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RESEARCH ARTICLE

MANAGEMENT OF GLOBUS HYSTERICUSAND ROLE OF ANTIDEPRESSANTS.

Seema Batool Shah[1], Raja Salman Khurshid[2] and Altaf Ahmad Malla[3]

1. Postgraduate Scholar, Department of Psychiatry, Government Medical College, Srinagar.
2. Consultant ENT, Department of Health, J&K Health Services.
3. Associate Professor, Department of Psychiatry, Government Medical College, Srinagar.

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Abstract

Objective/Hypothesis: To study the treatment response of Globus pharyngeus to ppi/prokinetic combination, and the role of antidepressants in non-responders. The purpose of this study is to devise a guideline for managing Globus pharyngeus which otherwise is a poorly understood and managed condition.

Study design: It is a prospective non-randomised study where OPD visiting patients have been followed over a course of 6 to 12 months.

Methods: 54 patients of Globus pharyngeus diagnosed, with any organic condition ruled out, were put on esomeprazole-domperidone/levosulpride combination. Patients were followed over 3 weeks and 6 weeks period. The non-reponders were put on antidepressant fluoxetine in addition. The response was again gauged at 6 weeks and 12 weeks.

Results: 11 patients responded fairly well to the initial treatment of esomeprazole-domperidone/levosulpride. Rest of the 43 patients were put on Fluoxetine in addition and followed over 6 weeks and 12 weeks' time. Out of them, 29 patients responded to a varied extent and the remaining either did not respond or were lost to follow-up.

Conclusion: Only a minority of the Globus pharyngeus patients seem to respond to acid suppressant/prokinetic agents. Involvement of a psychiatrist early in the care of these patients is recommended as quite a number of non-responders to the routine treatment do well if managed with anitidepressants as well pointing to the underlying mood ailments.

Introduction:-

"Globus sensation" is often described as the sensation of a lump in the throat associated with dry swallowing or the need for dry swallowing, which disappears completely during eating or drinking and for which no organic cause can be established. 1Earlier, as evidenced by literature, it used to be refered as 'globushystericus' because it was believed to be associated with psychological disorders in women.Malcomson coined the more accurate term "globuspharyngeus" in 1968 after discovering that most patients experiencing globus did not have a hysterical personality.2

Etiology of globuspharyngeus is uncertain. However, most of the recent work has suggested several mechanisms in isolation or not uncommonly in combination are to blame for the manifestation of globuspharyngeus; these include

Corresponding Author:- Seema Batool Shah
Address:- Postgraduate Scholar, Department of Psychiatry, Government Medical College, Srinagar.

psychological factors, gastro-esophageal reflux (GOR), pharyngeal dysmotility, hypertonic upper oesophageal sphincter (UOS), and local anatomic abnormalities.1,3,4Several reports have indicated that there is a close relationship between esophageal acid reflux and globus sensation. It has been reported that there is a high prevalence of esophageal motor abnormalities, including upper esophageal sphincter (UES) dysfunction 4,5, in patients who complain of globus sensation resistant to PPI therapy without any organic diseases, although the evidence obtained has been inconsistent. It has been reported that several psychological problems or social stress have often been considered to cause or trigger globus sensation6. In the past, several studies have shown that higher levels of psychological distress including anxiety or depression in patients with globus sensation7, although a few data showed that there were no differences in the psychological states between patients with globus sensation and normal controls. 8 A recent study showed that globus patients with laryngopharyngeal reflux (LPR) exhibited weaker psychological symptoms than non-LPR globus patients, and globus patients who did not respond to PPI had significantly higher anxiety scores 9, indicating a close relationship between psychological states and globus sensation. The mainstays of its treatment are explanation and reassurance as for other functional gastrointestinal diseases.10

After explanation and reassurance, several possible treatment options based on the causes of globus sensation should be provided, such as anti-reflux therapy, therapy for improving gastrointestinal dysmotility, treatment for decreasing the perception of globus sensation (visceral hypersensitivity), antidepressants and others.

Materials And Methods:-

This is a 1 year study of the treatment responses of Globus pharyngeus/hystericus carried out at MMABM Hospital, Anantnag, wherein consecutive 54 patients of globuspharyngeus seen in OPD in a 6 month period were assessed over next few months to a year and a half. Patients were seen and examined in the ENT and Psychiatry OPDs of the said hospital with the resistant cases further treated at Psychiatry hospital, Government Medical College, Srinagar. All the patients presenting with globus symptoms in the ENT OPD underwent complete ENT examination with stress on laryngeal and hypopharyngeal examination. Patients having associated symptoms of dysphagia underwent barium swallow test or upper GI endoscopy to rule out any possible organic causes.Only the patients with no organic issues were included in this study.

After taking informed consent, all the included patients were sent to psychiatry OPD for evaluation. Socio-demographic data (age, sex, residence, educaton, occupation, marital status, family type, per capita income) were collected in a semi-structured questionnaire. Patients were screened using Mini-International Neuropsychiatric Interview (MINI), English version; 5.0.0. Final DSM-IV TR diagnosis was done by two expert psychiatrists.

Patients with a clear diagnosis of Globus pharyngeus were initially managed with a ppi (Esomeprazole) and a prokinetic agent (domperidone/itopride/levosulpride)and followed up in 3 weeks and 6 weeks' time to look for the response. The non-responders were put on antidepressant Fluoxetine in addition and further followed in 6 weeks. Fifty four (54) patients of Globus pharyngeus were involved in this study who visited our OPD fromJuly, 2020 to June, 2021.

Results:-

Following facts were noteworthy:

1. Incidence: From July, 2020 to June, 2021, 4458 patients visited our ENT OPD in MMABM hospital. Out of these, 54 patients were diagnosed as Globus Pharyngeus by our set criteria, which gives an incidence of 12 per 1000 OPD visiting patients, or incidence of 1.2%.
2. Sex and age: Majority of these patients were females. Eight (08) out of the 54 patients seen were males. Age of these patients ranged from 16 to 56 years, with the majority belonging to fourth decade of life.
3. Associated symptoms: Majority of these patients presented with the sensation of a lump in the throatand no other symptoms. A few patients (about 15 of 54) also reported dry cough and contact hawking (features of pharyngeal hypersensitivity). Ten (10) patients also had some degree of hoarseness, either occasional or chronic.
4. Associated psychiatric issues: out of 54 patients refered to department of Psychiatry, 40 were found to have psychiatric comorbidities as diagnosed by DSM-IV TR. Out of them 20 had MDD, 5 had undifferentiated somatoform disorder, 6 had Panic disorder, 6 had GAD and 3 patients were diagnosed with Hypochondriasis. These are tabulated for ease of reference as below(Table 1)

5. Seasonal variations: A significant number of these patients presented in and around the winter season. Also during the course of follow-up many of these patients improved coinciding with the change in season.
6. Treatment responses: Out of the 54 patients, 11responded very well to an esmoperazole plus domperidone/levosulpride combination. Rest of the 43 patients were managed with antidepressant fluoxetine in addition to ppi-prokinetic combination. And out of them 29patients showed improvement in symptoms. Rest of the 14 patients either did not respond or fell off the study.

S. No	Psychiatric diagnosis DSM-IV TR	No. of diagnosed cases
1	Major Depressive Disorder	20
2	Undifferentiated Somatoform disorder	5
3	Panic disorder	6
4	Generalised Anxiety Disorder	6
5	Hypochondriasis	3
6	No Psychiatric Issues	14

Discussion:-

Moloy and Charter11 found the globus symptom as the seventh most common initial complaint among the first-visit patients to a general otolaryngology clinic with prevalence rate was reported to be around 4%. Hsu and colleagues12 reported that 2.3% of the patients of ENT referrals had the symptoms of globushystericus. The lesser incidence in our study may be because of smaller sample size and more strict criteria of inclusion.

Thompson and Heaton13 reported that a mild transient “lump in the throat” during stressful situations has been experienced by up to 45% of the general population, often in young or middle-aged persons, with an equal distribution among men and women. Moloy et al11 had reported that relative to men, women are affected three times more commonly at 50 years of age and below and with equal frequency above 50 years. In our study we observed that the female patients outnumbered males by more than three times.

Globus may be associated with throat irritation, soreness, dryness, catarrh, or constant throat clearing.14 A few patients in our study reported dry cough and contact hawking , and a few more patients also had some degree of hoarseness, either occasional or chronic.

Dearyet al15in their studies found that globus patients had significantly elevated psychological distress,including anxiety, low mood and somatic concern. In our study the results were close to A. Debnath et al16 who in their series of 53 patients found that 79.25% had co-morbid psychiatric disorders and 32.01% had multiple diagnoses. They also found that psychiatric disorders among the patients of globus were major depressive disorder, obsessive compulsive personality disorder, undifferentiated somatoform disorder, generalized anxiety disorder and panic disorder with agoraphobia, borderline personality disorder, obsessive compulsive disorder and dysthymia and hypochondriasis. As mentioned 40 out of 54 patients (74%) in our study had psychiatric disease associations, with major depressive disorder being the commonest association followed by panic disorder, generalised anxiety disorder, undifferentiated somatoform disorder, and hypochondriasis.

Many studies have stressed that no seasonal variation in incidence s found in globuspharyngeus, and men and women responded similarly to treatment.11But quite significantly we observed these cases clustered around the winter months which may be an inconsistent finding in our study as we collected our sample patients in about 7 months around the winter season. It needs a bigger study on our part to confirm the findings.

Current evidence shows that the clinical response to PPI in patients with globus sensation is variable17 and that the symptom improves more slowly than typical GERD symptoms such as heartburn or regurgitation following acid-suppression therapy.Since we made it a point to follow the patients at 3 weeks after start of treatment the response rate to ppi was much less than expected. One recent study that investigated the effectiveness of double doses of PPI in GERD patients with globus sensation showed that the response rate with PPI was 44.4%.18But in our cases the response rate was only about 21% at 3 weeks which increased with prolongation of treatment and increase in treatment dosage. A recent study suggested that stimulation of gastric emptying or esophageal clearance in addition to inhibition of gastric acid secretion may be an effective treatment for LPR. Ezzatet al19 reported that adding

prokinetics, such as cisapride and itopride to PPIs to treat LPR reduced the recurrence of symptoms including globus sensation.

The central focus in this particular study was the psychiatric evaluation of the patients of globuspharyngeus with the application of latest diagnostic criteria by expert Psychiatrists. A close relationship has been reported between psychological states including depression and globus sensation. The use of antidepressant Fluoxetine thus was legitimised in all the ppi non-responders. Out of 43 patients 29 responded well to the addition Fluoxetine, giving a response rate of 67.4%. The visceral hypersensitivity is considered one of features of globus sensation20, and might be modulated by antidepressant therapy. A small series of anti-depressants have also been found to be beneficial for some globus patients with concomitant psychiatric disorders, such as panic, somatization, major depression, and agoraphobia.21,22

Conclusion:-

The aetiology of Globus Pharyngeus and thus its treatment is still under discussion. Application of variety of medications including ppi, prokinetics, antidepressants, and cognitive behaviour therapy as well as speech therapy point to the varied aetiology of the condition and the chronic irritating but essentially benign course of the condition. Involvement of Psychiatrist early in the course of illness is emphasized.

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