International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

PPI in Laryngopharyngeal Reflex as an Emerging Treatment Modality

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Abstract: ***Background: Laryngopharyngeal reflux is a highly prevalent disease and commonly encountered in the otolaryngologists office. Laryngopharyngeal reflux is different from classical gastroesophageal reflux disease in many ways. Laryngopharyngeal reflux refers to backflow of stomach contents into the throat that is into the hypopharynx. Proton pump inhibitors have become the treatment of choice even though conflicting results exists in their response. Treatment requires acid suppression to be as complete as possible and treatment failure is not uncommon Material and methods: About 70 patients diagnosed as a case of LPR on the basis of reflux finding score and reflux symptom index were included in the study. We tried to evaluate the role of PPi in LPR management by observing the effect of PPi on reflux finding score and reflux symptom index . Results: Foreign body sensation was the most common symptom present in 74 of patients followed by frequent clearing of throat in 64 and cough in 56 of patients. Mean RSI of all patients was 24.75 before treatment with proton pump inhibitors. After 8 weeks of therapy with PPi mean RSI dropped to 13.25 and after 16 weeks of PPi therapy mean RSI dropped to 13.25. Significant change in RSI occurred after first 8 weeks of therapy in total and in all age groups and no further significant change occurred in the next 8 weeks Conclusion: RFS of more than 7 and RSI of more than 13 are assoc iated with high risk of LPR. Even though we did not find any patient who did not respond, but vas reported in literature treatment failures are not uncommon. Still we need to perform more well designed, prospective large scale, probably mullticentric studies to find the role of PPi in LPR as many studies don't favour PPi over placebo.***

1. Introduction

Laryngopharyngeal reflex is defined as the retrograde flow of stomach content to the larynx and pharynx whereby this material comes in contact with the upper aerodigestive tract.[1] in contrast gastroiesophageal reflex disease is the flow of stomach acids back into the esophagus. Acid reflex diseases are highly prevalent and GERD and LPR are epidemic.[2,3,4,5,6] . The most common symptom of LPR are excessive throat clearing, coughing, hoarseness, globus pharyngeus. 1 Laryngoscopic findings are also non specific. The most common laryngoscopic finding is reflux laryngitis.[7]The most frequently observed LPR related findings are interarytenoid erythema or hypermeia, infraglottic edema (pseudo sulcus), ventricular obliteration, posterior commissure hypertrophy and pachydermia, granuloma or granulation tissue formation and which excessive endo laryngeal mucous.[8] Pseudosulcus vocalis also known as infra-glottic oedema, is a pattern of oedema on the ventral surface of vocal fold that extends from the anterior commissure to the posterior larynx. The presence of pseudo sulcus alone is suggestive of a diagnosis of LPR.[9] A normal laryngeal examination cannot rule out the presence of LPR.[10] Belfasky etal developed simple non invasive, economical instruments reflux symptom index and reflex finding score to help in the diagnosis of LPR. Reflux finding score 11 ia an 8 item clinical severity rating scale basesd on fibreoptic findings. The scakle includes rating scale based on their fibreoptioc findings. The scale includes most common laryngeal findings related to LPR. It has been concluded that any individual with RFS greater than 7 has more than 95% probability of having LPR.RFS ranges from 0-26(the worst score). Reflux symptom index 12 on the other hand is is a 9 item self administered outcome instrument. This index appears to be valid and is highly reproducible. An RSI of mlore than 13 is considered to indicate LPR. It ranges from 0-45(woprst possible score). Treatment of LPR consists of dietary changes and changes in habits such as weight loss, quiting smoking, avoiding alcohol, and not eating immediately before bedtime. Dietary restrictions include caffine, chocolate, gasified beverages, fat, tomato sauce, red wine 1. The drugs most commonly used for the treatment of LPR are PPIs. Which suppress acid production by directly acting on the H-K ATPase of parietal cells PPIs not only prevent the exposure of the upper aerodigestive tract, but also reduce the damage resulting from the enzymatic activity of pepsin, which requires an acid medium for activation.[13]Responsze to empiric treatment with PPI (the omeprazole test) is a more common and acceptable initiual diagnostic strategy for uncomplicated LPR8. Clinical evidence indicates that pharmacologic intervention should comprise a minimum of 3 months of treatment with PPIs administered twice a day(40 mg omeprazole or an equivalent PPI), 30 to 60 minutes before a meal. This period is important because it provides the highest concentration of drug during the period of stimulation of proton pump by food consumption .[1,14] Rabeprazole can achieve the optimal acid suppression since the first administration and can maintain this advantage in the following days of therapy.

2. Material and Methods

This prospective study was conducted in Dr Ulhas Patil Medical college jalgaon Maharashtra for a period of 2 years from jan 2017 to jan 2019.About 70 patients of different age groups having different symptoms of LPR attending ENT OPD were included in the study. Patients were divided into different age groups. Reflux symptom index and reflux finding score were used to diagnose LPR. Inclusion criteria patients of different age groups with symptoms of LPR for the last 1 month and with both reflux symptom index (RSI)>13(table 1) and reflux finding score (RFS)>7(table 2)

Table 1: Reflux symptom index

Complaint	Yes/no Duration
1.Hoarseness or problem with voice	
2.Frequent clearing of throat	
3. Excessive throat mucus or postnasal drip	
4. Difficulty in swallowing food, liquids or pills	
5. Coughing after having eaten or after lying down	
6. Breathing difficulties or chocking episodes	
7. Troublesome or annoying cough	
8. Sensations of something sticking in throat or a lump in throat	
9. Heartburn , chest pain , indigestion or stomach acid coming up	

Each point is ranked from 0(no problem) to 5(severe problem). It ranges from 0to 45 (worst possible score).

Table 2: Reflux finding score

1. Pseudosulcus	0 absent, 2 percent
2. Ventricular obliteration	0 none, 2 partial, 4 complete
3.Eryrhema/hyperemia	0 none, 2 arytenoid only, 4 diffuse
4. Vocal cord edema	0 none , 1 mild, 2 moderate, 3 severe, 4 obstructing (polypoidal)
5. Diffuse laryngeal edema	0 none , 1 mild , 2 moderate , 3 severe,4 obstructing
6. Posterior commisure hypertrophy	0 none , 1 mild 2 moderate,3 severe, 4 obstructing
7. Granuloma formation	0 present, 2 absent
8. Thick endolarygeal mucus	0 present , 2 absent

It ranges from 0 (lowest possible) to 26(highest possible) Exclusion criteria Patients with reflux finding score less than 7 and/or reflux symptom score less than 13 . patients with history of antireflux medication in the preceding one month. Patients with signs of like infection, malignancy. Procedure All the patients underwent complete ENT examination including indirect laryngoscopy, flexible laryngoscopy. The diagnosis of LPR on first visit was done on the basis of symptom scoring called reflux index symptom and laryngosc opic findings called reflux finding score Follow Up patients were followed for first 16 weeks, on two occasions first at 8 weeks then at 16 weeks. On each follow up visit patient s symptoms were evaluated with reflux symptom index and laryngoscopic finding scored with reflux finding score Role of proton pump inhibitor proton pumps like omeprazole 20 mg twice daily. Esomeprazole 20 mg twice daily, rabeprazole 20 mg twice daily , pantaprazole 40 mg twice daily and lansoprazole 30 mg twice daily were used in the study. RFS and RSI was used to assess patients at first visit. Effect of PPi on reflux finding score and reflux symptom index at each follow up visit was used to assess the role of PPi. RESULTS Total number of patients included in the study were 70. 42(60%) cases were females and 28(40%) were males. Male to female ratio in the study was 2:3. Age of the patients varied from 10 -50 years. No patient was less than 1o years of age. Maximum numbers of patients were in the age group of 31 to 40 years forming about 40 percent of the study group. Mean age of the study population was 38 years.

Table 3: Percent distribution of symptoms (RSI)

Symptoms	Total number of patients	Percentage
Hoarseness	25	36
Frequent clearing of throat	44	64
Excess throat mucus	23	34
Difficulty in swallowing foods, liquids or pills	35	50
Cough after eating or after lying down	21	30
Breathing difficulties	21	30
Trouble some or annoying cough	39	56
Foreign body sensation	51	74
Heartburn, chestpain, indigestion, or stomach acid coming up	35	50

Table 4: Changes of RSI with PPi therapy

Age	Number of patients	Pretreatment (RSI)	Post-treatment after 8 weeks	Post treatment after 16 weeks
0-10	0	0	0	0
11-20	6	24	13	14
21-30	20	26	14	14
31-40	30	25	13	14
41-50	14	24	14	15
Total		24.75	13.5	14.25

Foreign body sensation was the most common symptom present in 74 of patients followed by frequent clearing of throat in 64 and cough in 56 of patients. Mean RSI of all patients was 24.75 before treatment with proton pump inhibitors. After 8 weeks of therapy with PPi mean RSI dropped to 13.25 and after 16 weeks of PPi therapy mean RSI dropped to 13.25. Significant change in RSI occurred after first 8 weeks of therapy in total and in all age groups and no further significant change occurred in the next 8 weeks.

Table 5: Percentage distribution of signs (Reflux finding score)

Findings	Number of patients	
Pseudo sulcus	35	50
ventricular obliteration	53	76
Erythema/hyperaemia	61	88
Vocal fold edema	36	52
Diffuse laryngeal edema	36	52
Posterior commisure hypertrophy	42	60
Granulation/granuloma	28	40
Thick endolaryngeal mucus	28	40

Table 6: Changes of RFS with PPi therapy

Age group	Number of patients	Pre treatment (RFS)	Post treatment RFR after 8 weeks	Post treatment RFS after 16 weeks
0-10	0	0	0	0
11-20	6	13	10	6
21-30	20	15	11	7
31-40	30	13	11	6
41-50	14	13	10	7
Total	70	13	11.5	6.5

3. Discussion

Most common symptom in the study was found to be globus sensation in 74% of patients followed by frequent clearing of throat in 64% of patients and troublesome or annoying cough in 56% of study population. Least common symptom was breathing difficulty. Other studies have also found globus pharyngeus as most common symptom like studies of Mesallam and Stemple, Karkos and Yates, Issing and Karkos, while some studies have found other most common symptom of LPR like throat burning (Pieter Noordzi and Khidir), Hoarseness in 71% (Koufmann), cough(Eubanks et al) Frequent clearing of throat (Toros and Toros).[15,16,17,18,19,20,21] Most common laryngoscopic sign in the study was found to be erythema/hyperaemia in 88% of patients followed by ventricular obliteration in 76% of patients and posterior commisure hypertrophy in 60% of patients. Other studies have also found erythema as most common sign like studies Book and Rhee, Mesallam and Stemple, Karkos and Yates and Toros and Toros.[15,16,21,22]In contrast to our study other authors have noted other most common laryngoscopic signs like posterior commisure hypertrophy by Belfasky and Postma, partial ventricular obliteration by Tezer and Kockar. We noted pseudo sulcus in only 50% of our study groups where as Belfasky et al in a study of 30 patients diagnosed on the basis of pH monitoring found pseudo sulcus in 70% of study subjects and concluded that sensitivity and specificity of pseudo sulcus in the diagnosis of LPR are 70 and 77% respectively. We used RSI and RFI to assess the role of PPi. We found significant improvement in both signs and symptoms after 4 months of PPi therapy. Symptomatic improvement was obvious after 2 months of therapy but laryngeal signs took 4 months to show improvement Our study showed similar results to other studies done for response of RFS to PPi like studies of Belfasky and Postma. Bilgen and Ogut. Overall physical findings did not change significantly after 8 weeks of therapy but it changed so after 16 weeks of therapy and this is in accordance with the literature. Similar results were obtained in other studies like study by Belfasky and Postma Belfasky et al. These difference in their study compare to our study is that we diagnosed LPR on the basisd of RSI and RFS and they diagnosed it on the basis of pH monitoring. First study to use PPi in LPR was by Kamel who used omeprazole. The PPis are most commonly given before meals in most of the studies. Twice daily dosing is usually employed to better control both nocturnal and daytime esophageal acid exposure. We used omeprazole 20 mg twice daily, esomeprazole 20 mg twice daily, Rabeprazole 20 mg twice daily as compared to higher doses used in other studies. Our study after PPi therapy found dramatic response in signs and symptoms and showed unexpectedly 100% response rate with PPi therapy, even though there are different respose rates reported in literature. We observed overall in patients with twice daily PPi for treatment of laryngopharyngeal reflux resulted in good response rate and treatment must be continued for atleasst 4 months. Laryngeal signs may take more time to resolve as al;so reported in literature. Treatment of LPR for more than6 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 pre-mature. This conclusion concurs with the view of consensus conference report 1997 on LPR that suggested twice daily PPi treatment to be continued for a minimum of 6 months.

4. Conclusion

Our patients of LPR responded witin 2 months of therapy, although laryngeal signs took more time to resolve, about 4 months. In most patients with LPR two daily PPi is needed and it should be prescribed nit for less than 4 months . Our results are in accordance with the recommendations of concensus conference report (1997) and American academy of otolaryngology and head and neck surgery. The reflux finding score and reflux symptom index of Wake Forest Universitynare valuable tools for diagnosing LPR as used in our study.RFS of more than 7 and RSI of more than 13 are assoc iated with high risk of LPR. Even though we did not find any patient who did not respond, but vas reported in literature treatment failures are not uncommon. Still we need to perform more well designed, prospective large scale, probably mullticentric studies to find the role of PPi in LPR as many studies don't favour PPi over placebo. Conflict of interest nil source of finding self Ethical clearance taken from the ethical committee.

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