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ORIGINAL RESEARCH

Role of Reflux Finding Score (RFS) and Reflux Symptom Index (RSI) as potential predictors for Proton Pump Inhibitor response in patients with Globus Pharyngeus

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ABSTRACT

Background: Globus pharyngeus is a multifactorial disorder with a mostly unidentified cause, which is defined as a non-painful sensation of a lump, foreign body, or tightness in the throat. Over 4% of all ENT clinic patients complain of globus sensation, which is quite common among the general population. Since the major cause of the globus is found to be GERD (Gastroesophageal reflux disease), the most practical therapeutic management of the globus would be empirical proton pump inhibitors (PPI) as a first attempt. Reflux symptom index (RSI) and reflux finding score (RFS) were initially used to document the clinical severity of laryngopharyngeal reflux (LPR) and to assess treatment efficacy. The RFS and RSI scores were used in this study to investigate the response rate and clinical predictors of symptom response to PPI treatment in patients with globus pharyngeus. **Materials and methods:** This Prospective interventional study was performed in the department of E.N.T at tertiary care teaching hospital in rural karnataka over 18 months. A sample of 100 globus pharyngeus patients was selected and evaluated using RSI and RFS on enrollment. They were treated with a twice-daily dose of esomeprazole 40mg for 2 months and RSI & RFS were readministered. Pre and post-treatment scores were compared and changes in the severity of globus pharyngeus correlated with the change in scores. **Results:** Before the treatment, 65% of the patients had RSI >13 and 66 % of the patients had RFS >7, after the treatment RSI was significantly reduced, with patients having RSI >13 being 12 % and RFS score >7 seen in only 1% of the patients. Further evaluation showed that a statistically significant reduction was seen in RSI with a p-value of 0.017 and RFS scores with a p-value of 0.0001. Evaluation of mean RSI and RFS scores between responders and non-responders did not show any significant difference pre and post-treatment symptoms concerning globus pharyngeus. **Conclusion:** The empirical treatment of all globus pharyngeus patients with esomeprazole is not effective. Globus pharyngeus was relieved with esomeprazole in patients whose symptoms were due to laryngopharyngeal reflux. Esomeprazole was not universally helpful in globus patients with high RSI and RFS scores. Also, RSI and RFS cannot be used as predictors for PPI response in globus pharyngeus patients according to our study.

Keywords: GERD (Gastroesophageal reflux disease), proton pump inhibitors (PPI), Reflux symptom index (RSI), Reflux finding score (RFS), Laryngopharyngeal reflux (LPR).

INTRODUCTION

Globus pharyngeus is a multifactorial condition with a largely unknown etiology and is defined as a non-painful sensation of a lump, foreign body, or tightness in the throat (1). Over 4% of all ENT clinic cases involve globus sensation, which is very common in the general population(2). It affects both men and women equally and peaks in incidence around middle age.

Conditions such as GERD (Gastro esophageal reflux disorder), abnormal upper esophageal sphincter function, esophageal motor disorders, pharyngeal inflammatory causes, such as pharyngitis, tonsillitis, and chronic sinusitis, upper aerodigestive malignancy, hypertrophy of the base of the tongue, retroverted epiglottis, thyroid conditions, cervical heterotopic gastric mucosa, rare laryngopharyngeal tumors, psychological factors, and stress may contribute to globus pharyngeus. According to recent studies,

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major etiological factors for globus pharyngeus include GERD, disturbed upper esophageal sphincter (UES), psychological illness, and stress(3).

It is challenging to establish a true diagnostic investigation and treatment for this multifactorial condition (3). Typically, patients with typical globus symptoms do not need any additional testing beyond an outpatient nasolaryngoscopy(4).

Since GERD is the primary cause of globus, empirical anti-reflux therapy would be the most practical diagnostic and therapeutic management of globus (3). Additionally, meta-analysis research has produced conflicting findings regarding the effectiveness of PPI in treating patients with LPR, including those with globus pharyngeus(5–7).

There is currently little information available on the function of PPIs in the primary complaint of globus pharyngeus (8). In patients with globus pharyngeus sensation, clinical predictors of symptom response to PPI are also infrequently described (9).

LPR (Laryngopharyngeal reflux) has non-specific signs and symptoms that can be confused with other laryngeal conditions brought on by postnasal discharge, neurogenic mechanisms, smoking, allergies, infections, vocal abuse, and other non-pathological variations(10). For evaluating the severity of LPR symptoms, Belafsky proposed the reflux symptom index (RSI). He also created the reflux finding score (RFS), which is based on endolaryngeal signs, to document the physical findings and severity of LPR (11,12). Therefore, this study aims to investigate the response rate and clinical predictors of symptom response to PPI treatment in patients with globus pharyngeus, using RFS and RSI. Both instruments were initially used to record the clinical severity of LPR and assess the effectiveness of its treatment. (11,12). However, both tools might be equally useful for diagnosing suspected LPR patients whose main symptom is globus pharyngeus. Additionally, both tools might be useful in predicting how such a treatment will be effective.

MATERIALS AND METHODS

Source of data: This Prospective interventional study was performed in the department of E.N.T at tertiary care teaching hospital in rural Karnataka over 18 months.

Sample size: The sample collection study included 100 patients with the primary complaint of globus pharyngeus. The sample size has been concluded from the statistical records of globus pharyngeus patients who have visited the ENT OPD.

Sampling procedure: A sample of 100 patients with the primary complaint of globus pharyngeus was selected by convenient sampling technique from patients attending ENT OPD for one and a half years.

Study design: A prospective interventional study.

Inclusion criteria

1. Age >18years and <65years.
2. Patients with complaints suggestive of Globus pharyngeus.

Exclusion criteria

1. Infectious laryngitis.
2. Known autoimmune disorders.
3. History of previous bariatric surgery or anti-reflux surgery.
4. Previous history of radiotherapy.
5. Recent use of PPIs for ≥ 6 month

Statistical Analysis

- After entering the data in a Microsoft excel sheet, the pre and post-test scores were compared using the paired t-test for normally distributed data (RSI scores) and the Wilcoxon signed ranks test for non-normallydistributed data (RFS scores).
- Potential predictors of PPI response (RSI and RFS combined as well individually) were explored using a binary logistic regression.
- Spearman's correlation was performed to determine the association between baseline RSI and RFS.
- p-values < 0.05 were considered statistically significant. Success rates were expressed with their 95% CI.

Method of collection of data

- A detailed history consisting of general information and symptoms of globus pharyngeus followed by an ENT examination was undertaken after written informed consent. Patients were asked the Reflux symptom index (RSI) questionnaire and were also assessed by video laryngoscopy for documenting Reflux finding score (RFS) on enrolment.
- Routine blood investigations like Complete blood picture, ESR, and Peripheral smear were done to rule out anemia and any other infective causes.
- All the patients were treated with a twice-daily dose of Esomeprazole 40 mg for 2 months.
- RSI and RFS were readministered after 2 months for evaluation.
- Post-treatment RSI and RFS were compared with pretreatment scores. Changes in the scores after the treatment was correlated with changes in the primary complaint of globus pharyngeus.

RESULTS

In this study, majority of the patients with globus pharyngeus were between the age groups of 51-60 years (35 %) followed by 41-50 years (24 %). Majority of the study population in this study were females (60 %) as compared to males (40%).

The total Reflux Symptom index was evaluated in the study before initiating treatment and majority of the patients had RSI above 13 (65%) and RSI less than 13 was found in 35% of the patients. (Table 1)

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Reflux Symptom index	Frequency	Percentage
≤ 13	35	35
> 13	65	65

Total Reflux Finding Scores were evaluated in the study and majority of the patients before treatment had RFS above 7 (34 %) and RFS less than 7 was found in 66 % of the patients. (Table.2)

Reflux Finding Score	Frequency	Percentage
≤ 7	66	66
> 7	34	34

The total Reflux Symptom Index was evaluated in the study and the majority of the patients before treatment had RSI above 13 (12%) and RSI less than 13 was found in a majority of the patients 88 % of the patients. (Table.3)

Total Reflux Symptom Index	Frequency	Percentage
≤ 13	88	88
> 13	12	12

The total Reflux Finding Scores were evaluated in the study and the majority of the patients before treatment had RFS above 7 (34 %) and RFS less than 7 was found in 66 % of the patients. (Table.4)

The Total Reflux Finding Score	Frequency	Percentage
≤ 7	99	99
> 7	1	1

The comparison of total reflux symptom scores has been compared between the pre and post-treatment by Chi-Square test and there was a significant improvement in the total symptom scores from 35 patient's pre-treatment to 88 patients at the end of treatment with a p-value of 0.017. (Table.5)

The total Reflux Symptom index	Post-Treatment			P value
Pre-Treatment	≤ 13	> 13	**Total**	**0.017**
≤ 13	35	0	35	
> 13	53	12	65	
Total	88	12		

The total reflux finding scores before and after treatment were compared by Chi-Square test and the reflux finding scores improved significantly after treatment from 66 patients having less than 7 scores before treatment to 91 patients after treatment with a p-value of 0.0001.(Table.6)

Total Reflux Finding Score	Post-Treatment		Total	P value
Pre-Treatment	≤ 7	> 7		**0.0001**
≤ 7	66	0	66	
> 7	25	9	34	
Total	91	9	100	

The total reflux symptom index as well as the reflux finding scores showed a significant (P value < 0.05) reduction within the responders and non-responders groups on doing paired t-test. (Table.7)

The Total Reflux Symptom Score	Responders N=44 (mean)	Non-Responders N=56(mean)	P value @
PRE-TREATMENT	15.11 ± 4.5	14.79 ± 4.5	.722
POST-TREATMENT	9.23 ± 3.7	9.59 ± 4.1	.650
P value#	.0001	.0001	

The total Reflux Finding Scores	Responders N=44(mean)	Non-Responders N=56(mean)	P value @
PRE-TREATMENT	6.5 ± 2.41	6.3 ± 3.5	.702
POST-TREATMENT	3.4 ± 1.8	4.2 ± 2.8	.082
P value#	0.0001	<0.0001	

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On comparing the mean RSI scores of responders and non-responders using the unpaired t-test, there was no significant difference found before (p-value of 0.722) and after treatment (p-value of 0.650). Similarly, on comparison of mean RFS scores of responders and non-responders using unpaired t-test, there was no significant difference found before (p-value of 0.702) and after treatment (p-value of 0.082).

On evaluation, there was no significant correlation found between the reflux symptom index and reflux finding scores with the outcome of treatment in the Globus pharyngeus. (Table.8)

Correlation		The total Reflux Symptom index	Total Reflux finding Scores
The outcome of the treatment	R	-0.157	-0.130
	P value	0.572	0.199

On performing spearman's correlation with total RSI, spearman's coefficient R (rho) value was found to be -0.157 and the p-value was 0.572 and with total RFS, R (rho) value was found to be -0.130, and p-value was 0.199 showing nil correlation.

Multivariate logistic regression analysis was performed to ascertain the predictive capability of age, gender, RSI total score, and the RFS total scores. On evaluation, there was no significant effect of the RSI and RFS on the Globus Pharyngeus Outcome. (Table.9)

	B	S.E.	P-Value	Exp(B)	95% C.I. for EXP(B)	
Age	-0.015	0.018	0.404	0.985	0.95	1.021
Gender (1)	0.362	0.447	0.418	1.436	0.598	3.448
RSI total score	0.027	0.046	0.56	1.027	0.939	1.123
RFS total score	0.035	0.076	0.644	1.036	0.892	1.202

DISCUSSION

The globus is a feeling of a lump in the throat in which the movement of food is unrestricted. The fact that globus is unrelated to swallowing and may even get better with swallowing is a crucial distinction. Most globus patients do not describe a history of food dysphagia.(13)

The Globus pharyngeus was first described by Hippocrates over 2500 years ago. The ailment was first accurately described in 1707 by Purcell, who postulated that globus was caused by pressure on the thyroid cartilage brought on by the neck's strap muscles contracting. Due to its frequent correlation with menopause or psychogenic conditions, globus used to be referred to as "globus hystericus." Malcomson, however, first used the more proper terminology "globus pharyngeus" in 1968 after learning that the majority of globus patients lacked a hysterical personality and found an association with gastroesophageal reflux(3,14–16).

Gastroesophageal reflux (GER) has been proposed to be a primary etiology, perhaps accounting for 23%–68% of globus patients, although there is still much disagreement regarding the causal significance of GERD in individuals with globus. Malcomson was the first to connect GERD to the sensation of globus by using a barium swallow to identify reflux in more than 60% of globus patients.

Cherry et al. demonstrated that 10 out of 12 people complained of globus when acid was pumped into the distal esophagus, while Koufman discovered that 58% of patients with globus had abnormal pH findings. In a study that involved 25 patients with globus and hoarseness and 24-hour double-probe pH monitoring, 72% of the participants showed pathologic reflux, and the globus symptom score was considerably greater in GERD patients than in those without(3,18–20).

The correlation between GERD and the globus sensation has been explained by two fundamental mechanisms: (1) Laryngopharyngeal reflux (LPR), is the direct irritation and inflammation of the laryngopharynx due to retrograde movement of gastric contents; (2) Vasovagal reflex hypertonicity of the UES caused by acidification or distention of the distal esophagus.

Additionally, it has been proposed that abnormal UES function may contribute to globus sensation. According to research, people with globus feeling experience elevated UES pressure substantially more frequently than controls (28% vs. 3%), which suggests that hypertensive UES may be a contributing factor to globus. A patient with globus and extremely high UES pressure also experienced a remission of the globus symptom and a drop in UES pressure after receiving a botulinum toxin injection into the cricopharyngeal muscle.

Other causes for globus pharyngeus include pharyngeal and esophageal motor disrders , pharyngeal inflammatory disorders, upper digestive tract malignancies, Tongue base hypertrophy, retroverted epiglottis, cervical heterotrophic gastric mucosa, stress and other psychological factors. (23-32)

LPR is a non-specific illness, and its symptoms and physical findings might be mistaken for other laryngeal conditions brought on by things like smoking, allergies, infections, vocal abuse, postnasal discharge, neurogenic causes, and non-pathological variations. For evaluating the intensity of LPR symptoms, Belafsky et al. presented the reflux symptom index (RSI). They also created the reflux

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finding score (RFS), which is based on eight endolaryngeal indicators, to record the physical findings and severity of LPR. RFS and RSI may not be reliable diagnostic techniques for LPR in patients with globus, since Park et al showed that they have limited specificity in globus patients(3). (Table.10 and table. 11)

Reflux Symptom Index (RSI)						
0 =no problem 5= severe problem						
1. Hoarseness or a problem with voice	0	1	2	3	4	5
2. Clearing of throat	0	1	2	3	4	5
3. Excess throat mucous or postnasal drip	0	1	2	3	4	5
4. Difficulty swallowing food, liquids, or pills	0	1	2	3	4	5
5. Coughing after eating 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 the throat orlump in the throat	0	1	2	3	4	5
9. Heartburn, chest pain, indigestion, or stomachacid coming up.	0	1	2	3	4	5

Reflux Finding Score (RFS)	
Subglottic Edema	2= present, 0 = absent
Ventricular Obliteration	2= partial, 4 = complete
Erythema/Hyperemia	2=arytenoids, 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	2=present, 0= absent
Thick Endo laryngeal Mucus	2 =present, 0 = absent

The management of laryngopharyngeal reflux (LPR) typically involves dietary and lifestyle modifications, long-term proton pump inhibitor (PPI) therapy, alginate preparations, and anti-reflux surgery. In the present study, all patients with a clinical diagnosis of globus pharyngeus were treated with a PPI (esomeprazole), regardless of whether they exhibited the classical symptoms of LPR. Following the completion of therapy, although there was a statistically significant improvement in the Reflux Symptom Index (RSI) and Reflux Finding Score (RFS), a substantial proportion of patients did not experience clinical relief from globus pharyngeus. Contrary to findings in other studies, we did not observe that empirical treatment of all clinically diagnosed globus pharyngeus cases with PPIs yielded significant clinical benefit.

LIMITATIONS

The study included a total of 100 patients, which limits the ability to generalize the findings to the broader population. Implementing randomization and blinding could have enhanced the accuracy and reliability of the results. Additionally, the absence of advanced diagnostic tools, such as manometry, restricted the ability to exclude cricopharyngeal spasms as a potential cause of globus pharyngeus.

CONCLUSION

Globus pharyngeus is a multifactorial condition with a high prevalence in the general population. Gastroesophageal reflux disease (GERD) is often identified as a major contributing factor, leading to the common use of empirical anti-reflux therapy as an initial treatment. In this study, empirical treatment with esomeprazole resulted in a significant improvement in both the Reflux Symptom Index (RSI) and the Reflux Finding Score (RFS), with a p-value of < 0.05. However, this improvement in RSI and RFS did not correlate with significant symptomatic relief from globus pharyngeus.

The persistence of globus symptoms may be attributable to other factors, such as cricopharyngeal spasm, upper esophageal sphincter (UES) dysfunction, or functional etiologies. Consequently, it was concluded that esomeprazole is not universally effective in the empirical treatment of globus pharyngeus. Additionally, this study demonstrated that RSI and RFS are not reliable indicators of responsiveness to proton pump inhibitor (PPI) therapy in patients with globus pharyngeus.

Nevertheless, the findings suggest that RSI and RFS can be valuable tools for clinicians in assessing disease severity and monitoring therapeutic response. The study's limitations precluded deriving a predictive model for PPI efficacy, and further research with a larger sample size and a healthy control group is necessary to clarify these relationships.

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