

Effects of a proton pump inhibitor on laryngeal irritation in patients with laryngopharyngeal reflux

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Abstract

Objective: To evaluate laryngeal irritation before and after treatment using the reflux symptom index (RSI) in patients diagnosed with laryngopharyngeal reflux (LFR).

Methods: A total of 30 patients who were diagnosed with LFR after 24 hours of dual-probe pH monitoring were included in the study. RSI was applied to the patients before and after treatment. In evaluating the patients' symptoms, throat clearing need and post-nasal drainage, which are frequently observed in LFR, were evaluated post-treatment. The patients were followed for 3 months during proton pump inhibitor treatment. Data regarding the patients' LFR symptoms were obtained after 3 months, and the responses to treatment based on reflux symptom scale scores, post-nasal drainage, and throat clearing need were evaluated and compared with those pre-treatment.

Results: The decrease in the RSI for postnasal drainage value was statistically significant after treatment. The decrease in the throat clearing RSI value was statistically significant after treatment.

Conclusion: In patients with persistent postnasal drainage and throat clearing need complaints, if no infection source is identified, the patients should be evaluated by 24-hour pH monitorization in terms of LFR, irrespective of the presence or absence of laryngoscopic findings.

Keywords: Laryngopharyngeal reflux, pH monitoring.

Özet: Proton pompa inhibitörlerinin larengofarengal reflü hastalarında larengal irritasyon üzerine etkisi

Amaç: Larengofarengal reflü (LFR) tanısı konmuş hastaların tedavi öncesi ve tedavi sonrası larengal irritasyon bulguları, reflü semptom indeksi (RSİ) kullanılarak değerlendirildi.

Yöntem: 24 saatlik çift problu pH monitörizasyonu sonucuna göre LFR tanısı alan 30 hasta çalışmaya dahil edildi. RSİ sorgulaması hastalara tedavi öncesi ve tedavi sonrası uygulandı. Hastalar 3 aylık proton pompa inhibitörü tedavisi sonrası geniz akıntısı ve boğaz temizleme ihtiyacı açısından reflü semptom indeksi kullanılarak tekrar değerlendirildi. Daha sonra geniz akıntısı ve boğaz temizleme ihtiyacı tedavi öncesi ve tedavi sonrası karşılaştırıldı.

Bulgular: Geniz akıntısında tedavi sonrası RSİ değerinde istatistiksel olarak anlamlı azalma saptandı. Boğaz temizleme ihtiyacında tedavi sonrası RSİ değerinde istatistiksel olarak anlamlı azalma saptandı.

Sonuç: Uzun süreden beri devam eden geniz akıntısı ve boğaz temizleme şikayeti olan hastalarda, herhangi bir enfeksiyon odağı saptanamıyorsa; hastalar LFR açısından laringoskopik bulgular olsun ya da olmasın 24 saatlik pH monitörizasyonu ile değerlendirilmelidir.

Anahtar sözcükler: Larengofarengal reflü, pH monitörizasyonu.

Gastroesophageal reflux (GER), the spontaneous and effortless regurgitation of stomach contents into the oesophagus, has one of the highest prevalence rates of all gastrointestinal system diseases.^[1] GER was first defined by Winkelstein in 1935 as "peptic esophagitis" in adults.^[2] By the end of the 19th century, it was reported that GER

might cause complications other than those involving the oesophagus.^[3] The transport of stomach contents (without bellowing and vomiting) to a point higher than the upper oesophageal sphincter is defined as extraoesophageal reflux, supra-extraoesophageal reflux, or laryngopharyngeal reflux (LFR).^[3]

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Laryngopharyngeal reflux is an atypical form of GER. LFR is associated with a large number of pulmonary, otorhinolaryngologic, and odontopathic diseases.^[3] Diseases associated with otorhinolaryngology include dysphagia, odynophagia, globus (lump in the throat), sore throat laryngitis, constant throat clearing need, post-nasal drainage, laryngeal contact ulcers, posterior glottic erythema-oedema, laryngeal granuloma, cancer of the larynx or pharynx, laryngospasm, sinusitis, stridor and vasomotor rhinitis.^[3-5]

While the associations of these diseases with LFR are strong, the causality is open for discussion based on epidemiological data. There are two theories regarding the role of GER in the pathogenesis of these diseases: microaspiration and irritation of the oesophageal reflex mechanism.^[3,6] The microaspiration theory is based on the histopathologic damage caused to laryngopharyngeal tissue by aspirated acid and pepsin. The oesophageal reflex theory is based on irritation of the vagus nerve. Due to their close relationship during embryologic development, both the respiratory tract and oesophagus are innervated by the vagus nerve. For this reason, excitement of the oesophagus may trigger laryngopharyngeal events such as bronchospasm, coughing, and chest pain.^[2,3]

A reflux symptom index (RSI) consisting of nine parameters was developed by Belafsky and Koufman to obtain information on the existence and progress of LFR symptoms and to facilitate pre- and post-treatment comparisons^[7] (Table 1). This index is widely used in the follow up of reflux symptoms.

For patients with post-nasal drainage and a feeling of foreign matter in the throat that persists despite treatment, LFR should be considered. In this study, we evaluated laryngeal irritation before and after treatment using the RSI in patients diagnosed with LFR using a 24 hours dual-probe pH monitoring, anamnesis, and examination.^[8]

Materials and Methods

Patients who admitted to Taksim Training and Research Hospital's Otorhinolaryngology Clinic between January and June 2013 were evaluated. Ethics committee approval was obtained for the study. Patients who had been diagnosed with LFR, had undergone laryngoscopic examinations, and had reflux symptom scores >13 were evaluated. Among the patients, 30 who were diagnosed with LFR after 24 hours of dual-probe pH monitoring were included in the study. A detailed otorhinolaryngological examination was performed on selected patients; no rhinosinusitis or allergic rhinitis, and no pathology in the nasal cavity or oropharynx were detected. The patients had undergone no treatment for allergic rhinitis or rhinosinusitis.

Our study evaluated the results of 30 patients who experienced at least one reflux attack at the proximal probe of the pH-meter and were treated.^[9] The youngest of these patients was 24 years of age and the oldest was 62.

All symptoms of LFR are based on subjective data; at present, no quantitative measurement method is available. For this reason, the disease is diagnosed according to the patient's treatment response. Therefore, our aim was to record reflux attacks in symptomatic patients after 24-

Table 1. Reflux symptom index.

Grade the effect on you of the problems below during the recent months, according to the scale on the right.	0: No effect whatsoever 5: Intense effect					
	0	1	2	3	4	5
1. Have you had any hoarseness or vocal problems?	0	1	2	3	4	5
2. Have you had extreme post-nasal drainage?	0	1	2	3	4	5
3. Do you need to clear your throat?	0	1	2	3	4	5
4. Do you have a sticking feeling in your throat?	0	1	2	3	4	5
5. Do you cough after meals or going to bed?	0	1	2	3	4	5
6. Do you ever feel that you cannot breathe and might suffocate?	0	1	2	3	4	5
7. Have you ever experienced chronic coughing or a coughing fit?	0	1	2	3	4	5
8. Do you have difficulty in swallowing solid or liquid food?	0	1	2	3	4	5
9. Do you ever feel burning or sticking in your chest and have brackish water come into your mouth?	0	1	2	3	4	5

hour pH monitoring and to evaluate their post-treatment symptoms.

To date, the most commonly used diagnostic test for LFR detection remains ambulatory 24-hour dual-probe pH monitoring.^[9] Smit et al., in 1998, described a relatively easy and reliable technique for the placement of the proximal probe.^[10] This method has been used in our study. The catheter was conveyed to the oesophagus together with a transnasal fibre-optic endoscope; at the point at which the sign in the proximal recorder was lost behind the arytenoids, the catheter was fixed to the patient's nose. Therefore, the proximal recorder remained just above the upper oesophageal sphincter. In the record obtained from the proximal channel, each instance of a decrease in pH to <5.0, in parallel with a pH drop in the distal channel, was accepted as an "LFR attack".^[11]

The reflux symptom scale was applied to the patients before and after treatment. In evaluating the patients' symptoms, throat clearing need and post-nasal drainage, which are frequently observed after hoarseness, were evaluated post-treatment. The patients were followed for 3 months during proton pump inhibitor (PPI) treatment. Data regarding the patients' LFR symptoms were obtained after 3 months, and the responses to treatment based on reflux symptom scale scores, post-nasal drainage, and throat clearing need were evaluated and compared with those pre-treatment.

Statistical analysis

The data obtained were analysed using the Statistical Package for the Social Sciences for Windows 21.0 (SPSS Inc., Chicago, IL, USA). Standard statistical methods (averages and standard deviations) were used to evaluate the data. A matched-group Wilcoxon test was implemented for the evaluation of repetitive groups. Pearson's correlation was implemented to analyse relationships between parameters. The findings were evaluated using 95% confidence intervals and a 5% significance level.

Results

A Wilcoxon test for matched groups indicated that the difference between the arithmetic average TC RSI value before

Table 2. Difference between throat clearing (TC) before and after RSI application.

Measurement	Before		After		N	Z	p
	Mean	SD	Mean	SD			
TC RSI	3.514	0.731	1.919	0.640	37	-5.461	0.000

Table 3. Difference in post-nasal drainage (PND) before and after treatment.

Measurement	Before		After		N	Z	p
	Mean	SD	Mean	SD			
PND RSI	3.541	0.767	1.838	0.688	37	-5.557	0.000

and after treatment was statistically significant ($Z=-5.461$; $p=0.000$). The average TC RSI value before treatment ($x=3.514$) was higher than the value after treatment ($x=1.919$).

A Wilcoxon test for matched groups indicated that the difference between the arithmetic average PND RSI value before and after treatment was statistically significant ($Z=-5.557$; $p=0.000$). The average PND RSI value before treatment ($x=3.541$) was higher than that after treatment ($x=1.838$) (Tables 2 and 3).

A statistically significant relationship was found between the before-treatment PND and TC RSI values ($r=0.657$; $p=0.000$). Therefore, the TC pre-treatment RSI value increased with increases in the pre-treatment PND RSI value (Table 4).

A statistically significant relationship was found between the TC post-treatment RSI value and the PND post-treatment RSI value ($r=0.677$; $p=0.000$). Therefore, the TC post-treatment RSI value decreased with decreases in the PND post-treatment RSI value (Table 5).

Discussion

Laryngopharyngeal reflux, an atypical clinical manifestation of GER, is the regurgitation of stomach contents

Table 4. Relationship between TC and PND before treatment.

	Average	Standard deviation	TC pre-treatment RSI value	PND pre-treatment RSI value
TC pre-treatment RSI value	3.514	0.731	1.000	
PND pre-treatment RSI value	3.541	0.767	0.657**	1.000

Table 5. Relationship between TC and PND post-treatment.

	Average	Standard deviation	TC pre-treatment RSI value	PND pre-treatment RSI value
TC post-treatment RSI value	1.919	0.640	1.000	
PND post-treatment RSI value	1.838	0.688	0.677**	1.000

through the upper oesophageal sphincter without any belching or vomiting. Contact between acid and pepsin in the stomach contents with the trachea, pharynx, and oral cavity mucosa can cause non-specific symptoms of irritation and mucosal lesions in the upper respiratory tract or digestive system.

Currently, the most important reason of increasing laryngopharyngeal reflux frequency is the understanding that previously known symptoms such as globus faringus, post-nasal drainage, chronic coughing and throat clearing need may be due to reflux. LFR may be diagnosed by means of a careful symptom query, a full otorhinolaryngological examination in which the larynx is analysed in detail, information from laboratory examinations for reflux determination and measurement, and responses to empirical reflux treatment.^[8]

The most sensitive and specific test for LFR is ambulatory 24-hour dual-probe pH monitoring.^[9] In evaluating the results of pH monitoring, the technical difficulties associated with such examinations and the fact that reflux may vary among individual patients should be taken into account. In patients with intermittent LFR, pH monitoring may not detect reflux if it does not manifest on the day of the evaluation.

Due to variation in reflux behaviour, an evaluation of the response to empirical treatment is a valid diagnostic method for LFR. Regarding medical treatment, acid suppression may be implemented through changes in lifestyle and the regulation of daily habits. For acid suppression therapy in patients with LFR, PPIs have a higher probability of success than H₂ receptor blockers; the treatment duration should be at least 3 months.^[12]

The terminology used for laryngeal lesions developing in connection with reflux includes non-standardised terms. Erythema and oedema on the arytenoids and posterior parts of the vocal folds were first termed “posterior laryngitis” or “acid laryngitis.” Terms such as “reflux laryngitis” and “peptic laryngitis” were also used to describe such an appearance. The term “laryngeal pachydermia” was used for mucosal thickening and interarytenoid granuloma due to mucosal epithelial proliferation,

parakeratosis, and dyskeratosis observed histopathologically; patients with this presentation should be regarded as possibly having reflux laryngitis.^[3-5] Irregular chronic non-specific laryngitis may develop secondary to reflux within the vocal fold epithelium; however, as this observation can also be encountered in vocal fold carcinoma, malignancy should be eliminated before a diagnosis of reflux laryngitis.^[13]

It should be noted that examinations of the larynx in patients with LFR could produce normal findings. In a study of 97 patients at Ankara University’s Medical Faculty using 24-hour pH monitoring, 48% of symptomatic patients with normal larynx examinations had LFR, and 39% of patients with LFR had normal larynx examination results.^[14]

For this reason, the existence of reflux symptoms is more important than the presence of findings. It is advisable to conduct 24-hour pH monitoring for symptomatic patients. Likewise, our study involved 30 patients with an RSI score of 13, in whom 24-hour pH monitoring was implemented and who experienced at least one reflux attack.^[9] During this procedure, the pH-meter base value was set to 5 because pepsin exhibits proteolytic activity even at this pH value.^[11]

A minimum of one reflux attack was identified in all symptomatic patients. RSI forms were completed by the patients, and treatment with two doses of pantoprazole (40 mg) for 3 months was started. Three months later, the RSI form was completed again to evaluate the treatment responses in terms of frequent throat clearing need and post-nasal drainage. In this study, other possible pathologies in patients with throat clearing need and post-nasal drainage complaints were eliminated, and these complaints were demonstrated to be associated with LFR. In addition, these complaints were reduced by PPI use.

It has been reported that secretion increases throat clearing need and post-nasal drainage, possibly as a neurologic or mucosal response to acid reflux contacting the respiratory mucosa.^[3,6] This situation may cause a misdiagnosis of allergic rhinitis in patients with no rhinological problem. For this reason, LFR symptoms and the pres-

ence of reflux should be investigated following the performance of detailed otorhinolaryngological and endoscopic examinations.

The possibility of reflux should be considered in all patients with post-nasal drainage and throat clearing need complaints lasting longer than 3 months with no findings of other possible pathologies. As acid accumulates in the laryngeal area, patients may clear throat, which produces an intense air stream and enables mucus discharge, to obtain relief. The mechanism underlying this symptom is post-nasal drainage.^[6]

Most patients who admit to polyclinics for medical attention for such complaints are undergoing asthma and allergic rhinitis treatment, and their symptoms do not decline. For this reason, patients presenting with such symptoms should be directed to an otorhinolaryngologist for a detailed examination. In patients with persistent postnasal drainage and throat clearing need complaints, if no infection source is identified, the patients should be evaluated by 24-hour pH monitorization in terms of LFR, irrespective of the presence or absence of laryngoscopic findings.

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The language of this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: <http://www.textcheck.com/certificate/VjEqRE>

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