Treatment of Clinically Diagnosed Laryngopharyngeal Reflux Disease

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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.


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.
We determined the incidence of HPSA-positive findings among patients diagnosed as having LPRD and compared the efficacy of 2 treatment regimens.

## METHODS

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 mouth) were included in this study, but we excluded patients with a history of smoking, alcohol intake, chronic rhinosinusitis, or treatment for LPRD.

All patients underwent laryngoscopic examination to confirm reflux signs, then 24 hours of pH monitoring was ordered (the pH test was considered to be positive for LPRD when the pH was lower than 4, HPSA testing was ordered when a fresh stool sample was obtained). Patients with negative HPSA test results received once-daily esomeprazole magnesium, 40 mg, for 4 weeks. Patients with positive HPSA test results were divided into 2 equal randomized groups: one was a control group that received only esomeprazole magnesium, 40 mg, for 4 weeks; the other was a study group that received triple therapy comprising esomeprazole magnesium, 40 mg, plus amoxicillin sodium, 1 g, and clarithromycin, 500 mg, for the same period. Two patients discontinued follow-up. Fifty-three patients (90%) showed marked improvement in symptoms, partial improvement occurred in 3 patients (5%), and 3 patients (5%) showed no improvement in symptoms (Table 1). In the practice of otolaryngology, it is now common to encounter patients with LPRD symptoms. Most of these pa-
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 Vaezi 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.18

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 shows 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 test with high sensitivity and specificity11,12.

Several authors suggested a correlation of HP infection and the degree of GERD,9,10,19,23,24 while others20 did not find any association between HP positivity and symp-

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.

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