

## Laryngeal Mucosal Changes in Patients in Laryngo-Pharyngeal Reflux before and after Treatment with Proton Pump Inhibitors

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### Abstract

To evaluate pre and post treatment results based on Laryngeal mucosal changes as assessed by direct video laryngoscopy/stroboscopy using Belafsky scores. In our study we have evaluated laryngeal changes in patients with dysphonia and RSI 10 before treatment and after 6 months of treatment with Tab. Pantoprazole and Tab. Mosapride. This prospective study was carried out on 50 patients attending the ENT out patient department of a tertiary care referral centre over a period of 18 months i.e. from Nov 2008 to Apr 2010. The study showed that prolonged therapy is required to treat laryngopharyngeal reflux (LPR) effectively and 24 h ambulatory dual probe pH metry and videolaryngoscopy to assess RFS are the most preferred diagnostic tools in LPR. Dr Speech software for voice analysis can give an objective assessment of voice changes in LPR before and after treatment. The treatment consisting of proton pump inhibitor (PPI) and prokinetic drugs proved to be effective in laryngopharyngeal reflux disease as improvement was seen in all the parameters including reflux findings score. According to results of our study, 24 h ambulatory dual probe pH-metry, Reflux Finding Score (RFS), can be used as indicators of efficacy of treatment.

**Keywords:** Laryngopharyngeal reflux (LPR), Prokinetic drugs, Dysphonia

### Introduction

Laryngopharyngeal reflux (LPR) is the retrograde movement of gastric contents (acid and enzymes such as pepsin) into the laryngopharynx leading to symptoms referable to the larynx/hypopharynx. Typical LPR symptoms include dysphonia/hoarseness, globus pharyngeus, mild dysphagia, chronic cough nonproductive throat clearing and sometimes Laryngospasm. Hoarseness is a common disorder. A recent study<sup>[1]</sup> suggested that up to

55% of patients with hoarseness have acid reflux, which affects their larynx. The diagnostic work of patients with LPR begins with thorough history and meticulous physical examination. Investigations for LPR include oesophagogram, oesophageal endoscopy (UGI endoscopy), manometry study, radionuclide scanning and acidification tests. Continuous pH monitoring studies are felt to be the gold standard study for LPR. Probes that sense pH changes can be placed at different locations in oesophagus and pharynx or hypopharynx. Dual pH

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probes can be used with one probe 5 cms above site of lower oesophageal sphincter and second probe above upper oesophageal sphincter to detect any reflux. Anti-reflux therapy includes drugs, lifestyle changes and sometimes surgery. These treatments are often used for patients with hoarseness, where no other cause has been found on examination. The treatment of laryngopharyngeal reflux (LPR) has seen phenomenal changes over time, often following the development of new medications. Initial treatment regimens involved antacids and dietary and lifestyle changes. The elimination or marked suppression of acid production by PPIs accomplished two things: It reduced exposure of damaged tissues to an acidic environment and, more importantly, it reduced the activity of pepsin, which requires an acidic pH level for activation. Pepsin retains 70% of its activity at a pH level of 4.5. Clinical trials confirmed the superiority of PPIs to H<sub>2</sub> receptor antagonists. H<sub>2</sub> receptor antagonists competitively inhibit histamine induced gastric secretion. All phases of secretion (basal, psychic, neurogenic and gastric) are suppressed whereas it has no effect on gastric and oesophageal motility. Patients with LPR have prolonged symptoms and delayed healing<sup>[2]</sup>. Unlike GERD, treatment for LPR must be more aggressive and prolonged to achieve resolution<sup>[3]</sup>.

LPR may manifest with other symptoms such as asthma exacerbations, otalgia, excessive throat mucus, halitosis, neck pain, odynophagia, postnasal drip etc. Such symptoms, however, are also nonspecific and extend along a broad range that can be seen in other medical conditions. Conversely, this same list cannot be treated as an inclusive one, either, as not all patients who experience LPR will be afflicted with all of the aforementioned symptoms.

There are no set guidelines for a definitive diagnosis of LPR. Much of the literature considers ambulatory 24-h. This study entails measuring the pH in the proximal and distal esophageal regions. A positive event is defined as a pH-drop in the proximal probe accompanied by a simultaneous decrease in the distal one. Although there does not appear to be a significant difference in results between sedated and unsedated individuals, dual-probe pH studies are susceptible to false positives that require manual correction.

Impedence studies are one developing technological advance that expands on the principles behind pH monitoring. This technique involves arranging multiple electrode pairs on a pH-probe-type catheter capable of tracking retrograde bolus transits suggestive of reflux.

Mucosal biopsies have been notable for its ability to measure the concentration of pepsin and CA-III. A pepsin immunoassay being developed has been postulated to be 100% sensitive and 89% specific for LPR. Spectro-photometric analysis of refluxate has garnered attention for its potential to evaluate for bile and pancreatic enzymes, two biochemical compounds that may possibly aggravate the laryngeal mucosal damage incited with LPR in addition to gastric acid and activated pepsin.

Treatment options for LPR can be divided into three main modalities: lifestyle modifications, pharmacological, and surgical. Lifestyle modifications are similar to changes suggested for individuals experiencing GERD. Patients should be instructed to avoid oral intake 2-3 h prior to lying supine and to elevate the head of the bed. Elevation should be undertaken with the placement of bed blocks as opposed to the use of additional pillows. In addition, patients are encouraged to sleep on their left side as the diaphragmatic crura is said to cause a natural kink in the gastroesophageal junction when a person is in the left lateral decubitus position. Weight loss is usually helpful if symptoms of both LPR and GERD are present. Patients are educated to avoid alcohol, caffeine, carbonated beverages, chocolate, tobacco, and foods that are fried, spicy, or contain citrus as these factors have been noted to exacerbate reflux.

Antacids and histamine-2 receptor antagonists (H<sub>2</sub>RA) were the mainstays of pharmacological therapy prior to the development of proton pump inhibitors (PPI) in the 1980<sup>0</sup>s. Aside from the symptomatic relief that antacids afford against the acidic component of gastric refluxate, H<sub>2</sub>RA's were prescribed to combat a histamine-regulated nocturnal acid breakthrough (NAB) that is felt to further exacerbate symptoms due to LPR. Early studies had concluded that the combination of H<sub>2</sub>RA and PPI therapy effectively controlled NAB only during the initial part of treatment, while later ones had suggested that there was an equivocal difference

with the addition of H2RA to an established twice daily PPI regimen.

The nonspecific nature of symptoms and the lack of set criteria for diagnosis, leaves LPR susceptible to a couple of foci of controversy. Although there are hallmark findings and symptoms associated with LPR, not all patients will present with these complaints nor exhibit all of the classic features. Consequently, these patients may be erroneously evaluated for allergies, asthma, sinusitis, smoking, and vocal abuse. In addition, up to 87% of healthy individuals have been noted to have at least one LPR physical exam finding despite remaining asymptomatic. Conversely, Ylitalo et al. in 2001 had shown that some people possessed a benign laryngeal examination despite complaints indicative of reflux [4]. Further compounding the problem posed by the absence of diagnostic guidelines, there is a poor level of inter-rater reliability which leads to a subjective diagnosis of LPR.

### Materials and Methods

This prospective study was carried out on 50 patients attending the ENT OPD of a tertiary care referral centre complaining of dysphonia due to Laryngopharyngeal reflux (with reflux score/symptom index more than 10) over a period of 18 months i.e. from Nov 2008 to Apr 2010. All the patients were subjected to detailed history taking, general physical examination, ENT examination, video laryngoscopy.

#### Inclusion Criteria

All patients having reflux score index more than 10 and reflux symptom index more than 10 were included in the study.

#### Exclusion Criteria

No local laryngeal pathology in the past.

Not having been treated for LPR with PPI and prokinetic drugs.

No previous history of surgery, Radiotherapy, intubation.

Known case of peptic ulcer/GERD on regular treatment

#### Study Protocol

This prospective study was carried out on 50 patients attending the ENT OPD of a tertiary care hospital complaining of dysphonia due to Laryngopharyngeal reflux (with reflux score index more than 10) over a period of 18 months i.e. from Nov 2008 to Apr 2010.

All the patients were subjected to detailed history taking, general physical examination, ENT examination, 24 h ambulatory dual probe pH monitoring, video laryngoscopy to assess RFS, pre and six months post treatment with Tab. Pantoprazole (40 mg BD) and Tab. Mosapride (5 mg TDS) and findings recorded. The other PPI and prokinetics were not given to avoid ambiguity.

*Videolaryngoscopy* to assess RFS was performed with the following devices: 8.0 mm rigid laryngeal telescope at 90° (Hopkins); 3.2 mm flexible fibro laryngoscope (Storz); light xenon source 350 watts (Storz); micro-camera (Karl Storz, ICCD, endocam, Germany). The examinations were carried out under topical anesthesia with 2 percent lidocaine spray. We instructed the subjects to produce deep breathing, comfortable production of sustained vowels/e/ and /i/, and inspiratory phonation. The reflux finding score (RFS) was used to assess laryngopharyngeal reflux (LPR) signs (subglottic edema, ventricular obliteration, erythema/hyperemia, vocal fold edema, diffuse laryngeal edema, posterior commissure hypertrophy, granuloma, and others). A score greater than 7 was strongly considered suggestive of LPR.

### Observations and Results

50 Patients presenting with dysphonia, Reflux Symptom Index [10 and Reflux Score Index [10 which is suggestive of LPR underwent complete ENT examination including ambulatory 24 h pH monitoring using a dual channel antimony probe, video laryngoscopy perceptual voice analysis using GRBAS score, SZ Ratio, pre and six months post treatment with Tab. Pantoprazole (40 mg BD) and Tab Mosapride (5 mg TDS) and findings recorded. The followings observations were made:-

- *Age and Sex Distribution* 50 patients were included in the study. 64% were females (n = 32) and 36% were males (n = 18). The ages

were ranging from 23 to 60 years with mean age of 41.4 years.

- *24 h pH metry Findings* Double probe 24 hr pH studies were conducted on 50 patients, of these 13 patients (26%) had negative or normal findings and 37 patients (74%) had abnormal pharyngeal reflux before taking treatment. After taking treatment for six months 26 patients (52.0%) showed no reflux episodes.

The data revealed that 13 patients had normal pH findings pretreatment out of which 11 patients (84.6%) remained asymptomatic after treatment and 2 patients (15.4%) showed abnormal reflux episodes. 37 patients had more than 1 reflux episodes pretreatment out of which 15 patients (40.5%) showed no abnormal reflux episode after taking treatment. *Video laryngoscopy and Reflux Finding Score Findings* The Reflux Finding Score was recorded in all patients, pretreatment and 6 months after treatment. The pretreatment Reflux Finding Score 7.88 improved to 3.96 post treatment. The Paired T-Test revealed *p* value to be 0.000 which is significant.

## Discussion

LPR is known as the main factor for various laryngeal diseases such as reflux laryngitis, subglottic stenosis, contact ulcer, or granuloma, vocal polyps and laryngeal cancer [5]. Almost half of the patients with dysphonia have LPR as a common causative factor [6] but its definite role in etiology or pathophysiology of dysphonia has not been clearly identified.

In our study we have evaluated and compared voice and laryngeal changes in patients with RSI 10 before treatment and after 6 months of treatment with Tab. Pantoprazole and Tab. Mosapride. In this study 50 patients with ages ranging from 23 to 60 participated (Mean 41.4 years) out of which 64% were females. 26% patients had normal findings on pH metry before starting the treatment and after taking the treatment 52% patients showed no reflux episode, the remaining 48% showed decrease in number of reflux episode.

LPR should never be considered physiologic, even a single pharyngeal episode of pH less than 4 is diagnostic of LPR. Therefore ambulatory 24 double

probe pH monitoring is the most suitable diagnostic method. On the other hand several studies proved that evident signs of LPR can be detected, even in patients with negative 24 h pH monitoring. It was also proved that pepsin is activated in values of pH higher than 4 [7]. For the esophagus, upto

An endoscopic laryngeal examination usually reveals the signs of LPR. Belafsky et al. [8] developed RFS and reported that it could be used effectively and reproducibly in the diagnosis and follow up of LPR. RFS has been widely used for its measuring efficacy of treatment and high reproducibility between observers. In the great majority of studies the RFS was used in the evaluation of clinical severity of LPR [8]. The score of more than 7 is indicative of LPR [9]. Videolaryngoscopy is a very simple method which can be easily repeated and well tolerated by the patients. The treatment of LPR needs to be more aggressive and prolonged as it usually takes 6 months or more for the laryngeal findings of LPR to resolve and some patients may require prolong treatment.

The results of our study confirmed that the treatment with Tab. Pantoprazole and Tab. Mosapride is very successful. In our study pretreatment mean RFS was 7.88, which became 3.96 after treatment which shows that the improvement was significant.

## Conclusions

50 patients with RSI 10 (suggestive of LPR) participated in this prospective study. All patients underwent 24 h ambulatory dual probe pH metry, videolaryngoscopy to assess Reflux Finding Score (RFS), perceptual and acoustic analysis of voice using GRBAS scale and Dr Speech software respectively to compare and evaluate laryngeal changes in patients with dysphonia in laryngopharyngeal reflux before and after treatment with proton pump inhibitors (PPI) and prokinetic drugs. All patients were given PPI (Tab. Pantoprazole 40 mg 1BD) and prokinetic (Tab. Mosapride 5 mg 1 TDS) for 6 months. After completion of the treatment all patients again underwent pH metry, videolaryngoscopy to assess Reflux Finding Score (RFS).

**Informed Consent:** written informed consent was taken from patients.

**Ethical Approval:** ethical committee approval was taken from the AIMSIR institutional committee of ethics.

**Source Of Funding:** funding source was self

**Conflict Of Interest:** there was no conflict of interest

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