patients with LPR, jitter and shimmer values are higher, stating that dysphonia in such patients will be more remarkable. Thus, for FD patients with LPR, we highly recommend that fixing this should be part of the treatment plans.

Conclusion

For FD patients with LPR condition, we highly recommend that LPR treatment should be part of the treatment plan.

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Variable	Intercept	LPR	Male	Age	LPR*Male	LPR*Age
R	0.839	-0.187	0.036	0.005	0.182	0.001
(3.82)	(-0.43)	(0.23)	(1.21) (0.72)		(0.13)	
B	1.011	-0.262	-0.086	0.0001	-0.003	0.005
(4.81)	(-0.64)	(-0.58)	(0.14) (-0.012)(0.63)			
H	1.094	-0.262	-0.111	0.005	0.154	0.003
(5.37)	(-0.66)	(-0.77)	(1.15) (0.66)		(0.36)	
mpt	15.05	-0.948	0.869	-0.023	-0.66	0.018
(10.6)	(-0.34)	(0.086)	(-0.80) (-0.41)		(0.32)	
F0	219.5	12.00	-77.26**	-0.195	6.817	-0.339
(16.6)	(0.46)	(-8.24)	(-0.73) (0.45)		(-0.65)	
mindB	49.76	2.174	3.421**0.084**-2.865**		-0.055	
(40.4)	(0.90)	(3.92)	(3.38) (-2.03)		(-1.13)	
maxdB 0.180*	97.84	9.147*	-2.560		-0.124**3.233	-
(35.6)	(1.70)	(-1.31)	(-2.25) (1.03)		(-1.67)	
%jitter	0.579	-0.564	-0.294	0.018*	0.171	0.008
(1.37)	(-0.68)	(-0.98)	(2.08) (0.35)		(0.47)	
%schimmer	2.100	-0.788	0.942	0.053**-0.161		0.014
(2.19)	(-0.42)	(1.39)	(2.75) (-0.15)		(0.36)	
DSH	0.593	-2.028	-1.669* 0.040	0.227	0.029	
(0.43)	(-0.74)	(-1.69)	(1.42) (0.14)		(0.52)	
NHR	0.114	-0.061	0.007	0.001	0.041	0.001
(3.31)	(-0.90)	(0.27)	(0.99) (1.02)		(1.00)	

Legends:

Table 1: The results of the regressions. The numbers in parentheses are t statistics. *, ** denote coefficients that are significant at 90%, and 95% confidence levels, respectively.