



## CLINICAL EVALUATION OF *TERMINALIA CHEBULA* FRUIT POWDER IN GLOBUS PHARYNGEUS

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### ABSTRACT

Globus pharyngeus (G.P.) is non-painful feeling of a lump with various degrees of foreign body sensation and dysphagic sensation annexed to it. GP is a rather intricate disease to manage but at the same time an innocuous one often having psychosomatic implications. Patients of G.P. always complains about gross enhancement in their globus features particularly in a anxiety or a depressive state of mind and they use to visit multiple physicians for the same complaint despite the fact that they are very well consoled about not having any sinister pathology. Gastro esophageal reflux disorder, hypertonicity of the upper oesophageal sphincter, unorganized oesophageal motility and excessive somatization are frequently related to this disorder. A rigid telalaryngopharyngoscopic examination, upper GI endoscopy and oropharyngeal examination is a prerequisite to rule out red flags of dysphagia before nominating a G.P. *Terminalia chebula* also know as Haritki in Ayurvedic literature is selected for the current clinical trial for the management of G.P. as it has got proven anti reflux, anti ulcerogenic, antispasmodic action, prokinetic activity and anxiolytic action by virtue of presence of various active constituents pharmacologically. This pilot study intends to explore the multiple pharmacological actions of *T. chebula* in G.P. by statistically evaluating the effectiveness of the drug by using Atul globus pharyngeus questionnaire (AGPQ) which is a modified version of Glasgow Edinburgh Throat Score and Reflux symptom index for the current study. *T. chebula* powder in 5 gm bed time dose for two months reflected highly statistically significant results on various parameters of Atul globus pharyngeus questionnaire parameters and also on Reflux symptom index parameters. Paired 't' test was used to statistically validate the outcome of the trial drug.

**KEYWORDS:** Globus pharyngeus (GP), Terminalia chebula, Upper oesophageal sphincter (UOS), Gastroesophageal reflux disease (GERD), Atul globus pharyngeus questionnaire (AGPQ), Reflux symptom index questionnaire.

### INTRODUCTION

Globus pharyngeus (GP) a persistent or intermittent non-painful sensation of a lump or foreign body in the throat, is a well-defined clinical symptom that is usually long-lasting, difficult to treat, and has a tendency to recur. This symptom frequently improves with eating and is generally unaccompanied by dysphagia or odynophagia.<sup>[1]</sup> Given the benign nature of globus pharyngeus, in most cases, reassurance rather than treatment or extensive investigation with rigid oesophagoscopy or contrast swallows is all that is needed. Swallowing is a complex motor reflex requiring coordination among the neurologic system, the oropharynx, and the esophagus. A number of disorders,

both benign and malignant, can interfere with this process and globus pharyngeus is a common related symptom. It is a common condition that accounts for approximately 4% of new referrals to ear, nose and throat (ENT) clinics, and it is reported by up to 46% of apparently healthy individuals, with a peak incidence in middle ago.<sup>[2,3]</sup> This condition is equally prevalent in men and women, though the latter are more likely to seek health care for this symptom.<sup>[4]</sup>

Hippocrates first noted globus pharyngeus approximately 2500 years ago.<sup>[5]</sup> In 1707, Purcell was the first to accurately describe the condition; he believed that globus resulted from pressure on the thyroid cartilage due to

contraction of the strap muscles of the neck. In the past, globus was described as “globus hystericus” because of its frequent association with menopause or psychogenic factors. However, Malcomson<sup>[6]</sup> coined the more accurate term “globus pharyngeus” in 1968 after discovering that most patients experiencing globus did not have a hysterical personality. The etiology of globus is still unknown but appears to be multifactorial. Various contributory factors are held responsible for this elusive but innocuous disorder but few have been documented for this globus sensation. Potential causes of globus are enumerated below:

1. Gastroesophageal reflux disease (GERD)
2. Abnormal upper esophageal sphincter function
3. Esophageal motility disorders
4. Chronic tonsillopharyngitis
5. Post nasal drip (PND)
6. Chronic sinusitis
7. Lymphoid tissue hypertrophy of the base of the tongue
8. Retroverted epiglottis
9. Thyroid diseases
10. Psychological factors and stress

The link between GERD and globus has been a matter of controversy for over forty years. Chevalier *et al.*<sup>[7]</sup> looked at globus patients with and without typical GERD symptoms. They found that 66.6% of the non reflux globus group and 80% of the GERD globus group had significant episodes of reflux (based on pH monitoring). In direct contrast, Chen *et al.* in a similar study found no evidence of reflux in globus patients based on ambulatory pH monitoring.<sup>[8]</sup> Reflux is, however, best detected by impedance. Anandasabapathy and Jaffin using multichannel intraluminal impedance and pH monitoring (MII-pH) have suggested that globus may also be due to non acid (NAR) reflux.<sup>[9]</sup> This latter study found non acid reflux and proximal reflux to be significant predictors of globus.

Hypertonicity of the upper oesophageal sphincter (UOS) has been suggested as a cause of globus, but several studies have yielded conflicting results. This has largely been due to possible technical difficulties in assessing UOS pressure profiles. It has long been recognised that the UOS pressure profile is asymmetrical, especially when using multilumen catheters. Therefore, earlier studies that have not taken this into account must be viewed with caution. Also, oral movement during swallowing and compression from surrounding structures complicates pressure readings. UOS pressure measurements obtained using circumferential transducers are regarded as being more reflective of true intraluminal pressure. Sun *et al.*<sup>[10]</sup> looked at twenty-four healthy volunteers and thirty-two patients with globus and found UOS pressure to be normal in most of the globus patients and could not suggest it as a possible aetiological factor. Interestingly they found that videofluoroscopic evidence of pharyngeal dysfunction especially laryngeal penetration had a strong association with globus.

Tokashiki *et al.*,<sup>[11]</sup> however, showed that perfusion of HCl into the distal oesophagus was related to a sensation of globus associated with a rise in UOS pressure. This rise in pressure was independent of the detection of a rise in pH in the hypopharynx. As its earlier name, globus hystericus, suggests, there has been a long history of links between globus and psychological factors. It is the fourth most discriminating symptom of a somatisation disorder after vomiting, aphonia, and painful extremities.<sup>[12]</sup> As most of the globus patients are quite rightly referred to ENT surgeons rather than to psychiatrists, a psychogenic basis must always be borne in mind. Gale *et al.*<sup>[13]</sup> in a detailed medical and psychological examinations including assessment with the Minnesota Multiphasic Personality Inventory (MMPI) of 4240 US male veterans demonstrated a 6.4% incidence of globus. This globus group scored higher in nine out of ten of the MMPI clinical scales. They concluded that in men there is a significant link to depression and somatization disorder and as a result other related treatable psychopathology should be investigated.

Recently there have been reports of very subtle changes in anatomy that when rectified have given relief of globus. Agada *et al.*<sup>[14]</sup> published a small series of patients with globus having “abnormally” retroverted epiglottises. The definition of a retroverted epiglottis is if the tip touches the tongue base when the tongue is protruded. Ulug and Ulubil<sup>[15]</sup> have presented a case of corniculate cartilage subluxation presenting with globus. Other postulated causes include Eagles syndrome (calcified stylohyoid ligament), impalpable thyroid nodules,<sup>[16]</sup> cervical osteophytes, lingual tonsils, or prominent greater cornu of the hyoid. More interestingly though Shiomi *et al.*<sup>[17]</sup> looked at the mucus in the epipharynx of patients with globus and compared it with that from healthy volunteers, they found that there were significantly increased concentrations of fucose and sialic acid (the main determinants of mucus viscosity) in the mucus of those with globus as compared to normal subjects. Though there is no evidence to suggest this, some ENT surgeons believe that globus may “simply” be a local sensory abnormality just like tinnitus.

### Investigation

The key is in taking a proper history. Pointers that would suggest sinister underlying pathology would include dysphagia, aspiration, regurgitation, weight loss, voice change, and pain. The presence of overt symptoms of GERD should be noted. The head and neck should be thoroughly examined. This should include transnasal fibre-optic laryngoscopy or if available transnasal flexible laryngo-oesophagoscopy (TNO). Any further investigation should be based on the findings at history and examination.

**A. Barium meal swallow:** In many ENT departments contrast swallows are the most popular radiological investigations used to investigate globus, with some departments historically using them to screen

patients for upper aero digestive tract malignancy. They have been favoured because they are safe (compared to rigid endoscopy), quick, and believed to increase diagnostic yield. Unfortunately there is particular concern that this modality may miss a malignancy. Barium swallow studies have been reported to identify benign lesions in up to one-third of patients with globus, and the most common findings include hiatal hernia and/or reflux (8%-18%), cervical osteophytes (0.4%-23%), and cricopharyngeal spasm (2.2%).<sup>[18,19,20,21]</sup> G.P. is shown to have poor correlation with barium meal swallow testing but definitely can add on in exclusion of various Space occupying lesion especially intraluminal esophageal disorders.

**B. Endoscopy:** Direct visualisation of the upper digestive tract is another means of investigating globus. The main drawback of this is that flexible oesophagoscopy often requires sedation, while rigid endoscopy requires a general anaesthetic and carries a small but significant risk of perforation. Lorenz *et al.*<sup>[22]</sup> carried out flexible endoscopies on patients that had been referred by ENT for further investigation of globus, and all of the patients had had a normal outpatient ENT examination and barium swallow. 62.7% of the patients were found to have pathology that could possibly have caused their globus though no sinister pathology was noted. Similarly, Nagano *et al.*<sup>[23]</sup> in their study found a 36.5% incidence of benign oesophageal pathology in patients with globus on flexible endoscopy, but again no malignancies were identified. Takwoingi *et al.*<sup>[24]</sup> retrospectively reviewed 250 patients that had undergone rigid endoscopy for globus. The most common recorded anomalies were cricopharyngeal spasm (4.8%) and reflux (4.4%). No tumours were found, and they concluded that rigid endoscopy played a limited role in the investigation of globus. The most recent major advance in endoscopy is transnasal oesophagoscopy (TNO). It combines the main advantages of both conventional flexible and rigid oesophagoscopy with none of the major disadvantages. It can be done with just topical anaesthesia and vasoconstriction. There is total examination of the upper digestive tract down to the stomach with the ability to take biopsies at the same time. It has been shown to be safe with a high patient satisfaction rate.<sup>[25]</sup> Transnasal esophagoscopy is the ideal investigation for those ENT surgeons who want a relatively safe, cheap, and quick way of visualising the upper digestive tract especially the hypopharynx and postcricoid regions. Where Transnasal esophagoscopy is available, almost 90% patients with globus can be discharged after their first visit

Endoscopy has been shown to be superior to barium swallow as a principal means of diagnosing upper aero digestive tract malignancy.<sup>[26]</sup> Excellent views of the pyriform fossa and the postcricoid area can be achieved by insufflating air via flexible esophagogastrosopy.<sup>[27]</sup> Moreover, this procedure enables full esophageal evaluation and diagnosis of reflux esophagitis and/or upper esophageal malignancy as a cause of globus. However, in general, endoscopy is known to have low

sensitivity and to be of limited value for the diagnosis of extraesophageal GERD. A study of 58 patients with pH-documented LPR found that only 19% had esophagitis or Barrett's metaplasia.<sup>[28]</sup> In another study of patients with suspected Laryngopharyngeal reflux symptoms, esophagitis was generally prevalent<sup>[29]</sup> but occurred least in patients with globus and throat symptoms.

**C. Videofluoroscopy:** Of 23 globus patients, who received videofluoroscopy, 8 patients showed abnormal results; 5 had laryngeal aspiration, 2 had barium stasis in the vallecula and pyriform sinuses, and 4 had poor pharyngeal elevation.<sup>[30]</sup> Although it is unlikely that this indicates a causal relationship, videofluoroscopy may help to identify pharyngeal dysfunction in a substantial proportion of globus patients.

*Terminalia chebula* is a traditional medicine belonging to the genus Terminalia, family Combretaceae, and is extensively cultivated in India. The dried ripe fruit of *T. chebula* is an important Indian herb used extensively in the indigenous system of medicine (Ayurvedic) for its homeostatic, antitussive, laxative, diuretic, and cardiogenic activities.<sup>[31]</sup> Phytochemical analysis of *T. chebula* shows the presence of gallic acid, ellagic acid, tannic acid, ethyl gallate, chebulic acid, chebulagic acid, corilagin, mannitol, ascorbic acid (vitamin C), and other compounds.<sup>[32]</sup> Various source lists *T. chebula* as having 30-35% tannin content having positive effect on the gastric and intestinal motility and hence resolving GERD features.<sup>[33,34,35]</sup> Thus, phytochemical analyses of *T. chebula* extract composition are necessary and provide useful information. *Terminalia chebula* significantly increased gastric emptying and has got a prokinetic action. The enhancement of gastric emptying was comparable to that produced by metoclopramide.<sup>[36]</sup> *T. chebula* has got a well recognised normalization effect on the GI motility<sup>[37]</sup> which perhaps will counter the clinical features of GERD related globus sensation.

Various contributory factors are responsible for the globus sensation but GERD, stress related generalized anxiety and UOS spasticity are the most important acknowledged factors responsible. By virtue of presence of potent antiulcerogenic properties, antispasmodic action to relieve UES action, proven prokinetic action and anti anxiety function *T. chebula* is selected for the current clinical trial for the management of G.P. related clinical features. Role of *T. chebula* in G.P. is relatively new domain of investigation and hence this trial may be considered as a pilot clinical study because no literature in citation indices or in classical texts is available regarding this ambit.

## MATERIALS AND METHODS

The present work is randomised, single blind, prospective, crossover and single centre study comprising patients of either sex in the age group 16-70 years. The patients for the research were selected from Department of Shalakya Tantra OPD, Chaudhary Brahm Prakash Ayurved Charak Sansthan, Khera Dabar,

Najafgarh, India. Patients who have got their 70 degree rigid telaryngopharyngoscopic, upper G.I. endoscopy and oropharynx examination done to establish a G.P. Globus pharyngeus patients abiding inclusion/exclusion and criteria of assessment were selected for the current trial after having written and informed consent from the patient to participate in the study on a recorded and standardized Performa. The patient was also briefed about the research protocol, intervention, duration of trial, route of administration of drug and possible undesirable effects, prior to the consent. An official permission from institution's research ethical committee and hospital research committee as a prerequisite was also requested for the trial vide communication letter no. CBPACS/SKT/Res./2016-1A.

### Statistical analysis

The data was analysed for statistical significance by using statistical package for social sciences (SPSS Inc. Chicago, USA, 17.0). The student's 't' test (paired) was used to analyse the data for the level of significance. The related 't' test was used to analyse intra differences in pre/post protocol. For all analysis the 'p' value used for statistical significance was 0.05.

### Selection of the patients

40 patients of established G.P. were selected for the current trial and a fine powder of *T. chebula* is given 5 gm in bed time dose (atleast 1 hr. post prandial) for two months. All the patients have to screened with 70 degree, 8mm rigid telaryngopharyngoscopic, upper G.I. endoscopy with sedation and oropharynx examination for any red flags viz. oropharyngeal growth, suspected oesophageal malignancies and post laryngeal space occupying lesions. Selected patients of G.P. were offered Atul globus pharyngeus questionnaire (AGPQ) and Reflux symptom index questionnaire before and after completion of the trial. Fortnightly visitation for the patients was advocated for the evaluation of possible outcome of the therapy, added complaints and possible unwanted effect of the drug.

### Inclusion criterion

- Patients age between 16-70 years.

- Patients having normal rigid telaryngopharyngoscopic, upper G.I. endoscopy and oropharynx examination.

### Exclusion criterion

- Patients having intractable GERD features/heartburn.
- Patients having Oropharyngeal malignancies.
- Patients having Oesophageal malignancies.
- Patients which has got red flags viz. true dysphagia, voice change, hematemesis and weight loss.
- Patients not willing to participate in Atul globus pharyngeus questionnaire (AGPQ) and Reflux symptom index questionnaire.
- Patients who can have their rigid telaryngopharyngoscopic, upper G.I. endoscopy and oropharynx examination done.

### Criteria of assessment for the present study/Grading and scoring

Atul globus pharyngeus questionnaire (Table 1) is used for the grading and scoring of the subjective sensations of the patients. This self designed questionnaire is frequently used in our ENT unit for the possible G.P. patients who are clinically suggestive of low risk group i.e. no history of true dysphagia, voice change, hematemesis and weight loss. Patients in this low group also have got intermittent dysphagia (dysphagia more for saliva than for bolus/liquids) and non alcoholic-non smoker young patient. Atul globus pharyngeus questionnaire (AGPQ) is a modified version of Glasgow Edinburgh Throat Score which is sometimes used for the evaluation of G.P.<sup>[38]</sup> Point scoring and symptom complex is altered/modified to make it more in accordance with the G.P. patients to comprehend an AGPQ. Apart from the use of Reflux symptom index (Table 2) was also considered for the present clinical trial in order to correlate G.P. features with GERD. Reflux symptom index is a 5 point rating scale to validate the patients of GERD which is an established factor in G.P. patients. Reflux symptom index is a questionnaire which is frequently used in various clinical studies to evaluate the degree of subjective GERD features.<sup>[39,40,41]</sup>

**Table 1: Atul globus pharyngeus questionnaire (AGPQ)**

| Symptom   | Grade 1 | Grade 1 | Grade 2  | Grade 3 | Grade 4     | Grade 5    |
|---|---------|---------|----------|---------|-------------|------------|
| Feeling of something in the throat                          | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Pain in the throat  | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Irritation of the throat                                    | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Difficulty in swallowing food                               | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Repeated clearance of throat                                | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Throat closing off/choking episodes                         | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Increased sense of saliva trickling down the throat         | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Feeling of dysphagia more for saliva than of solids/liquids | No      | Mild    | Moderate | Severe  | Very severe | Unbearable |
| Increased spitting  | No      | Mild    | Moderate | Severe  | Very severe | Unbearable |
| Increased Consciousness For swallowing of saliva            | No      | Mild    | Moderate | Severe  | Very severe | Unbearable |

**Table 2: Reflux symptom index**

| Complaint  | Grade 0 | Grade 1 | Grade 2  | Grade 3 | Grade 4     | Grade 5    |
|--|---------|---------|----------|---------|-------------|------------|
| Hoarseness or a problem with your voice                                  | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Clearing your throat   | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Excess throat mucus or postnasal drip                                    | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Difficulty swallowing food, liquids, or pills                            | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Coughing after you ate or after lying down                               | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Breathing difficulties or choking episodes                               | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Troublesome or annoying cough  | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Sensations of something sticking in your throat or a lump in your throat | No      | Mild    | Moderate | severe  | Very severe | Unbearable |
| Heartburn, chest pain, indigestion, or stomach acid coming up            | No      | Mild    | Moderate | severe  | Very severe | Unbearable |

**OBSERVATIONS AND RESULTS**

*T. chebula* powder 5 gm bed time dose for two months reflected highly statistically significant results on various parameters of Atul globus pharyngeus questionnaire parameters (Table 3) and also on Reflux symptom index parameters (Table 4). Paired 't' test was used to statistically validate the outcome of the trial drug. All the clinical pictures related to G.P. shows significant reduction including pain in the throat, irritation of the

throat, repeated clearance of the throat and acid reflux symptoms. Sensation of lump in the throat, choking episodes and increased spitting also responded positive after the completion of the treatment with *T. chebula* powder. Simultaneous resolving in Atul globus pharyngeus questionnaire parameters and also on Reflux symptom index parameters strongly suggests the importance of GERD in the globus sensation.

**Table 3: Effect of T. chebula powder on Atul globus pharyngeus questionnaire (AGPQ) parameters in G.P.**

| Clinical features   | n  | Mean |      | X(d)<br>B.T.-A.T. | S.D.+/- | S.E.+/- | 't'<br>value | 'p'<br>value | Remark |
|---|----|------|------|-------------------|---------|---------|--------------|--------------|--------|
|   |    | B.T. | A.T. |                   |         |         |              |              |        |
| Feeling of something in the throat                          | 40 | 3.15 | 2.30 | 0.85              | 0.74    | 0.12    | 5.11         | < 0.0001     | HS     |
| Pain in the throat  | 40 | 3.15 | 2.55 | 0.60              | 0.74    | 0.12    | 4.35         | < 0.0001     | HS     |
| Irritation of the throat                                    | 40 | 3.63 | 2.15 | 1.46              | 0.54    | 0.09    | 12.08        | < 0.0001     | HS     |
| Difficulty in swallowing food                               | 40 | 2.70 | 1.85 | 0.85              | 0.46    | 0.07    | 6.64         | < 0.0001     | HS     |
| Repeated clearance of throat                                | 40 | 3.70 | 2.48 | 1.23              | 0.46    | 0.07    | 11.28        | < 0.0001     | HS     |
| Throat closing off/choking episodes                         | 40 | 2.45 | 1.63 | 0.83              | 0.50    | 0.08    | 7.42         | < 0.0001     | HS     |
| Increased sense of saliva trickling down the throat         | 40 | 3.73 | 2.63 | 1.10              | 0.55    | 0.09    | 8.62         | < 0.0001     | HS     |
| Feeling of dysphagia more for saliva than of solids/liquids | 40 | 3.43 | 1.68 | 1.75              | 0.84    | 0.13    | 10.3\5       | < 0.0001     | HS     |
| Increased spitting  | 40 | 2.68 | 1.50 | 1.17              | 0.47    | 0.07    | 10.71        | < 0.0001     | HS     |
| Increased Consciousness For swallowing of saliva            | 40 | 2.33 | 1.50 | 0.83              | 0.47    | 0.07    | 7.52         | < 0.0001     | HS     |

**Table 4: Effect of *T. chebula* powder on Reflux symptom index parameters in G.P.**

| Complaint  | N  | Mean |      | X(d)<br>B.T.-A.T. | S.D.+/- | S.E.+/- | 't'<br>value | 'p'<br>value | Remark |
|--|----|------|------|-------------------|---------|---------|--------------|--------------|--------|
|  |    | B.T. | A.T. |                   |         |         |              |              |        |
| Hoarseness or a problem with your voice                                  | 40 | 2.40 | 1.85 | 0.55              | 0.50    | 0.08    | 3.84         | < 0.0001     | HS     |
| Clearing your throat   | 40 | 2.65 | 1.68 | 0.98              | 0.77    | 0.12    | 5.19         | < 0.0001     | HS     |
| Excess throat mucus or postnasal drip                                    | 40 | 2.43 | 1.73 | 0.70              | 0.90    | 0.14    | 3.20         | < 0.05       | S      |
| Difficulty swallowing food, liquids, or pills                            | 40 | 2.65 | 1.65 | 1.00              | 0.48    | 0.08    | 8.83         | < 0.0001     | HS     |
| Coughing after you ate or after lying down                               | 40 | 2.43 | 1.85 | 0.58              | 0.71    | 0.11    | 4.30         | < 0.0001     | HS     |
| Breathing difficulties or choking episodes                               | 40 | 2.68 | 1.93 | 0.75              | 0.66    | 0.10    | 5.86         | < 0.0001     | HS     |
| Troublesome or annoying cough  | 40 | 1.60 | 1.35 | 0.25              | 0.55    | 0.09    | 2.50         | < 0.05       | S      |
| Sensations of something sticking in your throat or a lump in your throat | 40 | 3.70 | 2.48 | 1.23              | 0.46    | 0.07    | 11.28        | < 0.0001     | HS     |
| Heartburn, chest pain, indigestion, or stomach acid coming up            | 40 | 2.43 | 1.80 | 0.63              | 0.87    | 0.14    | 5.60         | < 0.0001     | HS     |

## DISCUSSION

Globus is a sensation of a lump, something stuck, or tightness in the throat. Classically, a lump, it may be a hair or crumb like (foreign body) sensation, a constriction or a choking. The symptom is considered functional when no organic explanation is detected. Globus is a clinical diagnosis and not a diagnosis of exclusion. A complete head and neck examination including fiberoptic laryngoscopy is more than adequate to confidently discharge the classic globus pharyngeus patients. The introduction of transnasal oesophagoscopy in one stop globus clinics has meant that with appropriate training otolaryngologists can nowadays complete a thorough upper aero digestive tract examination, thus avoiding the need for any other investigations such as barium swallows or rigid oesophagoscopies under general anaesthesia. Over investigating these patients can often add unnecessary stress to a group of patients who already seem to have higher levels of depression, anxiety, and other somatic concerns.

Association of G.P. with reflux disorders including non acid reflux, hypertonicity of the UOS, hypertrophy of tongue base lymphoid tissue and somatization of the patients is advocated in various clinical studies. *Terminalia chebula* also known as Haritki in Ayurvedic literature is selected for the current clinical trial as it has got proven anti reflux, anti ulcerogenic, antispasmodic action, prokinetic activity and anxiolytic action by virtue of presence of various active constituents pharmacologically.

*Terminalia chebula* Retz. (Family-Combretaceae), is called the 'King of Medicine' and is always listed at the top of the list of 'Ayurvedic Materia Medica' because of its extraordinary pharmacological actions. The whole plant possesses high medicinal value and traditionally used for the treatment of various ailments for human being. *Terminalia chebula* which exhibited a number of medicinal activities due to the presence of a large number of different types of phytoconstituents. The fruit of the tree possesses diverse health benefits and has been used as traditional medicine for household remedy against various human ailments since antiquity.

*T. chebula* behaves as gastrointestinal prokinetic agent and hence effectively manage the GERD features which have got strong association with globus symptoms.<sup>[42,43]</sup> *Terminalia chebula* methanolic extract further provided significant anti-ulcer protection against aspirin induced ulcers and GERD related reflux esophagitis.<sup>[44]</sup> The anti-ulcer activity of the methanolic extract of *Terminalia chebula* fruits was evaluated in the pylorus ligation and ethanol induced ulcer models of the wistar rats proved them to be a potent anti-ulcer agent.<sup>[45]</sup> Histopathological changes observed in the pylorus ligation model have showed the degeneration, hemorrhage, edematous appearance of the gastric tissue.<sup>[46]</sup> Anti ulcerogenic property of the *T. chebula* may be attributed to its competent GI motility enhancer and thus less exposed oesophageal and gastric mucosa to the gastric acid contents.

Globus was first described by Purcell in 1707 who coined the term globus hystericus, (globus originating from the Latin meaning "ball" and "hystericus" reflecting the supposed psychological component of the disorder). Traditionally patients presenting with globus symptoms were referred to psychiatrists and a study demonstrated that these subjects were significantly higher on neuroticism and low on extra-version scales and have significantly elevated levels of psychological distress, including anxiety, low mood, and somatic concern when compared with the control subjects. Chebulinic acid is an ellagitannin found in the fruits of *Terminalia chebula*. It has the molecular formula of  $C_{41}H_{32}O_{27}$  and molecular weight of 956.67658 [g/mol]. It is isolated from the fruits of *Terminalia chebula* by high-speed counter-current chromatography.<sup>[47]</sup> Chebulinic acid displayed behavioural profile that is consistent with an antidepressant and anxiolytic actions.<sup>[48,49]</sup>

Somatization and alternate anxiety-depressive illness along with heightened anxiety which is associated with G.P., *T. chebula* as a trial drug was found to be effective in managing the globus features. Patients of G.P. always complain about gross enhancement in their globus features particularly in an anxiety or a depressive state of mind and they use to visit multiple physicians for the same complaint despite the fact that they are very well consoled about not having any sinister pathology.<sup>[50,51]</sup> Perhaps change in the swallowing pattern, increased GERD in a stressed condition, altered food habits, escalated smoking and repeated conscious salivary swallowing makes a condition of Hypochondriasis.<sup>[52]</sup> Cyberchondria, which is unfounded escalation of concerns about common symptomology based on review of search results and literature online also complicates the picture in multiplicity of the patients. Cyberchondria is a growing concern among many healthcare practitioners as patients can now research any and all symptoms of a disease, illness or condition, and manifest a state of medical anxiety. Intermittent spasmodic events are frequent positive finding in manometric studies of oesophagus thus the validated antispasmodic function of *T. chebula* may effectively play its part in relieving the cricopharyngeus spasm which is an important contributor for UOS.<sup>[53]</sup>

## CONCLUSION

Globus pharyngeus is a difficult to treat clinical entity with psychosomatic implications. The most convincing etiological factor in triggering this globus sensation is GERD including a non acid reflux. G.P. patients used to visit multiple physicians for their disturbing but innocuous clinical features. UOS hypertonicity, altered esophageal motility behaviour, somatization and recently Cyberchondria also complicate the picture in a G.P. patient. *Terminalia chebula* is used for the current clinical trial in 5 gm bed time dose and found to be effective on Atul globus pharyngeus questionnaire parameters and also on Reflux symptom index parameters. This effectiveness of this trial drug may be

attributed to its proven pharmacological actions viz. including anti reflux, anti ulcerogenic, antispasmodic action, prokinetic activity and anxiolysis.

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