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Original Research Article

A clinical study of symptomatic profile and response in objective and subjective parameters to proton pump inhibitor in laryngopharyngeal reflux

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ABSTRACT

Background: The study was conducted to identify the various clinical presentations and findings in cases of LPR and also to study the role of proton pump inhibitor in the management of laryngopharyngeal reflux by observing the effect of proton pump inhibitor on reflux finding score (RFI) and reflux symptom index (RSI).
Methods: A prospective, interventional, cohort study of 50 diagnosed cases of LPR with RSI >13 and RFS >7 (based on fibreoptic laryngoscopic findings) at the time of initial presentation was done. They were treated with a 6 month course of oral cap omeprazole (20 mg twice daily 30 minutes before meals) and followed up at 0, 4, 8 and 24 weeks for any improvement in RSI and RFS scores.
Results: Most frequent symptoms detected in the cases were frequent clearing of throat, dry cough and sensation of lump in the throat all of which showed significant improvement at follow up at 4 weeks. Most common finding on fibreoptic laryngoscopy was erythema and diffuse laryngeal oedema, both of which showed significant improvement on follow up.There was also a significant change in RSI and RFS after receiving Omeprazole at 4 weeks, 8 weeks and at 24 weeks duration ($p < 0.0001$).
Conclusions: This study dealt mainly with study of combination of clinical features that LPR presents time line of improvement of these features with capsule omeprazole. It is proposed that a presumptive diagnosis of LPR can be made based on the criteria of RSI and patients be given an empirical therapeutic trial including behavioral and dietary recommendations and 6 months of twice-daily proton-pump inhibitor therapy for an excellent clinical response.

Keywords: Laryngopharyngeal reflux, Reflux symptom index, Reflux finding score, Proton pump inhibitor

INTRODUCTION

Laryngopharyngeal reflux has been reported in upto 10% of patients, presenting to an ENT OPD.[1] Laryngopharyngeal reflux is a known etiological factor behind the development of various conditions of the upper aero-digestive tract like recurrent laryngospasm, cricoarytenoid joint fixation and stenosis as well as many other otolaryngology related conditions, including globus pharyngeus, cervical dysphagia, carcinoma and subglottic stenosis.

A nine-item reflux symptom index (RSI) is a preset questionnaire introduced by Belafsky et al answered by the patient himself to find out the severity of laryngopharyngeal reflux.[2] RSI also evaluates treatment efficacy, which has excellent reproducibility and criterion-based validity.

Flexible fibreoptic laryngoscopy (FOL), an OPD procedure, is used to detect the findings of laryngopharyngeal reflux. Reflux finding score (RFS) is an 8 item clinical severity rating scale based on FOL findings.[3] RFS helps physicians identify subtle findings of reflux, evaluation of severity of laryngeal tissue injury and to know treatment outcome.

Proton pump inhibitors (PPI) are an important therapeutic agent in the management of laryngopharyngeal reflux (LPR). Effective medical treatment has been claimed to reverse the Reflux Finding Score. However, unlike in GERD, response to PPI therapy in patients with LPR has been described as highly variable and may need prolonged and aggressive therapy.[4]

Ambulatory 24-hour double-probe (simultaneous oesophageal and pharyngeal) pH monitoring is considered as the 'gold standard' investigation to diagnose LPR. However, American gastroenterological association monitoring has reserved diagnosis of LPR by pH monitoring for patients who do not respond to initial acid suppression.[5] Also pH monitoring is a cumbersome procedure and is not suitable to be carried out in an OPD setup. In this study we used the criteria of Reflux Symptom index and reflux symptom score were used in this study to diagnose LPR. RSI and RFS have been found to have a high comparability with the gold standard double probe 24 hour pH monitoring.[2,3,6]

This study was intended to observe various presentations and findings in a presumptive case of LPR. Further, the study assessed the effect of omeprazole on the recorded symptoms and findings over the duration of the study. The purpose of the present study was to assess the various clinical presentations and findings in cases of LPR and also to study the role of proton pump inhibitor in the management of laryngopharyngeal reflux by observing the effect of proton pump inhibitor on RFS and RSI.

METHODS

The study was a prospective, interventional, cohort study. Study population consisted of all patients visiting the out-patient department of ENT with symptoms of laryngopharyngeal reflux which includes dysphagia, chronic cough, dysphonia, globus sensation, hoarseness, sore throat, throat clearing and upright reflux (daytime reflux), who were screened.

Patients below 18 years of age, patients with other obvious cause of symptoms and signs like infection/ malignancy and patient with history of taking anti-reflux medication/prokinetic agents or histamine-2 receptor blockers in the preceding one month were excluded from the study. The patients were administered a preset questionnaires to assess his/her perception of severity of symptoms. Each symptom was scored on the self-assessment scale of 0 to 5. The RSI was thus obtained as presented in Table 1.

Patients underwent detailed ENT evaluation and those patients with an obvious aetiology for the clinical presentations like infections or malignancy, were treated accordingly and were excluded from the study. After exclusion, 62 patients were subjected to FOL in the OPD, under local anesthesia (4% lignocaine spray). To avoid bias, FOL was performed by an independent experienced ENT specialist, who was blinded to clinical information and RSI of the patients. Reflux Finding Score was calculated as given in Table 2.

Table 1: Reflux symptom index.

Symptoms						
Within the last MONTH, how did the following problems affect you?	0 = no problem 5 = severe problem					
1. Hoarseness or a problem with your voice	0	1	2	3	4	5
2. Clearing your throat	0	1	2	3	4	5
3. Excess throat mucus or postnasal drip	0	1	2	3	4	5
4. Difficulty in swallowing food, liquids or pills	0	1	2	3	4	5
5. Coughing after you ate or after lying down	0	1	2	3	4	5
6. Breathing difficulties or choking episodes	0	1	2	3	4	5
7. Troublesome or annoying cough	0	1	2	3	4	5
8. Sensations of something sticking in your throat or a lump in your throat	0	1	2	3	4	5
9. Heartburn, chest pain, indigestion or stomach acid coming up	0	1	2	3	4	5
Total						

52 adult patients of both genders with symptoms of laryngopharyngeal reflux for the last 1 month and with RSI ≥13 and RFS ≥7 were recruited into the study. RSI ≥13 has been found to be highly suggestive for LPR in a study by Belafsky et al.[2] RFS greater than 7 has more than 95% probability of having LPR.During the study period, 2 patients were lost to follow up. Hence a total of 50 patients were followed up till the end of the study.

Table 2: Refulx finding score.

Findings	Score
Subglottic edema	2 = present 0 = absent
Ventricular obliteration	2 = partial 4 = complete
Erythema/hyperaemia	2 = arytenoids only 4 = diffuse
Vocal cord edema	1 = mild 2 = moderate 3 = severe 4 = polypoid
Diffuse laryngeal edema	1 = mild 2 = moderate 3 = severe 4 = obstructing
Posterior commissure hypertrophy	1 = mild 2 = moderate 3 = severe 4 = obstructing
Granuloma/granulation	2 = present 0 = absent
Thick endolaryngeal mucus	2 = present 0 = absent
Total	

Patients were given empirical treatment with proton pump inhibitor (cap omeprazole 20 mg), twice daily, 30 min before meals. On follow-up at 4 weeks, 8 weeks and 24 weeks patients were re-evaluated and RSI and RFS were calculated. Statistical analysis of the data was done and conclusion was drawn. RSI and RFS scores were analyzed at 0, 4, 8, 24 weeks using paired t-test.

RESULTS

Of the total 50 patients enrolled in the study 29 patients (58%) were females and 21 patients (42%) were males. 42 percent of the patients (n=21) were in the age range of 30 to 40 years. 34 percent of the patients were more than 50 years old and 22 percent were in the age range of 40-50 years. There was a significant reduction ($p < 0.005$) seen in the mean RSI scores at 4, 8, 24 weeks of follow up as iilustrated in Table 3. There was also a significant reduction ($p < 0.005$) seen in the mean RFS scores at 4, 8, 24 weeks of follow up as displayed in Table 4.

Table 3: Average reflux symptom index.

RSI	M (1)	M (2)	M (3)	M (4)
Mean	16.50	11.94	9.12	5.44
SD	1.66	1.79	2.00	2.08

M (1): RSI in patients. M (2), M (3), M (4): RSI at 04, 08 and 24 weeks post treatment with omeprazole respectively.

Table 4: Average reflux finding score.

	M (1)	M (2)	M (3)	M (4)
Mean	8.12	6.60	5.22	4.34
SD	0.96	0.67	0.79	0.75

M (1): RFS in patients. M (2), M (3), M (4): RFS at 04, 08 and 24 weeks post treatment with omeprazole respectively.

Most common symptom in this study was found to be frequent clearing of throat, seen in 98% of patients, followed by sensation of lump in throat and troublesome cough in 96% of patients each. Less common symptoms observed were, post nasal drip/excessive throat mucus (80%), heartburn/chest-pain/indigestion (76%), and hoarseness of voice (68%), dysphagia (66%), cough after eating (56%) and dyspnoea/choking (38%).

There was statistically significant improvement seen in all the symptoms considered in RSI ($P < 0.05$) at first four weeks, in this study as given in Figure 1. Maximal change was observed in throat clearing, post nasal drip/excessive throat mucus, dysphagia, cough, lump in throat sensation and heartburn/chest pain/indigestion. Improvement to lesser extent, however statistically significant was observed with symptoms of hoarseness and dyspnoea/choking. At 08 weeks duration, all symptoms showed significant improvement, the least being dyspnoea/choking, as compared to initial scores. There was no significant difference in severity of dyspnoea/choking as experienced by patients at 04 and 08 weeks of omeprazole therapy. Again at 24 weeks all symptoms reduced in severity. Hence, it can be assumed that dyspnoea/choking is the least and last affected symptom after omeprazole therapy.

Most common laryngoscopic sign in this study was found to be erythema/hyperaemia in 84% of patients followed by diffuse laryngeal oedema in 82% of patients, posterior commissure hypertrophy (56%) and vocal cord oedema in 50% of study population. Other less common findings were thick endolaryngeal mucus (38%), granuloma/granulation (24%), ventricular obliteration (22%) and subglottic oedema (14%).

In this study, there was statistically significant improvement seen in the findings of erythema, vocal cord oedema, diffuse laryngeal oedema, posterior commissure hypertrophy at 4 weeks of therapy as shown in Figure 2. No significant change was seen in the findings of ventricular obliteration, thick endolaryngeal mucus, subglottic oedema and granuloma/granulation, as compared to initial findings. The findings of subglottic oedema and thickened endolaryngeal mucus show significant improvement at 8 and 24 weeks of therapy. However, ventricular obliteration and granuloma/ granulation tissue remain least responsive even at 24 weeks of therapy.

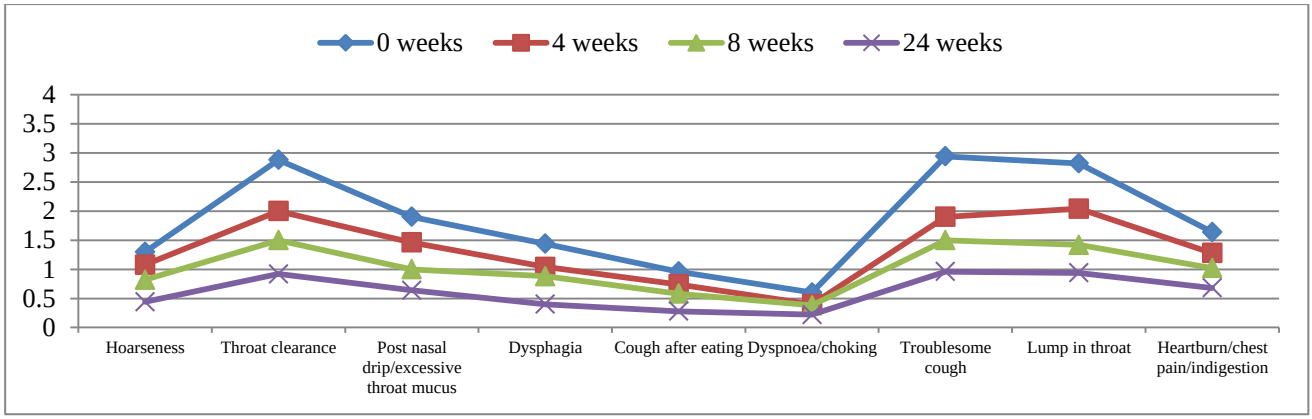

Figure 1: Graph showing response in symptom profile to omeprazole.

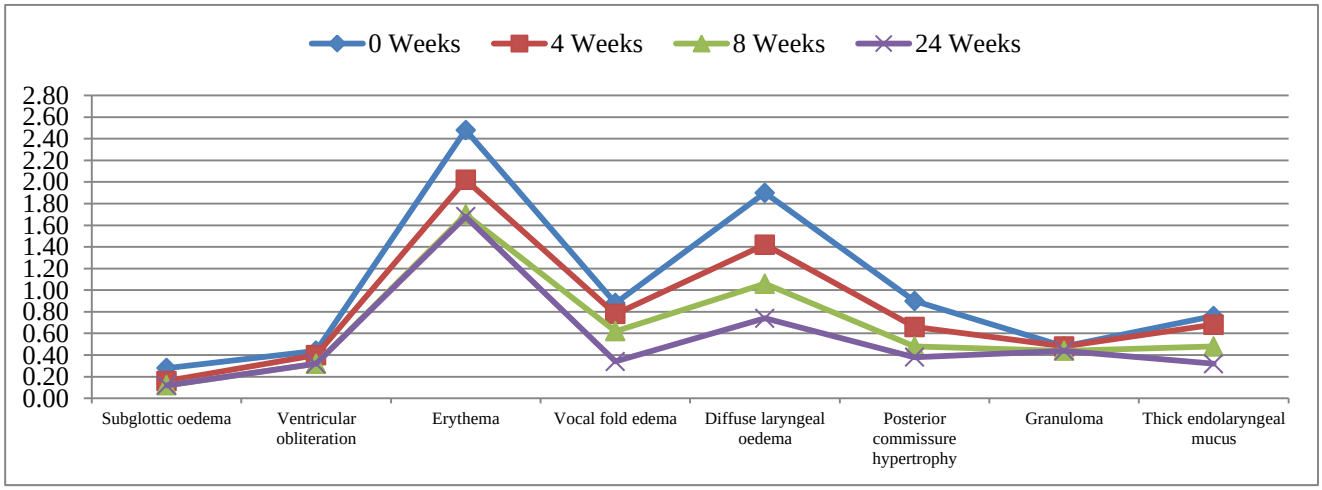

Figure 2: Graph showing response in laryngeal findings to omeprazole.

In the study, there was a significant change in RSI and RFS after receiving omeprazole at 4 weeks, 8 weeks and at 24 weeks duration ($p < 0.0001$).

Non responders in the present study, encountered 2 cases of resistance to PPI at the end of 24 weeks of treatment in terms of insignificant reduction in RSI and RFS. These patients continued to show RSI ≥13 and RFS ≥7 even after 24 weeks of omeprazole therapy.

DISCUSSION

Approximately, 50% of all patients presenting with voice or swallowing disorder exhibit features of laryngo-pharyngeal reflux. Several studies on LPR have found globus pharyngeus as the most common symptom, while some studies have found other symptoms of LPR more common like throat burning, hoarseness, cough.[7-11] In our study most common symptom of LPR was found to be frequent clearing of throat in 98%, which was similar in the study by Toros et al.[12] Other common symptoms seen in our study were sensation of lump in throat and troublesome cough in 96% of patients each. Dyspnoea/choking (38%) was least common symptom seen our patients.

On FOL, the most common sign in our study was found to be erythema/hyperaemia in 84% of patients, which is similar to the findings in various other studies.[7-9,12] Diffuse laryngeal oedema was seen in 82% of our patients. Least common findings were granuloma/granulation (24%), ventricular obliteration (22%) and subglottic oedema (14%). Other authors have noted the most common laryngoscopic signs to be posterior commissure hypertrophy and partial ventricular obliteration which was not seen in our study.[3,13]

Symptomatic improvement in patients in our study was seen after 2 months of therapy however improvement in laryngeal signs took 4 months. These results are similar to studies by Belafsky et al and Bilgen et al.[3,14] Overall RFS showed significant change at 4 weeks of therapy and again at 8 and 24 weeks of therapy and this is similar to various other studies.[2,3]

There is currently no accepted protocol for the most effective treatment for LPR. Among the unresolved issues are the dosing and length of therapy with PPIs and the role of histamine-2 receptor antagonists (H_2RAs) in those unresponsive to PPIs alone. Studies using H_2RAs

have produced only mild to moderate improvement at best as reported by Koufman and Vaezi et al.[1,15]

Metz et al, in their study found that 60% of patients with reflux laryngitis treated with PPI (20 mg omeprazole) for 1 month had symptomatic improvement. In this study after PPI therapy dramatic response in signs and symptoms in patients was seen with 96% response rate with PPI therapy.[16]

Treatment of LPR of more than 6 months may be indicated to attain full resolution of physical findings and to reduce the risk of return of symptoms. Termination of treatment based on the presumption that LPR symptoms are getting better alone may be premature. This study concurs with the view of consensus conference report 1997 on LPR that suggested twice daily PPI treatment needs to be continued for a minimum of 6 months.[17]

Present study encountered only 2 cases of resistance to PPI at the end of 24 weeks of treatment in terms of insignificant reduction in RSI and RFS. In a study by Amin et al increased frequency of resistance to PPI (56%) was encountered owing to once daily dosage of proton pump inhibitors followed by them.[18] Amin et al suggested that increased dosage or frequency of proton pump inhibitors could result in reduced rates of such failure of resistance to treatment.[18] We used twice daily dosage of proton pump inhibitors in this study. Twice-daily dosing is usually employed to better control both nocturnal and daytime oesophageal acid exposure. The likely other mechanisms proposed for resistance to proton pump inhibitors are non-compliance by the patients, impaired bioavailability and associated motility disturbances of oesophagus.[19-22]

CONCLUSION

Laryngopharyngeal reflux is common among the middle aged individuals with a gender predilection for women. This study dealt mainly with combination of clinical features that LPR presents including RSI and RFS scores and time line of improvement of these features with capsule omeprazole. We conclude that an presumptive diagnosis of LPR can be made based on the criteria of RSI and patients be given an empirical therapeutic trial including behavioral and dietary recommendations and 6 months of twice-daily proton-pump inhibitor therapy for an excellent clinical response.

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