Section: ENT

Original Research Article

EFFECT OF PROTON PUMP INHIBITORS IN LARYNGOPHARYNGEAL REFLUX DISEASE

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Abstract

Background: Laryngopharyngeal reflux disease (LPRD) is a very common disease seen in the ENT outpatient department. Reflux symptom index (RSI) and Reflux findings score (RFS) are used to diagnose LPRD clinically. This study aims to find out the effect of Proton pump inhibitors in the treatment of Laryngopharyngeal Reflux diseae. **Study Design:** Prospective study with quasi experimental design. **Materials and Methods:** 85 patients with symptoms suggestive of laryngopharyngeal reflux disease were studied. Patients were evaluated using Reflux Symptom Index, a set of nine self-assessment questions that are graded from 0 to 5 (with a total score of 0 – 45) according to severity and those with a score of 3 or more in any of the symptom scores were selected and subjected to endoscopic examination, for the assessment of reflux finding score. Subjects were evaluated as 2 (two) groups. Group 1: Pretreatment group - Patients with Laryngopharyngeal reflux disease that was evaluated for reflux symptom index and reflux finding score. Group 2: Posttreatment Group – Patients in the pretreatment group after treatment who were again studied for reflux symptom index and reflux finding score. The Pretreatment group acted as control for posttreatment group. **Result:** The mean reflux symptom index was 20.2 in pretreatment group and 11.2 posttreatment, with medians of 20 and 11 respectively. The pretreatment mean reflux finding score was 9.9 and post treatment was 6.0, with medians of 9 and 5 respectively. All the components of both reflux symptom index and reflux finding score showed significant reduction, following 6 weeks of treatment with proton pump inhibitors. **Conclusion:** LPRD is more common in the age group of 31-40 years. LPRD is more common among females Proton pump inhibitors are highly effective in controlling laryngeal reflux symptom index and laryngeal reflux finding score.

INTRODUCTION

The term Laryngopharyngeal Reflux (LPR) was coined by James and is accepted by the American Academy of Otolaryngology: Head and Neck surgery.[1]

Laryngopharyngeal reflux disease (LPRD) was first described by von Leden and Moore, in the 1960, but it did not come to the forefront of otolaryngology practice until Koufman's landmark thesis on the subject in 1991.[1,2] Laryngopharyngeal reflux disease is an extraesophageal variant of gastroesophageal reflux disease that affects the larynx and pharynx.[3,4]

The other terms used for this in otorhinolaryngology practice are 'extra esophageal reflux', 'chronic laryngitis' and 'supra esophageal complication of gastroesophageal reflux'.[4] Recent studies in this field evidently proves that laryngopharyngeal reflux represents a complex spectrum of abnormalities and it is therefore important to understand the basic scientific concepts relevant to this disease and also the appropriate clinical care of patients with laryngopharyngeal reflux. Laryngeal abnormalities may be caused either by direct injury or damage by a secondary mechanism.[5-7]

It has been shown experimentally that as few as three reflux episodes per week can produce severe laryngeal damage.[1] Direct injury occurs when acid and pepsin comes into contact with laryngeal mucosa, resulting in mucosal damage.[6,8]

Irritation of the distal esophagus by acid may cause a reflux mediated by the vagus nerve, resulting in chronic cough and throat clearing which may in turn

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produce traumatic injury to laryngeal mucosa.[7,9] The incidence of patients presenting to an Otolaryngologist with GERD has been estimated to be 4 percentage to 10 percentage.[10] As otolaryngologists are now more diligent in looking for signs of laryngopharyngeal reflux, such as posterior laryngeal edema and erythema, obliteration of the laryngeal ventricles and inter arytenoid hypertrophy.[2,11]

The treatment for laryngopharyngeal reflux based on these findings has become increasingly common.[2,12] Though Laryngopharyngeal reflux disorder is a common scenario in clinical practice, it is usually under reported, misdiagnosed or neglected for want of a definitive diagnosis. Because of the lack of convincing evidence regarding diagnostic techniques, causation in individual patient and deficient studies that have produced conflicting conclusions; the diagnosis and management of LPRD remains controversial. The prevalence of laryngopharyngeal reflux disease is very high.[13,14] There are no epidemiological studies to show us the prevalence of laryngopharyngeal reflux disease in India. According to Koufman, 50 percentage of all patients presenting to their centre with laryngeal and voice disorders had laryngopharyngeal reflux as documented by dual pH probe studies.[13,15]

Because of the high prevalence of the disease and potential serious consequences including laryngeal carcinoma, it is important to be familiar with contemporary perspectives on this disorder.[13,16,17] In this study, we would like to evaluate whether proton pump inhibitor therapy would aid in reducing the abnormal 'reflux finding score' in laryngopharyngeal reflux disease.[18,19]

MATERIALS AND METHODS

Study Design

This was a prospective study with quasi experimental design to know the effect of proton pump inhibitors on the reflux symptom score and reflux finding score in laryngopharyngeal reflux disease.

Study Population and Setting:

85 patients between the age group of 18 to 80 years, who came to the outpatient department of Otorhinolaryngology with symptoms suggestive of laryngopharyngeal reflux disease, were included in the study.

Period of Study

January 2023 to December 2023

Study Groups

Subjects were evaluated as 2 (two) groups.

Group 1: Pretreatment group:

Patients with Laryngopharyngeal reflux disease, who fulfill the criteria of inclusion and exclusion, were included in the study and their reflux symptom index and reflux finding score were studied.

Group 2: Posttreatment Group

Pretreatment group was again studied for reflux symptom score and reflux finding score. The Pretreatment group acts as control for posttreatment group.

Equipment used: Flexible Nasopharyngo Laryngoscope – Karl Storz

Procedure: Those patients who fulfilled the inclusion and exclusion criteria were enrolled and subjected to endoscopic examination. Patients were evaluated using Reflux Symptom Index, a set of nine self-assessment questions that are graded from 0 to 5 (with a total score of 0 to 45) according to severity and those who were having a score of 3 or more in any of the symptom scores were selected for endoscopic examination for the assessment of reflux finding score after getting consent. 2 drops each of Nasal decongestants (Xylometazoline) and 4 percentage Xylocaine was instilled in the patient's nostril for nasal decongestion and local anaesthesia.

Xylocaine viscous 10 ml was administered orally to the patient. The patient was advised not to swallow and retain the preparation for 2 minutes, to anaesthetize the throat. Flexible nasopharyn-golaryngoscope was introduced with proper lubrication through nostril and guided to the laryngopharnx and the larynx was assessed.

Patients whose reflux finding scores were above 7, were given Proton pump inhibitors (Pantoprazole 40 mg twice daily 1 hour before food),[8] for a duration of 6 weeks and were evaluated again with Reflux Symptom Index and endoscopic examination

Endoscopic examination was done by the study investigator and confirmed by an expert who was not below the post of an Assistant professor. We recorded the Reflux Symptom Index and Reflux Finding Score on the proforma along with a set of questions regarding their dietary, history and habits.

Those patients whose reflux finding scores were above 7 were given 6 weeks of Proton pump inhibitors in the prescribed dose (Pantoprazole 40 mg twice daily)

In the follow up, patients were again assessed with Reflux symptom index questionnaire and a repeat nasopharyngolaryngoscopy was done and Reflux Finding Score recorded.

Sample Size,[20]

$$N = \frac{\left(Z_{crit} + Z_{pwr}\right)^2 X\ 4\ X\ \sigma^2}{D^2}$$

Z_{crit} (95% Confidence Interval) = 2.576 (Standard Normal Deviate corresponding to selected significance criteria.

Z_{pwr} (0.95) = 1.645 (Standard normal Deviate Corresponding to selected Statistical power)

σ - Assumed standard deviation

D – minimum expected difference between the two means

Power = 0.95 (95%)

$$N = \frac{(2.576 + 1.645)^2\ X\ 4\ X\ 3^2}{3^2}$$

$$= 72$$

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Since we are doing a non–parametric analysis, power efficacy of 5 percentages extra was also considered. Since we expected a loss of follow up in approximately 10 percentages of patients, the sample size was upsized by 10 percentage. Hence the total sample size has been upsized to 82.

As the same group act as the control and comparator the sample size of one group is 41, ie, 41 patients were studied pretreatment and posttreatment.

Inclusion Criteria

a. Patients with symptoms suggestive of laryngopharyngeal reflux disease with a reflux symptom index of 3 or more in any of the symptom scores.
b. Patients with symptoms suggestive of laryngopharyngeal reflux disease with a reflux finding score of more than 7 as per laryngeal endoscopic examination.
c. Patients who were between the age group of 18 and 80.

Exclusion Criteria

a. Those who were taking proton pump inhibitors for the past one month.
b. Patients who were hypersensitive to proton pump inhibitors.
c. Those who were on any regular drugs.
d. Pregnant women.
e. Those who did not give consent.
f. Patients below 18 years of age.
g. Patients above 80 years of age.
h. Patients with other co-existing laryngeal pathology

Parameters to be studied

Reflux Symptom Index,[1]

Within the past month, how did the following problems affect the patient?

It was ranked from 0 to 5 (0- no problem to 5- severe problem)

- Hoarseness or a problem with your voice
- Clearing of throat
- Excess mucous production in the throat or postnasal drip
- Difficulty in swallowing food, liquid, or pills
- Coughing after you have eaten or after lying down
- Breathing difficulty / choking episodes
- Troublesome/ annoying cough
- Sensation of something sticking in your throat or a lump in your throat
- Heartburn, chest pain, indigestion or stomach acid coming up

Reflux Finding Score,[1] (endoscopic grading scale for laryngopharyngeal reflux disease) score 0-26more than 7 is significant

- Subglottic edema 0- absent 2- present
- Ventricular edema 2- partial 4- complete
- Erythema/hyperemia 2- arytenoids only 4- diffuse
- Vocal fold 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 tissue 0- absent 2 present
- Thick endolaryngeal mucus 0- absent 2- present

Statistical analysis:

- Data was entered into Microsoft Office 365 Excel for windows 7
- SPSS Version17.0 for Windows was used to analyze the data
- Quantitative variables were described by mean, sd, Median, minimum and maximum.
- Qualitative variables were described by percentage distribution.
- For Scores with non-normal (Non-Gaussian) distribution non-parametric test, Wilcoxon's signed rank test was used for comparison of pretreatment and posttreatment scores.
- Between groups comparisons of quantitative variables were analyzed by t test or ANOVA.
- Paired comparisons of qualitative variables were analyzed by McNemar test.o A p - value of 0.05 was considered as level of significance..

RESULTS

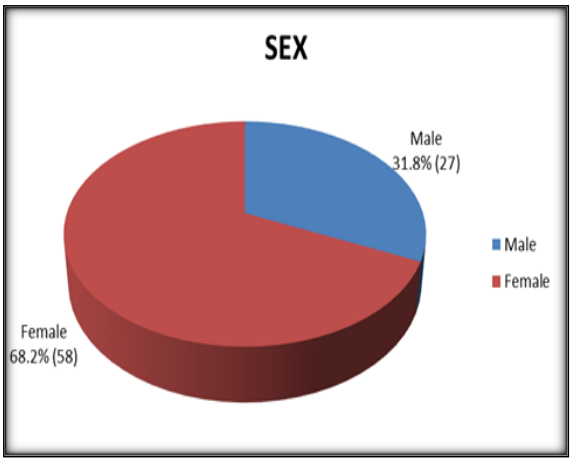

Figure 1: Distribution of Patients based on Sex

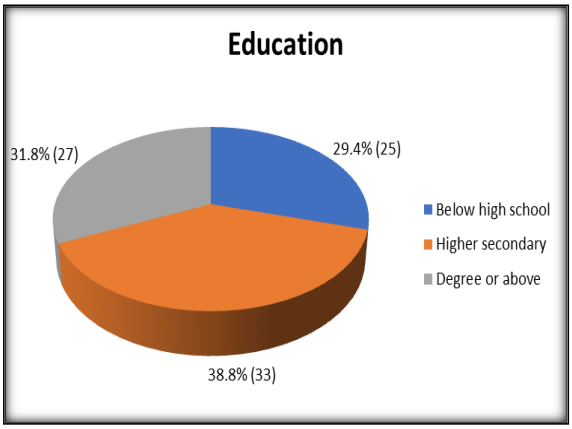

Figure 2: Distribution of Patients based on Education

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In our study, 85 patients in the age group of 19 to 74 years were included. The mean age was 43.7 years. Out of all patients, 7 were lost to follow up after 6 weeks, and therefore reflux symptom index and reflux finding scores were analyzed using the remaining 78 patients. But in the sample size calculation we expected 10 percentage would be lost to follow up, that is 8. According to the statistics only 41 patients were required for the study. But there were 78 patients with proper follow up. This figure is more than the number expected for the adequate strength of the study.

When we have considered habituations among the patients 16, 16 and 8 out of 85 had a habit of smoking, alcohol consumption and tobacco chewing respectively.

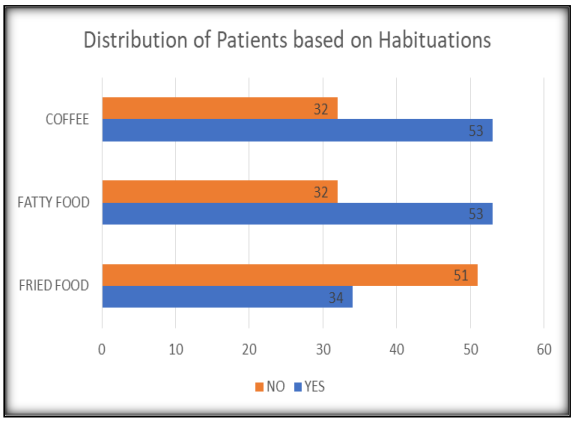

Figure 3: Distribution of Patients based on Habituations

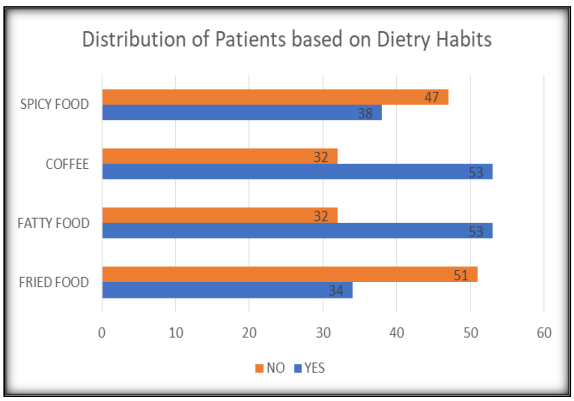

Figure 4: Distribution of Patients based on Dietry Habits

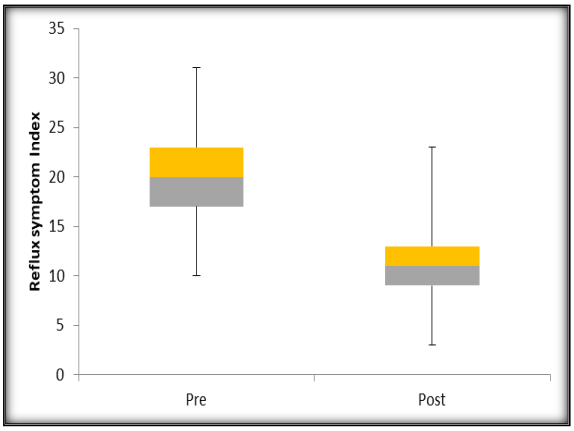

Figure 5: Boxplot Diagram Describing Reflux Symptom Index. Among Pretreatment and Post Treatment Group

Lower and upper end of the whisker represents minimum and maximum index. Lower border of the box represents First quartile and the upper border represents the Third quartile and the middle line (the line of separation of the two coloured box) represents the median index.

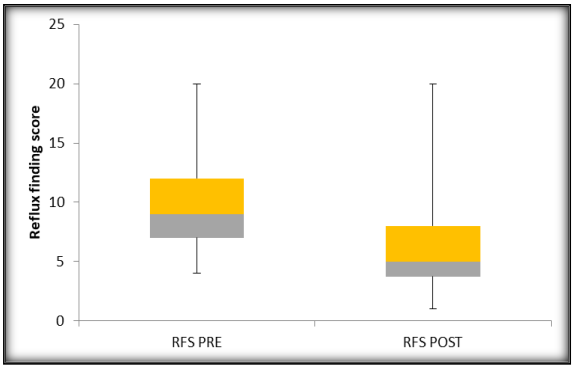

Figure 6: Boxplot Diagram Describing Reflux Finding Score. Among Pretreatment and Post Treatment Group

Lower and upper end of the whisker represents minimum and maximum index. Lower border of the box represents First quartile and the upper border represents the Third quartile and the middle line (the line of separation of the two coloured box) represents the median index.

Table 1: Distribution of Patients based on age

Age in years	Frequency	Percent
<30	19	22.4
31-40	23	27.1
41-50	18	21.2
51-60	15	17.6
>60	10	11.8
Total	85	100.0

Majority of Patients were females.

Table 2: Comparison of Reflux Symptom Index among Pre-treatment and Post treatment Group

Reflux Symptom Index	Pre treatment	Post treatment
Mean	20.2	11.2
SD	4.6	4.5

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Minimum	10.0	3.0
First quartile	17.0	9.0
Median	20.0	11.0
Third quartile	23.0	13.0
Maximum	31	23
Wilcoxon signed Rank test – z	7.483	
P	<0.001	

Table 3: Comparison of Reflux Finding Score among Pre-treatment and Post treatment Group

Reflux Finding Score	Pre-treatment (N=85)	Post-treatment (N=78)
Mean	9.9	6.0
SD	3.7	4.1
Minimum	4.0	1.0
First quartile	7.0	3.8
Median	9.0	5.0
Third quartile	12.0	8.0
Maximum	20	20
Wilcoxon signed Rank test – z	7.133	
P	<0.001	

Table 3a: Percentage of Reduction in Reflux Symptom Index

SEX	N	Percentage reduction in RSI		t	p
		Mean	Sd		
Male	27	44.8	13.7	.218	.828
Female	51	43.9	19.7		

Table 4: Comparison of Percentage Reduction in Reflux Finding Score among Males and Females

SEX	N	Percentage reduction in RFS		T	P
		Mean	SD		
Male	27	43.4	24.2	.699	0.487
Female	51	39.1	26.7		

Table 5: Percentage of Reduction in Reflux Symptom Index Based on Habits

		N	Percentage reduction in SI		t	p
			Mean	SD		
Smoking	Yes	16	42.1	18.2	.534	0.595
	No	62	44.8	17.8		
Alcoholism	Yes	16	44.6	17.9	.092	0.927
	No	62	44.1	17.9		
Tobacco Chewing	Yes	6	41.2	18.2	.431	0.668
	No	72	44.5	17.8		

Table 6: Comparison of Mean age and Age group with maximum patients with other studies

	Our Study	Patigaroo SA et al. (2011)	Mattoo O et al. (2012)
Mean age	43.7	38.0	42.3
Age group with maximum patients	31 – 40	31 – 40	31 – 40

Table 7: Comparison of Gender wise distribution with other studies

Our Study		Belafsky et al. (2002)		Patigaroo et al. (2012)		Preetam Chapitty (2014)	
Male	Female	Male	Female	Male	Female	Male	female
31.8%	58.2%	56%	44%	40%	60%	49.8%	50.2%

Table 8: Comparison of change in Reflux Symptom Index with Other Studies

Our Study		Belafsky et al. (2002)		Mattoo et al. (2012)	
Pretreatment	Posttreatment	Pretreatment	Posttreatment	Pretreatment	Posttreatment
20.2	11.2	21.2	12.8	20.7	8.9

Table 9: Comparison of pretreatment and posttreatment reflux finding score with other study

Our Study		Patigaroo et al.	
Pretreatment	Posttreatment	Pretreatment	Posttreatment
9.9	6.0	12	6.5

[Table 2] compares reflux symptom index of pre-treatment and post treatment groups. The mean pre-treatment symptom index of 20.2 was reduced to 11.2. The minimum score in the pre-treatment group was 10 while that of the post treatment group was 3. The maximum score in the pre-treatment group was 31 while that of post treatment group was 23. All the scores were analyzed using Wilcoxon signed rank test which gave a p value <0.001 which is highly significant.

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[Table 3] shows a comparison of Reflux Finding Scores in the pre-treatment and Post treatment groups. The mean score in the pre-treatment group was 9.9. A reduction in the mean pretreatment score to 6.0 is seen in the post treatment group. The standard deviation among pre-treatment and post treatment group were 3.7 and 4.1 respectively. The Minimum score in pre-treatment group was 4 where as in post treatment group it was 1. The maximum value being, 20 for both the groups. All the values were analyzed statistically, Wilcoxon signed test gave a p value <0.001 which was highly significant.

[Table 3a] The above table and figure shows a mean percentage reduction of 44.8% in males and 43.9 among females. Statistically there is no significant relation between the reduction in reflux finding index and sex. ANOVA gave a p value of 0.823.

[Table 4] showed a mean percentage reduction of 43.4 among males and 39.1 among females. On statistically analyzing the mean reduction in reflux finding score it gave a p value of 0.487 which is not significant.

[Table 5] shows Mean percentage reduction in reflux Symptom Index among different habituations. This study did not show any relation with habits and reduction in Reflux symptom score after treatment. The p values for smoking, alcoholism and tobacco chewing after analysis were >0.05 which is not statistically significant.

DISCUSSION

The present study was aimed to evaluate the effect of Proton pump inhibitors on the reflux symptom index and reflux finding score among those who suffer from Laryngopharyngeal reflux disease. This study included 2 groups each group comprising of 85 patients, of which the pretreatment group acts as the control and the same patients after treatment act as the test group. Those patients with other co-existing laryngeal pathology, patients who are hyper sensitive to proton pump inhibitors, who are on proton pump inhibitor therapy for the past one month and pregnant women were excluded from the study.

In a study of 50 Indian patients with LPRD by Suhail Amin Patigaroo and colleagues (Aligarh, Uttar Pradesh) in 2011; 40% belonged to the age group of 31-40 years with a mean age being 38.[21] Another study by Mattoo O and colleagues (2012) in Srinagar showed a mean age of 42.3 years.[12] We also observed a peak incidence of LPRD in the 3140 years age group, with the mean age being 43.07 years. We had 22.4% in the age group of less than 30 years, 21.2% in the age group of 41-50 years, 17.6% in the age group of 51-60 years and the least being (11.8%) in the age group of greater than 60 years.

Gender based distribution of the subjects in our study revealed that 31.8% were males and 58.2% females. However Belafsky and colleagues in North Carolina, United States (2002) showed a male predominance of 56% in his study of 25 patients.[15] In the Indian context, Suhail A Patigaroo and colleagues (2012), observed that 60% of the patients with LPRD were females.[21] Another study by Preetam Chappity and colleagues (2014) conducted in New Delhi showed an almost equal distribution among males and females in their study of 234 Indian patients with LPRD.[22]

An assessment of the educational qualification of the subjects showed that 29.4% that is 25 patients had only primary school education, 38.8% (33 patients) possessed higher secondary education and 31.8% (27 patients) had a collegiate education.

Among the 85 patients personal history of smoking was present in 18.8% (16 patients), alcoholism 18.8% (16 patients) and tobacco chewing 9.4% (8 patients).

The association of LPRD with dietary habits was observed as follows. 60% i.e. 51 patients used to take fried food, 55% (47 patients) used to take spicy food, 37.6% (32 patients) used to take fatty food regularly and 37.6% (32 patients) used to drink coffee.

Effect of Treatment on the Outcome:

The effect of treatment of LPRD were assessed primarily based on Reflux Symptom
Index and Reflux finding Score

Effect of treatment on Reflux Symptom Index:

In our study the mean reflux symptom index for pretreatment group was 20.2 and it was reduced to 11.2 in the posttreatment group. Wilcoxons signed rank test was done for the pretreatment and posttreatment group and it gave a z value of 7.483 and p <0.001 which is highly significant.

A study by Belafsky and colleagues in North Carolina, United States among Americans showed a reduction of mean Reflux symptom index from 21.2 to 12.8 among pretreatment and posttreatment group.[15] Another study by Mattoo and colleagues in Indian population, showed a reduction of mean RSI from 20.7 to 8.9 between pretreatment and posttreatment group when treated with twice daily dose of PPI and Domperidone for a duration of 4 months.[12] The results obtained from both the studies were comparable to ours.

In our study an attempt has been made to compare the reduction in each component of the reflux symptom index. There was no literature available where such a comparative pre and posttreatment analysis of each component of the reflux symptom index has been done.

Effect of treatment on Reflux finding score:

In our study the comparison of reflux symptom index of pretreatment group with that of the posttreatment group showed a difference of 3.9 i.e. a reduction from 9.9 to 6 with 6 weeks of treatment. The data was analysed used Wilcoxons signed rank test and it showed a p value <0.001 which is highly significant.

Suhail A Patigaroo and colleagues' in their study of 50 Indian patients with LPRD, showed a mean

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reduction in Reflux finding score from 12 in the pretreatment to 6.5 in the posttreatment group. These values are comparable to our study.[21]

We also made an attempt to compare each component of the Reflux finding score among the pretreatment and posttreatment group, which was not done in previous
studies.

Our study didn't show any gender difference, in the reduction of reflux symptom index or reflux finding score.

There was no relation with dietary habits and habituation in the reduction of reflux symptom index or reflux finding score, except for an incidental finding of a statistically significant p value of 0.036 in patients who consume fatty food. No strict dietary and lifestyle modification/ restrictions were imposed on the patients. So the comparison with dietary habits and habituations is outside the scope of this study.

CONCLUSION

LPRD is more common in the age group of 31-40 years. LPRD is more common among females Proton pump inhibitors are highly effective in controlling laryngeal reflux symptom index and laryngeal reflux finding score.

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