**Online First**

Treatment of Clinically Diagnosed Laryngopharyngeal Reflux Disease

Tarek Fouad Youssef, MD; Mohamed Rifaat Ahmed, MD

**Objectives:** To determine the incidence of *Helicobacter pylori* (HP) stool antigen (HPSA) in patients with laryngopharyngeal reflux disease (LPRD), and to make a comparison of 2 treatment regimens that have been used based on the presence or absence of HPSA positivity in patients with LPRD.

**Design:** Randomized controlled study.

**Setting:** Suez Canal University Hospital, Ismalia, Egypt.

**Patients:** A total of 212 patients with symptoms of LPRD.

**Intervention:** Patients were evaluated by laryngoscopy, ambulatory pH monitoring for 24 hours, and HPSA testing. Esomeprazole magnesium as a monotherapy was evaluated vs triple therapy in patients with HP infection.

**Main Outcome Measures:** To determine the incidence of HPSA in patients with LPRD, and to make a comparison of 2 treatment regimens that have been used based on the presence or absence of HPSA positivity in patients with LPRD.

**Results:** Persistent dry cough and a feeling of a lump in the throat (globus sensation) were the most frequent symptoms of LPRD, while posterior laryngeal inflammation was the main laryngoscopic finding. Results from the HPSA test were positive in 57% of the studied group. Patients with negative HPSA were treated with esomeprazole as single modality with a reported improvement score of 96.6%. Patients with positive HPSA test results were divided into 2 groups: 1 received only esomeprazole, with reported improvement in 40%, whereas the second group was treated with esomeprazole, plus amoxicillin sodium and clarithromycin (triple therapy) and reported a 90% incidence of symptom improvement.

**Conclusion:** The incidence of HP infection in patients with LPRD in our study was 57%. Triple therapy showed a higher cure rate in patients with HPSA-positive test results.


**Gastroesophageal reflux disease (GERD) is defined as a backward flow of gastric contents into the esophagus.** Beaver et al. suggested that laryngopharyngeal reflux disease (LPRD) means a backward flow of the stomach contents up to the throat. The clinical symptoms usually occur secondary to a refluxate of hydrochloric acid and pepsin. The gastric refluxate in the larynx might be the causative factor in posterior laryngeal inflammation, laryngeal contact ulcers, and laryngeal granuloma formation. It is associated with many otolaryngology disorders, such as reflux laryngitis, cervical dysphagia, globus pharyngeus, chronic cough, laryngeal or tracheal stenosis, and laryngeal carcinoma. The incidence of laryngopharyngeal symptoms is greater than expected.

There is a complex multifactor set of pathophysiologic characteristics of LPRD besides simple acid reflux. *Helicobacter pylori* (HP) is a gram-negative, microaerophilic bacterium that can cause infection of the stomach and is also strongly linked to the development of duodenal and gastric ulcers. A relationship between the rates and degree of reflux esophagitis with HP infection has been reported, but to our knowledge, no relationship with reflux laryngitis has been reported. The HP stool antigen (HPSA) test is a rapid, noninvasive diagnostic method based on a sandwich enzyme immunoassay with antigen detection, which has a high sensitivity and specificity.

No standard guidelines are available for treatment of LPRD; proton pump inhibitors, twice daily for 8 weeks, have been recommended if HP is present. However, clinical guidelines may consider revision to add a triple therapy regimen.
esomeprazole magnesium, 40 mg, for 4 weeks,14 and the other randomized groups: one was a control group that received only with positive HPSA test results were divided into 2 equal ran-
dered (the pH test was considered to be positive for LPRD when 
firm reflux signs, then 24 hours of pH monitoring was or-
ment for LPRD.

We performed a randomized controlled study at Suez Canal University Hospital, Ismailia, Egypt. A total of 212 patients with LPRD symptoms (hoarseness, chronic unexplained cough, frequent throat clearing, a feeling of a lump in the throat [globus sensation], and a bad or bitter taste in the mouth3) were in-
cluded in this study, but we excluded patients with a history of smoking, alcohol intake, chronic rhinosinusitis, or treat-
ment protocol performed follow-up evaluation for all patients after the end of medical treatment.

METHODS

We determined the incidence of HPSA-positive find-
ings among patients diagnosed as having LPRD and com-
pared the efficacy of 2 treatment regimens.

RESULTS

The mean age of the 212 patients in the study was 32.4 years. Cough, the main LPRD symptom, was found in 105 patients (49%), followed by globus sensation in 98 patients (46%), frequent throat clearing in 78 patients (36%), a bad or bitter taste in the mouth in 69 patients (32%), and hoarseness in 54 (25%).

Red, irritated arytenoids was the main laryngoscopic finding in 116 patients (54%), followed by swelling of the vocal cords in 59 patients (27%), small laryngeal ulcers in 24 patients (11%), and laryngeal granulomas in 4 patients (2%).

Among the patients in the study, the HPSA test results were positive in 57% of cases, and we found them to be statistically nonsignificant in relation to patient sympt-
s (Table 1) (P < .05 was considered statistically sig-
nificant). Also, they were found to be nonsignificant in re-
lation to the laryngoscopic findings (Table 2).

Marked improvement in symptoms occurred in 87 of the 90 patients with negative HPSA test results who received once-
daily esomeprazole magnesium, 40 mg, for 4 weeks.14

The 122 patients with positive HPSA test results were randomized into 2 equal groups (61 patients each). The control group (61 patients) received only esomeprazole magnesium, 40 mg, for 4 weeks; 23 patients (40%) showed marked improvement in symptoms, partial improvement occurred in 9 patients (16%), while 25 patients (44%) reported no improvement. Four patients discon-
tinued follow-up.

The second study group (61 patients) received triple therapy comprising esomeprazole magnesium, 40 mg, plus amoxicillin sodium and clarithromycin. In both groups, treatment was daily for 4 weeks.

Figure. The clinical improvement in both controls and study patients with laryngopharyngeal reflux disease is seen. Triple therapy comprised esomeprazole plus amoxicillin sodium and clarithromycin. In both groups, treatment was daily for 4 weeks.

We determined the incidence of HPSA-positive find-
ings among patients diagnosed as having LPRD and com-
pared the efficacy of 2 treatment regimens.

LPRD Symptom

<table>
<thead>
<tr>
<th>LPRD Symptom</th>
<th>Positive (n=122)</th>
<th>Negative (n=90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic cough</td>
<td>59</td>
<td>46</td>
</tr>
<tr>
<td>Feeling of lump in throat</td>
<td>52</td>
<td>46</td>
</tr>
<tr>
<td>Frequent throat clearing</td>
<td>40</td>
<td>38</td>
</tr>
<tr>
<td>Bad/bitter taste</td>
<td>37</td>
<td>32</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>24</td>
<td>30</td>
</tr>
</tbody>
</table>

Table 1. Relationship Between Laryngopharyngeal Reflux Disease (LPRD) Symptoms With HPSA Test Results

Abbreviation: HPSA, Helicobacter pylori stool antigen.

All comparisons were nonsignificant (P < .05 was considered statistically significant).

Laryngoscopich Findings

<table>
<thead>
<tr>
<th>Laryngoscopic Findings</th>
<th>Positive (n=122)</th>
<th>Negative (n=90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red, irritated arytenoids</td>
<td>61</td>
<td>55</td>
</tr>
<tr>
<td>Swelling of the vocal cords</td>
<td>32</td>
<td>27</td>
</tr>
<tr>
<td>Small laryngeal ulcers</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Granulomas in the larynx</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2. Relationship Between Laryngoscopic Findings and HPSA Test Results

Abbreviation: HPSA, Helicobacter pylori stool antigen.

All comparisons were nonsignificant (P < .05 was considered statistically significant).

In the practice of otolaryngology, it is now common to en-
counter patients with LPRD symptoms. Most of these pa-

©2010 American Medical Association. All rights reserved.
tients have been seen in thoracic and gastroenterology departments with atypical GERD symptoms. Laryngopharyngeal reflux disease is a diagnostic dilemma given the lack of solid guidelines for diagnosis and management.

In a recent report, Barry and Vaeezi state,13 “more questions than answers” were given, which best describes the current state of knowledge of LPRD. Our current study contributed several more questions.

In 1 limb of the study, a trial was made to associate HP infection with the degree or severity of symptoms and laryngoscopic findings. It was shown clearly based on statistical analysis that HP has no relation with any of the symptoms or signs of HPSA-positive or HP-negative individuals.

The second limb of the study compared the efficacy of proton pump inhibitor monotherapy vs triple therapy, and we have shown in our results that triple therapy gave better results in patients with positive HPSA test results. This study presents as much raw data as possible in compliance with the most recent guidelines to enable future evidence-based meta-analysis.

Gastroesophageal reflux disease is a common acid-related disorder presenting with a broad spectrum of symptoms with or without complications.3 The incidence of laryngopharyngeal symptoms is greater than expected.3 There are more complex multifactorial pathophysiologic characteristics of LPRD than simply acid reflux.6 Laryngopharyngeal reflux disease is considered to be a variant of GERD in which the incidence of throat and laryngeal symptoms is more evident and encountered in practice more often than expected.10

A large number of studies have raised the issue of the role of HP infection and its role in the pathophysiologic mechanism of GERD, but the interest in its role in LPRD has not been adequately studied.17 An estimated prevalence rate of HP infection of 30% among the general population has been given and shown that it is quite common.18 Various theories and mechanisms have been proposed to clarify its role in GERD.

In our study, 212 patients with symptoms of LPRD and positive results from 24 hours of pH monitoring were evaluated clinically. The most common symptoms were dry, persistent cough (49%) followed by a globus sensation (46%); other studies have also reported a globus sensation or throat-clearing, voice change, persistent sore throat, dysphagia, and cough as the predominant symptoms.19-21

The common reported findings of LPRD are in the domain of posterior laryngitis; we reported red, irritated arytenoids in 54% and swollen vocal folds (27%); other reports20,21 found endoscopic abnormalities in up to 98% of patients with LPRD, including nonspecific hyperemia, usually of the posterior larynx.

In our study, the 57% incidence rate of positive HPSA test scores is higher than that reported by Haruma et al,21 who mentioned that in Japan there is a relationship between HP infection and LPRD with a reported incidence of 31% to 41%. Helicobacter pylori stool antigen testing is a relatively new, noninvasive diagnostic technique with high sensitivity and specificity.11,22

Several authors suggested a correlation of HP infection and the degree of GERD,2,10,19,23,24 while others2 did not find any association between HP positivity and symptoms; the latter is in agreement with our data, which failed to demonstrate such a connection, and this variable report adds more to the dilemma of diagnosing LPRD.

As mentioned in the introductory paragraphs, we did not aim to point to a specific treatment regimen, a task better left for meta-analysis trials, but our raw data showed that patients with LPRD and with negative HPSA test results benefit from esomeprazole magnesium, 40 mg, for 4 weeks, with marked symptom improvement in most cases. While the patients with positive HPSA test results who received only esomeprazole magnesium, 40 mg, for 4 weeks showed a 40% rate of improvement, the second study group of patients with positive HPSA test results receiving triple therapy showed a 90% rate of improvement. Reports of a more successful triple therapy in GERD26 are in agreement with our results, but still, no clear guidelines for treatment of LPRD are available.

In conclusion, the incidence of the HP infection in patients with LPRD in our study is 57%. Second, HP infection should be considered when treatment is prescribed to patients with LPRD because the standard therapy for GERD might be insufficient. Finally, the use of triple therapy (esomeprazole magnesium, 40 mg, plus amoxicillin sodium, 1 g, and clarithromycin, 500 mg) in the treatment of LPRD with HP infection might result in a higher cure rate.

Submitted for Publication: March 9, 2010; final revision received June 20, 2010; accepted July 22, 2010.
Published Online: September 20, 2010. doi:10.1001/archoto.2010.165
Correspondence: Mohamed Rifaat Ahmed, MD, Department of Otolaryngology–Head and Neck Surgery, Faculty of Medicine, Suez Canal University, Ismailia, Egypt (m_rifaat@hotmail.com).
Author Contributions: Both authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Analysis and interpretation of data: Youssef and Ahmed. Critical revision of the manuscript for important intellectual content: Youssef and Ahmed. Statistical analysis: Youssef and Ahmed. Obtained funding: Ahmed. Administrative, technical, and material support: Ahmed.
Financial Disclosure: None reported.

REFERENCES