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Original Research

The Effects of Empiric Antireflux Treatment on Laryngopharyngeal and Gastroesophageal Reflux Disease

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Abstract

Objectives: This study aims to investigate the effects of empiric lansoprazol therapy on laryngopharyngeal (LPR) and gastroesophageal (GOR) reflux symptoms and laryngological findings.

Methods: Sixty-seven patients with suspected LPR related symptoms were prospectively analyzed in this study. Following eleven symptoms were asked to patients using LPR symptom questionnaire; sore throat, throat burning, throat clearing, globus sensation, cough, halitosis, dysphonia, dysphagia, postnasal dripping, vocal fatigue and sputum. GOR symptoms were evaluated with the Frequency Scale for the Symptoms of Gastroesophageal Reflux Disease (FSSG) questionnaire consist of twelve symptoms. Posterior larynx, arytenoids and interarytenoid area were evaluated with a 70° endoscope. Erythema, edema and nodularity were graded separately using 4 point severity scale to examine laryngeal signs. All patients were treated using 30 mg lansoprazole once daily for four weeks. After the end of medication, symptoms and laryngoscopic signs were evaluated again with the same method. The pretreatment and posttreatment values were compared with statistical analyses.

Results: There was a statistically significant decrease in LPR symptom scores and total scores of FSSG. The severity of nodularity in the posterior larynx, arytenoids and interarytenoid area was improved after treatment. There was no statistically significant difference in erythema on each area larynx. Edema in the posterior larynx and interarytenoid area was improved but there was no change on the edema of arytenoids.

Conclusion: A short period of empiric antireflux treatment has a significant improving effect on all LPR symptoms and most of GOR symptoms. However, it was insufficient on laryngeal signs. Further research is needed to investigate longer times of treatment for the complete resolution of symptoms and signs.

Keywords: Gastroesophageal reflux; Laryngopharyngeal reflux; proton pump inhibitors.

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Laryngopharyngeal reflux (LFR) is the backflow of gastric contents that pass through the upper esophageal sphincter and enter into the laryngopharynx. Although it is similar to gastroesophageal reflux disease (GERD), which is defined as gastric contents escaping back into the esophagus, it differs concerning symptoms and signs. While retrosternal burning and regurgitation are typical symptoms of GERD, symptoms such as hoarseness, cough, dysphagia, and globus pharyngeus are at the forefront.[1,2] Therefore, the referral rates of patients with reflux symp-

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toms to the otolaryngology clinics have increased significantly in recent years.[3] LFR is present in many etiologies of laryngeal disease, such as reflux laryngitis, subglottic stenosis, laryngeal carcinoma, laryngeal granuloma, contact ulcer and vocal nodule.[4,5] Given that these symptoms and signs of larynx and pharynx are nonspecific and factors, such as smoking, infection, allergy and poor voice hygiene, may play a role in the etiology, the diagnosis of LFR becomes difficult.

The 24-hour pH monitoring used in the diagnosis of reflux is the gold standard. Its practical use is not very common in the diagnosis of LFR because its sensitivity is not as high as in GERD and it is an invasive test.[6] The proton pump inhibitor (PPI), which is generally accepted in the treatment of antireflux, is applied empirically at the first stage. There is no standard protocol, as there are different opinions regarding the duration and dosage of treatment. In our study, the effectiveness of one-month empirical lansoprazole treatment on laryngopharyngeal reflux symptoms, endoscopic larynx findings and gastroesophageal reflux symptoms was investigated.

Methods

In our study, 67 patients who presented to the otorhinolaryngology outpatient clinic and had LFR-related symptoms for at least three months were prospectively examined. Patients receiving antireflux therapy, the patients with upper respiratory tract infection, allergic symptoms, systemic disease and smokers were not included in this study. The patients' complaints were evaluated with the 11-item LFR symptom scoring questionnaire, including symptoms of laryngeal pain, sore throat, expectoration, postnasal discharge, need for throat clearing, dysphonia, vocal fatigue, cough, globus sensation, dysphagia and halitosis.

Patients rated their severity from zero to three according to the Likert-type scale as: 0: no symptoms), 1: mild (minimal awareness of symptoms, easily tolerated), 2: moderate (obvious awareness, disturbing but tolerable), 3: severe (difficult to tolerate, preventing daily activities)].[2] The complaints of GERD, including burning in the chest, bloating in the abdomen, feeling of heaviness after eating, throat burning. The desire to rub the chest, feeling sick and feeling of fullness in the throat after eating, feeling of throat pain after eating, bitter water coming into the throat, burping and chest pain while bending were questioned using The 12-item Frequency Scale for the Symptoms of Gastroesophageal Reflux Disease (FSSG) questionnaire. Symptoms were scored from zero to four (0: none, 1: rare, 2: sometimes, 3: frequent, 4: always).[7]

The laryngeal findings were evaluated by the same specialist blinded to the clinical condition of the patient. Using a rigid endoscope with a 70° rigid lens, the posterior larynx, interaritenoid region and arytenoids were evaluated separately for edema, erythema and nodular appearance. The findings were graded and scored from mildest to severe. (0: none, 1: mild, 2: moderate, 3: severe). Patients received a single dose of 30 mg lansoprozole consumed on an empty stomach, for one month. Suggestions for avoiding reflux-enhancing foods, using high pillows while sleeping, and not feeding before sleep were made. LFR and GERD symptoms and laryngeal findings were evaluated again with the same methods after treatment. Data before and after treatment were compared statistically. Our study was approved by the ethics committee (Date, 04.09.2009; decision no. 09-25). Informed consent was obtained from all patients.

Statistical evaluation was performed using SPSS 22.0 program. Continuous variables were expressed as mean±standard deviation and categorical variables as percentages. Before and after the treatment, LFR symptoms and endoscopic larynx findings, GERD symptoms were evaluated using the multi-eyed chi-square test or McNemar Test. FSSG score totals before and after treatment were evaluated with Wilcoxon Signed Ranks Test. In all statistical measurements, $p<0.05$ was considered the level of statistical significance.

Results

In this study, eleven of the patients were male (16.4%), and 56 were female (83.6%). Patients' ages ranged from 18 to 70 (mean 44.2±11.9) years. LFR symptom scores before and after treatment are summarized in Table 1. All LFR symptom scores showed a statistically significant improvement after treatment. Regardless of the severity of the symptoms, the most common symptoms were dysphonia and vocal fatigue (86.6%) and the least common symptom was halitosis (49.3%). While the symptom that improved mostly with treatment was sound fatigue, the symptom of throat-clearing showed the least improvement (Table 1).

A statistically significant improvement with treatment was seen endoscopically in the nodular appearance of the posterior larynx, interarytenoid region and arytenoids. Although there was no improvement in erythema in all three regions with treatment, there was a statistically significant regression in edema of the posterior larynx and interarytenoid region. There was no significant improvement in arytenoid edema (Table 2).

The FSSG scores before and after treatment are separately summarized in Table 3. When the total scores were compared, the value of 21.9±8.4 before treatment regressed to

Table 1. Comparison of pre- and post-treatment LFR symptoms

LFR Symptoms	Severity	Pre-treatment		Post-treatment		p
		Patients (n)	%	Patients (n)	%	
Throat pain	No	12	17.9	28	41.8	
	Mild	27	40.3	31	46.3	<0.001
	Moderate	17	25.4	5	7.5	
	Severe	11	16.4	3	4.5	
Sore throat	No	12	17.9	21	31.3	
	Mild	19	28.4	36	53.7	0.016
	Moderate	30	44.8	7	10.4	
	Severe	6	9	3	4.5	
Expectoration	No	22	32.8	29	43.3	
	Mild	20	29.9	22	32.8	<0.001
	Moderate	13	19.4	13	19.4	
	Severe	12	17.9	3	4.5	
Postnasal discharge	No	29	44.3	36	53.7	
	Mild	14	20.9	16	23.9	<0.001
	Moderate	16	23.9	12	17.9	
	Severe	8	11.9	3	4.5	
Need for throat clearing	No	11	16.4	17	25.4	
	Mild	15	22.4	30	44.8	<0.001
	Moderate	17	25.4	15	22.4	
	Severe	24	35.8	5	7.5	
Dysphonia	No	9	13.4	28	41.8	
	Mild	22	32.8	26	38.8	<0.001
	Moderate	24	35.8	12	17.9	
	Severe	12	17.9	1	1.5	
Vocal fatigue	No	9	13.4	29	43.3	
	Mild	28	41.8	25	37.3	0.002
	Moderate	23	34.3	10	14.9	
	Severe	7	10.4	3	4.5	
Coughing	No	19	28.4	33	49.3	0.002
	Mild	23	34.3	30	44.8	
	Moderate	17	25.4	4	6	
	Severe	8	11.9	--	--	
Globus	No	11	16.4	19	28.4	
	Mild	12	17.9	35	52.2	0.008
	Moderate	27	40.3	11	16.4	
	Severe	17	25.4	2	3	
Dysphagia	No	23	34.3	30	44.8	
	Mild	21	31.3	29	43.3	<0.001
	Moderate	16	23.9	7	10.4	
	Severe	7	10.4	1	1.5	
Halitosis	No	33	49.3	40	59.7	
	Mild	18	26.9	16	23.9	<0.001
	Moderate	9	13.4	9	13.4	
	Severe	7	10.4	2	3	

4.6±7.5 after treatment. When GERD symptom scores were examined separately, any significant change was not observed only in the complaint of feeling sick after eating. Regardless of the severity of the symptoms, the most common symptom was the presence of brackish water in the throat (86.6%) and the least common symptom was the desire to rub the chest (53.7%). While the symptom that improved the most with treatment was throat burning after eating, the symptom with the least improvement was a sense of food while swallowing (globus sensation) (Table 3).

Table 2. Comparison of the endoscopic findings of the larynx before and after treatment

Endoscopic findings of the larynx	Severity	Pre-treatment		Post-treatment		p
		Patients (n)	%	Patients (n)	%	
Posterior larynx	No	3	4.5	26	38.8	
	Mild	23	34.3	37	55.2	
Edema	Moderate	37	55.2	4	6.0	0.02
	Severe	4	6.0	--	--	
Erythema	No	2	3	28	41.8	
	Mild	18	26.9	34	50.7	0.9
	Moderate	44	65.7	4	6.0	
	Severe	3	4.5	1	1.5	
Nodular appearance	No	40	59.7	56	83.6	
	Mild	18	26.9	10	14.9	0.006
	Moderate	7	10.4	1	1.5	
	Severe	2	3.0	--	--	
İnteraryternoid region						
Edema	No	1	1.5	22	32.8	
	Mild	23	34.3	38	56.7	0.002
	Moderate	37	55.2	7	10.4	
	Severe	6	9.0	--	--	
Erythema	No	1	1.5	21	31.3	
	Mild	20	29.9	42	62.7	0.055
	Moderate	43	64.2	4	6.0	
	Severe	3	4.5	--	--	
Nodular appearance	No	41	61.2	61	91.0	
	Mild	20	29.9	6	9.0	<0.001
	Moderate	6	9.0	--	--	
	Severe	---	---	--	--	
Arytenoids						
Edema	No	1	1.5	18	26.9	
	Mild	26	38.8	42	62.7	0.746
	Moderate	35	52.2	7	10.4	
	Severe	5	7.5	--	--	
Erythema	No	1	1.5	19	28.4	
	Mild	26	38.8	43	64.2	0.51
	Moderate	36	53.7	5	7.5	
	Severe	4	6.0	---	--	
Nodular appearance	No	57	85.1	63	94.0	
	Mild	8	11.9	4	6.0	0.001
	Moderate	2	3.0	---	---	
	Severe	---	--	---	---	

Discussion

The backward escape of gastric contents from the stomach into the laryngopharyngeal region is defined as LFR. Although its mechanism has not been fully elucidated, it is argued that symptoms occur due to the dysfunction of the upper esophageal sphincter.[8] Up to 10% of patients presenting to the otolaryngology outpatient clinics have symptoms associated with LFR.[1] In our study, sore throat, laryngeal pain, expectoration, postnasal discharge, the need for throat clearing, dysphonia, vocal fatigue, cough, globus sensation, dysphagia and halitosis are frequently encountered among these symptoms. Although the presence of related symptoms and characteristic laryngeal findings are significant for the diagnosis of LFR, many researchers argue that laryngeal and pharyngeal findings can be very diverse.[9]

The diagnosis of LFR becomes more difficult, considering that the signs and symptoms can develop due to reflux, as

Table 3. Comparison of pre and post-treatment FSSG scores

FSSG SCORES	Severity	Pre-treatment		Post-treatment		p
		Patients (n)	%	Patients (n)	%	
Burning sensation on the chest	No	12	17.9	20	29.9	
	Mild	11	16.4	18	26.9	
	Moderate	23	34.3	18	26.9	<0.001
	Severe	14	20.9	11	16.4	
	Extremely severe	7	10.4	--	--	
Bloating	No	11	16.4	19	28.4	
	Mild	9	13.4	17	25.4	
	Moderate	15	22.4	22	32.8	0.001
	Severe	22	32.8	6	9	
	Extremely severe	10	14.9	3	4.5	
A sense of heaviness after eating	No	11	16.4	17	25.4	
	Mild	3	4.5	16	23.9	
	Moderate	23	34.3	21	31.3	0.005
	Severe	24	35.8	9	13.4	
	Extremely severe	6	9	4	6	
The desire to rub the chest	No	31	46.3	40	59.7	
	Mild	6	9	8	11.9	
	Moderate	15	22.4	13	19.4	0.01
	Severe	15	22.4	6	9	
	Extremely severe	--	--	--	--	
Feeling sick after eating	No	18	26.9	25	37.3	
	Mild	11	16.4	17	25.4	
	Moderate	16	23.9	16	23.9	0.06
	Severe	16	23.9	5	7.5	
	Extremely severe	6	9	4	6	
Throat burning after eating	No	19	28.4	29	43.3	
	Mild	6	9	14	20.9	
	Moderate	22	32.8	16	23.9	0.006
	Severe	15	22.4	7	10.4	
	Extremely severe	5	7.5	1	1.5	
Throat pain after the meal	No	10	14.9	22	32.8	
	Mild	10	14.9	11	16.4	
	Moderate	23	34.3	23	34.3	0.01
	Severe	19	28.4	6	9	
	Extremely severe	5	7.5	5	7.5	
Sense of fullness while eating	No	22	32.8	30	44.8	
	Mild	6	9	16	23.9	
	Moderate	20	29.9	14	20.9	0.02
	Severe	15	22.4	4	6	
	Extremely severe	4	6	3	4.5	
Globus sensation when swallowing	No	14	20.9	15	22.4	
	Mild	3	4.5	10	14.9	
	Moderate	23	34.3	29	43.3	0.04
	Severe	16	23.9	9	13.4	
	Extremely severe	11	16.1	4	6	
Brackish water in the throat	No	9	13.4	13	19.4	
	Mild	8	11.9	17	25.4	
	Moderate	26	38.8	28	41.8	0.03
	Severe	19	28.4	8	11.9	
	Extremely severe	5	7.5	1	1.5	
Burping	No	18	26.9	23	34.3	
	Mild	5	7.5	21	31.3	
	Moderate	22	32.8	15	22.4	<0.001
	Severe	19	28.4	8	11.9	
	Extremely severe	3	4.5	--	--	
Chest pain when bending forward	No	29	43.3	36	53.7	
	Mild	4	6	12	17.9	
	Moderate	16	23.9	16	23.9	0.004
	Severe	15	22.4	2	3	
	Extremely severe	3	4.5	1	1.5	

well as other causes, such as smoking, allergy, asthma, viral disease and voice misuse.

GERD is related to multifactorial causes such as disruption of the antireflux barrier, esophageal clearance and esophageal mucosal resistance due to the temporary relaxation of the lower esophageal sphincter.[10] The differing features of the laryngeal mucosa and lower esophageal mucosa also differentiate the effects of reflux. Thus, the symptoms and signs are also different. Therefore, the relationship of LFR with GERD has not been fully revealed. LFR signs and symptoms in patients diagnosed with reflux esophagitis by esophagogastroduodenoscopy have yielded different results in many studies.[11-13] In our study, LFR and GERD symptoms were evaluated separately, without comparing them.

The reliability of 24-hour dual-probe Ph monitoring, which is the gold standard in the diagnosis of acid reflux LFR, is debatable because of its invasiveness and lower sensitivity.[14] Thus, the positivity of symptoms, laryngeal findings, and regression of these values with empirical PPI treatment are considered more valuable in the diagnosis of LFR. Lack of laryngeal symptoms and signs with antireflux therapy suggests that the etiology may depend on other reflux components other than the presence of gastric acid. According to the studies performed, laryngeal damage due to LFR can also be induced by pepsin and bile acids in addition to gastric acid.[15,16]

Today, the widely accepted approach in the empirical management of LFR and GERD is PPI treatment applied twice daily for two or three months.[17] In GERD, typical reflux symptoms, such as a burning sensation in the chest, regress with antireflux therapy, while the response to treatment in LFR is not so obvious and varies much from patient to patient. According to some researchers, higher dose and longer-term antireflux treatment are required in LFR than GERD.[18] If there is no response to appropriate empirical treatment, instead of increasing the dose or extending the duration of treatment, it is necessary to review the diagnosis by considering the multifactorial physiopathology of reflux.[19]

In our study, we administered a single dose of empirical 30 mg lansoprazole treatment for one month to investigate the short-term results of empirical therapy. Significant improvement was observed in all symptoms of LFR and symptoms of GERD other than feeling sick after eating. There was a significant decrease in the total GSFS score after treatment.

Regarding endoscopic findings of the larynx, we could not achieve satisfactory results compared to symptoms. Although there was a significant decrease in the nodular appearance of the larynx, we could not detect a statistically significant improvement in erythema, but we observed a decrease in the severity of the symptoms.

In their study, Chun et al. applied antireflux therapy by combining six and 12 weeks of PPI alone or together with a prokinetic agent. They found more improvement in endoscopic findings of the larynx after long-term treatment compared to the short-term.[20] In addition, there are studies in which the same protocol was applied as in our study, and significant improvement was observed in all of the laryngeal findings.[21] The absence of a complete improvement in all symptoms and findings in the literature indicates that the search for the definitive treatment of reflux will continue.

As a result, different results in the literature make it difficult for us to establish a clear approach to the symptoms and signs of LFR and its relation to GERD. There is a need for a more detailed investigation of the multifactorial physiopathology of reflux, as well as studies with a higher number of cases regarding treatment time and combined approaches.

Disclosures

Ethics Committee Approval: Local Ethics Committe of Haydarpasa Numune Training and Research Hospital (09-25, 09.04.2009).

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Conflict of Interest: None declared.

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