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Association of Laryngopharyngeal Reflux and Gastroesophageal Reflux Disease

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Abstract

Background /Aims: Laryngo Pharyngeal Reflux (LPR) is the back flow of gastric contents to the laryngopharynx and upper aerodigestive tract, resulting in a constellation of laryngeal symptoms and signs. This project aimed to investigate the prevalence of Gastro Esophageal Reflux Disease (GERD) in patients with LPR and to analyze its associated factors.
Methodology: The patients with LPR were collected at our out-patient department consecutively from March 2011 to April 2013. These patients had a history of at least 2 months of one or more of the following symptoms; hoarseness, sore or burning throat, excessive throat-clearing, chronic cough, globus sensation, dysphagia. A common self-administered questionnaire, the Reflux Symptom Index was used during the interview for symptom assessment. The Los Angeles classification was used for the evaluation and diagnosis of GERD on endoscopy.
Results: Total 35 patients with LPR were enrolled in our study. Fourteen patients (40.00 %) had GERD by endoscopy. The infection rates of *Helicobacter pylori* were 16.67 % (2/12) and 17.65 % (3/17) in GERD and non-GERD patients, respectively. The body mass index (BMI) of LPR patients with GERD was significantly higher than the LPR patients without ($p = 0.015$). The other variables including age ($p = 0.105$), gender ($p = 0.778$), presence of ulcer ($p = 0.279$) or HP ($p = 0.948$) were not significantly different between the two groups of patients. In multivariate logistic regression analysis, BMI was still an independent correlate of GERD in LPR patients. (Odds ratio = 1.411; $p = 0.030$).
Conclusions: GERD is present in 40 % of LPR patients and the GERD patients have higher BMI than non-GERD.

Keywords: Laryngopharyngeal reflux; Gastroesophageal reflux disease; Body mass index

Abbreviations: Laryngopharyngeal reflux (LPR); Gastroesophageal reflux disease (GERD); Body mass index (BMI); Upper gastro intestinal (UGI)

Introduction

The term of Laryngo Pharyngeal Reflux (LPR) was adopted by the American Academy of Otolaryngology-Head and Neck Surgery in the 2002 Position Statement[1]. It refers to the retrograde flow of gastric contents to the laryngopharynx and upper aerodigestive tract, resulting in a constellation of respiratory and digestive symptoms[2]. It may lead to many laryngeal and esophageal diseases such as reflux laryngitis, laryngeal granuloma, laryngeal carcinoma, subglottic stenosis and esophageal adenocarcinoma[3,4]. The diagnosis and treatment of LPR remain controversial in the absence of reliable and solid evidence from high quality randomized controlled studies. Diagnosis of LPR is currently based on the combination of symptoms, 24-hour PH monitoring, laryngoscopic findings and the efficacy of empirical twice-daily PPI therapy[4]. The symptoms and signs of LPR are usually none-specific, such as hoarseness, dysphonia, sore or burning throat, excess throat-clearing, chronic cough, globus pharyngeus, dysphagia, postnasal drip and laryngospasm[5]. Based on ambulatory, 24-hour, double-probe pH monitoring, Belafsky developed a self-administered scoring system to analyze patient perception of possible LPR[6]. This Reflux Symptom Index (RSI) includes nine symptoms suggestive of LPR, scored from 0 to 5, with a maximum score of 45 (Table 1). The authors recommended that an RSI of 13 or greater than 13 was indicative of LPR.

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Table 1: The Reflux Symptom Index.

Within the last month, how did the following problems affect you?	0 = No problem, 5 = Severe					
1. Hoarseness or a problem with your voice	0	1	2	3	4	5
2. Clearing your throat	0	1	2	3	4	5
3. Excess throat mucus or postnasal drip	0	1	2	3	4	5
4. Difficulty swallowing food, liquids, or pills	0	1	2	3	4	5
5. Coughing after you ate or after lying down	0	1	2	3	4	5
6. Breathing difficulties or choking episode	0	1	2	3	4	5
7. Troublesome or annoying cough	0	1	2	3	4	5
8. Sensations of something sticking or a lump in your throat	0	1	2	3	4	5
9. Heartburn, chest pain, indigestion, or stomach acid coming up	0	1	2	3	4	5

The exact mechanisms of LPR have not been conclusively validated. The symptoms of LPR are induced by the direct effect of gastric refluxate, including gastric acid pepsin and bile salts, on the upper aerodigestive tract. Direct exposure from gastric contents can result in local inflammatory reactions of laryngeal mucosa[2]. Two studies have shown that pepsin in the larynx can cause depletion of two laryngeal protective proteins, including squamous epithelial stress protein and carbonic anhydrase isoenzyme[7,8]. This depletion may predispose larynx and vocal cords to reflux-induced inflammatory injury.

Gastro Esophageal Reflux Disease (GERD) is a condition induced by reflux of gastric contents into esophagus causing troublesome symptoms as heartburn and acid regurgitation[9]. The entities of GERD and LPR are not exactly the same. The aim of our study was to investigate the prevalence of GERD in patients with LPR. In addition, we analyzed the independent predictor of GERD in LPR.

Methodology

Patients

Between March 2011 and April 2013, 35 LPR patients were recruited consecutively from the out-patient department of Gastroenterology by two gastroenterologists in Taipei City Hospital, Ren-Ai Branch. These patients had a history of at least 2 months of one or more of the following symptoms; hoarseness, sore or burning throat, excessive throat-clearing, chronic cough, globus sensation, dysphagia. Other apparent causes of their symptoms had been ruled out (i.e., tumor, allergy, and upper respiratory tract infection, pulmonary, cardiovascular, and neurological disease). Exclusion criteria were as follows: an age of < 18 year-old, pregnancy, malignancy, previous surgical resection on the Upper Gastro Intestinal (UGI) tract. Patients who ever had smoking were not included in the study. Alcohol intake was rare in all patients. The patients were not receiving any medical treatment for these symptoms at the time of presentation. Informed consent was obtained from all participating patients. At the entry to the study a symptom questionnaire and complete medical history for all subjects were completed. A common self-administered questionnaire, the RSI developed by Belafsky et al [6], was used during the interview for symptom assessment. It is a nine-item questionnaire, each having a scale ranging from 0 (no problem) to 5 (severe), with a maximum score of 45 in total (Table 1). A patient with a total RSI score of 13 or greater than 13 was included in the study.

Endoscopy

Endoscopy of UGI tract was performed for all LPR patients as a diagnostic tool of GERD. The Los Angeles classification was used for the evaluation of endoscopic findings and the diagnosis of GERD[10,11]. The infection of *Helicobacter pylori* (*H. pylori*) was detected by either rapid urease test or biopsy.

Statistical Analysis

Data were summarized as mean ± SD. Data were compared between groups on the basis of GERD. Categorical variables were compared with the chi-square test or Fisher's exact test as required. Continuous variables were compared between groups by using the unpaired t-test. The Mann-Whitney test was used when it was appropriate. The independent factors related to the GERD were assessed by using multivariate logistic regression analysis. The $p < 0.05$ was statistically significant.

Results

Thirty-five patients who fulfilled patient criteria were studied. The demographic data of the patients were summarized in Table 2. There were 14 males and 21 females. The mean age of the 35 patients was 52.11 ± 13.48 (25–80) year-old. The mean body mass index (BMI) was 21.78 ± 2.82 (16.82–29.74) kg/m^2. Fourteen patients (40.00 %) had GERD by endoscopy. In the fourteen patients, nine patients were grade A and five patients were grade B by Los Angeles classification. The prevalence of *H. pylori* was 17.24 % (5 / 29) in LPR patients. The infection rates of *H. pylori* were 16.67 % (2 / 12) and 17.65 % (3 / 17) in GERD and non-GERD patients, respectively.

Table 2: Demographic data of 35 patients with laryngopharyngeal reflux and univariate analysis of risk factors associated with gastroesophageal reflux disease

Variable	Total (n = 35)	GERD (n = 14)	No GERD (n = 21)	*P*
Age (yr)	52.11 ± 13.48	56.64 ± 16.50	49.10 ± 10.39	0.105
Gender (male : female)	14 : 21	6 : 8	8 : 13	0.778
BMI (kg/m^2)	21.78 ± 2.82	23.16 ± 3.21	20.86 ± 2.14	0.015
Ulcer (+/-)	4 : 31	3 : 11	1 : 20	0.279
H. pylori (+/-)	5 : 24	2 : 10	3 : 14	0.948

GERD: gastroesophageal reflux disease, BMI: body mass index, *H. pylori: helicobacter pylori*.
Data are expressed as n or mean ± SD.

The LPR patients with GERD had significant higher BMI than the LPR patients without GERD (23.16 ± 3.21 vs. 20.86 ± 2.14 kg/m^2; $p = 0.015$). The other variables including age ($p = 0.105$), gender ($p = 0.778$), presence of ulcer ($p = 0.279$) or *H. pylori* ($p = 0.948$) were not significantly different between the two groups of patients (Table 2). In multivariate logistic regression analysis,

BMI was still an independent predictor of GERD in LPR patient. (Odds ratio = 1.411; p = 0.030).

Table 3: Multivariate logistic regression analysis of association between risk factors and gastroesophageal reflux disease in patients with laryngopharyngeal reflux.

Variable	Odds Ratio	95% CI	p
Age	1.035	0.974–1.101	0.267
Male Gender	1.598	0.280–9.124	0.598
BMI	1.411	1.034–1.926	0.030

BMI: body mass index.

Discussion

The investigative modalities used to diagnose LPR include ambulatory pH probe monitoring, laryngoscopy, endoscopy and symptom scoring systems[5]. Use the same criteria of LPR, Park *et al.* reported about 30 % of LPR patients showed GERD by UGI endoscopy[12]. Tauber *et al.*[13] and Rouev *et al.*[14] both described GERD in 43 % and 54 % of patients with laryngopharyngeal symptoms also by UGI endoscopy, respectively. The prevalence of GERD is estimated to be 10–20 % of the Western world with a lower prevalence in Asia[15]. Our study showed the prevalence of GERD was 40 % in LPR patients. These findings implicated that LPR and GERD may share retrograde reflux as a major mechanism of pathogenesis. Therefore, the prevalence of GERD seems to be higher in LPR patients than general population.

Four randomized controlled trials were reviewed by Gatta *et al.* in 2007, which showed no significant difference between PPI therapy and placebo in improving laryngopharyngeal symptoms[16]. Lam *et al.* discovered that twelve weeks treatment of rabeprazole (20 mg, twice daily) significantly improve reflux symptoms, compared with placebo, in patients with LPR[17]. Another RCT revealed twice-daily PPI therapy for 8 and 16 weeks were effective in patients with postnasal drip[18]. Despite divergent results, LPR patients are recommended to receive a trial of twice-daily PPI therapy for at least 2 months[19]. If the patient responds to therapy, it would be prudent to taper the dose of PPI to once-daily and then to minimally effective dose[5]. In LPR patients who show no improvement, other causes of symptoms should be explored. These patients should also be advised to adopt lifestyle modification including avoidance of smoking, heavy meals, alcohol and late meals. There is a definite relationship between GERD and obesity in general population[20]. In our study, BMI was the only independent risk factor of GERD in LPR patients. Since high BMI is associated with the presence of GERD in LPR patients, every patient with high BMI should be advised to lose weight before receiving an UGI endoscopy. In other words, the result may be useful in helping to select the patients who may benefit from acid - suppressive therapy.

H. pylori infection rate in Taiwan from a randomly selected population was 54.4 % in 1993[21]. Our study showed the prevalence of *H. pylori* was only 17.24 % in LPR population. The low infection rate of *H. pylori* gives us a hint that *H. pylori* might decrease the laryngopharyngeal symptoms. However, Cekin *et al.* found no association between *H. pylori* and LPR status determined on the basis of RSI and reflux finding score, which was based on findings on endoscopic examination of the larynx[22]. Generally speaking, the relationship between *H. pylori* infection and GERD is controversial[20]. In our study, the infection rates of *H. pylori* were not significantly different between GERD and non-GERD patients in LPR population. Because the number of patients is limited in our study, further research for elucidating the correlation between *H. pylori* infection and LPR should be followed.

In conclusion, GERD is present in 40 % of LPR patients. The finding of GERD on UGI endoscopy is related to BMI but doesn't correlate with age, gender, presence of ulcer or *H. pylori* infection in LPR patients.

Conflicts of Interest

All contributing authors declare no conflicts of interest.

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