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

Mehmet Külekçi, Ridvan Budun, Mehmet Özgür Avinçsal, Denizhan Dizdar, Seçkin Ulusoy, Ömer Necati Develioglu, Murat Topak

Department of Otorhinolaryngology, Gaziosmanpasa Taksim Training and Research Hospital, Istanbul, Turkey

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.\footnote{1} GER was first defined by Winkelstein in 1935 as “peptic esophagitis” in adults.\footnote{2} By the end of the 19th century, it was reported that GER might cause complications other than those involving the oesophagus.\footnote{1} 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).\footnote{3}

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 monitoring in terms of LFR, irrespective of the presence or absence of laryngoscopic findings.

Keywords: Laryngopharyngeal reflux, pH monitoring.

Özet: Proton pompa inhibitörlerinin larengofarengle refil hastalarında larengel irritasyon üzerine etkisi

Amaç: Larengofarengle refil (LFR) tanısı konmuş hastaların tedavi öncesi ve tedavi sonrası larengel irritasyon bulguları, refil semptom indeksi (RSI) kullanılarak değerlendirildi.

Yöntem: 24 saatlik çift proble pH monitörizasyonu sonucuna göre LFR tanısı alan 30 hasta çalışmaya dahil edildi. RSI sorgulaması hastalar tedavi öncesi ve tedavi sonrası uygulandı. Hastalar 3 aylık proton pompa inhibitörü tedavisi sonrası geniz akıntı ve boğaz temizleme ihtiyac açıdan reflü semptom indeksi kullanılarak tekrar değerlendirildi. Daha sonra geniz akıntıs ve boğaz temizleme ihtiyac tayin edildi.

Bulgular: Geniz akıntıda tedavi sonrası RSI değerinde istatistiksel olarak anlamlı azalma saptandı. Boğaz temizleme ihtiyacında tedavi sonrası RSI değerinde istatistiksel olarak anlamlı azalma saptandı.

Sonuç: Uzun süreden beri devam eden geniz akınıts ve boğaz temizleme şikâyeti olan hastalarda, herhangi bir enfeksiyon odağı saptanmamaşa, hastalar LFR açısından laringoskopik bulgular olunca da olmasa da 24 saatlik pH monitörizasyonu ile değerlendirilmelidir.

Anahtar sözcükler: Larengofaringeal refil, pH monitörizasyonu.
Laryngopharyngeal reflux is an atypical form of GER. LFR is associated with a large number of pulmonary, otolaryngologic, and odontopathic diseases.[3] Diseases associated with otolaryngology 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.[1-4]

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 otolaryngological 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.

<table>
<thead>
<tr>
<th>Grade the effect on you of the problems below during the recent months, according to the scale on the right.</th>
<th>0: No effect whatsoever</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Have you had any hoarseness or vocal problems?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Have you had extreme post-nasal drainage?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Do you need to clear your throat?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Do you have a sticking feeling in your throat?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. Do you cough after meals or going to bed?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Do you ever feel that you cannot breathe and might suffocate?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. Have you ever experienced chronic coughing or a coughing fit?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>8. Do you have difficulty in swallowing solid or liquid food?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>9. Do you ever feel burning or sticking in your chest and have brackish water come into your mouth?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
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 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=0.657**; 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
through the upper oesophageal sphincter without any bel-
lowing 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 irrita-
tion 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 faringeus,
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 otorhinolaryng-
ological examination in which the larynx is analysed in
detail, information from laboratory examinations for
reflux determination and measurement, and responses to
empirical reflux treatment.

The most sensitive and specific test for LFR is ambu-
latory 24-hour dual-probe pH monitoring. 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 monitor-
ing 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 sup-
pression 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 proba-
ability of success than H2 receptor blockers; the treatment
duration should be at least 3 months.

The terminology used for laryngeal lesions developing
in connection with reflux includes non-standardised
terms. Erythema and oedema on the arytenoids and poste-
rior 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 pachy-
dermia” was used for mucosal thickening and interary-
tenoid granuloma due to mucosal epithelial proliferation,
parakeratosis, and dyskeratosis observed histopathologi-
cally; patients with this presentation should be regarded as
possibly having reflux laryngitis. 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 laryngi-
tis.

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 sympto-
matic patients with normal larynx examinations had LFR,
and 39% of patients with LFR had normal larynx exami-
nation results.

For this reason, the existence of reflux symptoms is
more important than the presence of findings. It is advis-
able 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. During this procedure, the pH-meter base value
was set to 5 because pepsin exhibits proteolytic activity
even at this pH value.

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 patholo-
gies in patients with throat clearing need and post-nasal
drainage complaints were eliminated, and these com-
plaints 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 neuro-
logic or mucosal response to acid reflux contacting the res-
piratory mucosa. This situation may cause a misdiagno-
sis of allergic rhinitis in patients with no rhinological
problem. For this reason, LFR symptoms and the pres-

| 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 |
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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References


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