

The Relationship Between Upper Esophageal Sphincter Pressure and Psychological Status in Patients with Globus Sensation

Qiao-Li Lan
Xiao-Xiao Lin
Ying Wang
Bei-Bei Xu
Ke-Yue Shu
Xiao-Jin Zhang

Department of Digestive System,
Wenzhou People's Hospital, The Third
Affiliated Hospital of Shanghai University,
Wenzhou Third Clinical Medical College
of Wenzhou Medical University,
Wenzhou, 325000, People's Republic of
China

Correspondence: Ying Wang
Department of Digestive System,
Wenzhou People's Hospital, The Third
Affiliated Hospital of Shanghai University,
Wenzhou Third Clinical Medical College
of Wenzhou Medical University, No. 49 of
Cangzhou Road, Lucheng District,
Wenzhou, 325000, People's Republic of
China
Tel +86 13758454419
Fax +86 88059502
Email wangying268@outlook.com

Objective: To explore the correlation between changes in esophageal pressure and psychological status in patients with globus sensation.

Methods: A total of 40 patients with globus sensation who attended Wenzhou People's Hospital between August 2020 and February 2021 were divided into two groups based on the results of esophageal manometry: a high-pressure group and a non-high-pressure group. The duration of disease, clinical symptom score, and self-rating anxiety scale (SAS) were compared between the two groups to determine the relationship between changes in esophageal pressure and psychological status.

Results: All the patients before treatment were divided into a high-pressure group (n = 14) and a non-high-pressure group (n = 26) according to whether the resting pressure of the upper esophageal sphincter (UES) was greater than 104 mmHg. The differences between the high-pressure group and non-high-pressure group in duration of disease, clinical symptom score, and SAS were statistically significant (all $P < 0.05$). Anxiety was present in 12 patients in the high-pressure group and two patients in the non-high-pressure group. The difference between the the high-pressure group and non-high-pressure group in the incidence of anxiety was statistically significant ($\chi^2 = 21.04$ and $P < 0.001$). Pearson correlation analysis of the association between esophageal pressure and anxiety resulted in $R = 0.74$ and $P < 0.001$.

Conclusion: Patients with globus sensation who develop anxiety were more likely to have high pressure in the upper esophageal sphincter.

Keywords: globus sensation, high-resolution manometry, HRM, upper esophageal sphincter, clinical symptoms, psychological status

Introduction

Globus sensation is a persistent or intermittent sensation of a non-painful lump or foreign body in the throat; it occurs between meals, is not accompanied by dysphagia or painful swallowing, and is characterized by intractability, common recurrence, and the overlapping of multiple symptoms, with patients, repeatedly visiting the hospital.^{1,2} Previous research has found that nearly 50% of patients with globus sensation have repeated hospital visits, indicating that the condition seriously affects a patient's quality of life and consumes healthcare resources.³ The etiology and pathogenesis of globus sensation have not yet been completely clarified, but it is currently thought to be correlated with esophageal and motor dysfunction of the upper esophageal sphincter (UES).⁴ Mental and psychological factors, as well as esophageal hypersensitivity,⁵ are also important etiological factors.³

High-resolution manometry (HRM) with esophageal pressure topography is an evolution in esophageal manometry that measures pressure activity from sensors spaced at 1-cm intervals from the pharynx to the stomach.^{6,7} This technique detects not only focal dysmotility but also dysfunction and outflow obstruction caused by structural pathology. Studies have suggested that hysteria is related to increased pressure of the upper esophageal sphincter.⁸⁻¹⁰ We propose that HRM can increase the sensitivity of the physiological measurement to identify the cause of Globus sensation.

This study aimed to provide a detailed evaluation of esophageal pressure in patients with Globus sensation and to explore the psychological anxiety of patients with globus sensation, evaluate the effects of clinical treatment, and clarify the correlation between the characteristics of esophageal pressure changes and psychological status in patients with globus sensation.

Subjects and Methods

Study Subjects

A total of 40 patients with globus sensation who attended Wenzhou People's Hospital between August 2020 and February 2021 were enrolled in the present study.

Inclusion Criteria

(1) Patient met the Rome IV diagnostic criteria¹¹ (persistent or intermittent non-painful choking or foreign-body sensation in the throat, with no structural lesions on physical examination, laryngoscopy, or endoscopy; sensations occurring between meals; no dysphagia or painful swallowing); (2) no evidence of gastroesophageal reflux or eosinophilic esophagitis causing the symptoms; (3) no esophageal dysfunctional disease combined with histopathological abnormalities; (4) the symptoms had been present for at least six months before diagnosis, had met the above diagnostic criteria for the last three months, and occurred at least one day per week; (5) patient could tolerate treatment with flupentixol/melitracen; (6) patient was not pregnant or lactating.

Exclusion Criteria

Disease of oesophageal dynamic disorder with histopathological abnormalities; Reflux esophagitis; Primary oesophageal dynamic disorder

This study was conducted with approval from the Ethics Committee of Wenzhou People's Hospital (HY-2020183). This study was conducted in accordance with the declaration of Helsinki. Written informed consent was

obtained from all participants. All patients provided informed consent.

Examination Method

An esophageal HRM was conducted for all patients to clarify the characteristics of esophageal dynamics and post-therapeutic changes in globus sensation.

Pre-Examination Preparation

Esophageal motility drugs were discontinued one week before the examination, and the patient was instructed to fast for 12 hours for food and 6 hours for water before the examination. Explain examination procedures to patients prior to reduce anxiety.

Examination Process

The patients are placed in a sitting position and the pressure is calibrated. The catheter electrode is lubricated and inserted through the esophagus. After the catheter was inserted, making patients rest for 3–5 minutes, and then change to the supine position. Patients are instructed to repeat the swallowing action 10 times, swallowing 5mL of water each time. The following indicators were measured according to the HRM operation manual: UES resting pressure, lower esophageal sphincter (LES) resting pressure, UES residual pressure, LES residual pressure, and distal contraction integral (DCI).¹²

Clinical Subgroup Treatment

Patients were then randomly divided into two groups, a control group and a treatment group. Patients in the control group were given 10mg rabeprazole enteric-coated tablet 30 minutes before breakfast and 10mg mosapride citrate tablet in the morning, afternoon, and evening 30 minutes before meals. Patients in the treatment group were given 10mg rabeprazole enteric-coated tablet 30 minutes before breakfast, 10mg mosapride citrate tablet in the morning, afternoon, and evening 30 minutes before meals, and 0.5mg flupentixol/10mg melitracen tablet every morning after breakfast. The duration of all treatments was one month. All patients were provided with psychological counseling and comfort from the start to the end of the treatment.

Evaluation

There are independent staff to compare the changes in clinical symptoms and mental state before and after treatment in the control group and the treatment group to clarify the anxiety state and the clinical treatment effect.

The staff who participated in the evaluation received evaluation training and followed consistent standards. The staff were unaware of the grouping and treatment of patients in the meantime.

Evaluation of Clinical Symptoms

Symptom scoring and assignment method of globus sensation: No globus sensation = 0; occasional (no impact on life and work) = 1; sometimes (occasional impact on life and work) = 2; often (obvious impact on life and work and had a medical consultation) = 3; always (almost unable to work, continual impact on quality of life, repeated medical consultation) = 4. The changes in score before and after treatment were recorded, and the differences before and after treatment, as well as the differences between the two groups, were compared.

Evaluation of Therapeutic Effect

(1) Very effective (the main clinical symptoms completely disappeared after one month of medication); (2) effective (after one month of medication, the main clinical symptoms were reduced compared with those before medication); (3) ineffective (no significant improvement in the main clinical symptoms after treatment).

Evaluation of Psychological Status

Zung's self-rating anxiety scale (SAS) was used to evaluate each patient's psychological status. SAS score = cumulative score of each entry \times 100/80 (maximum total score of 80). Score $<$ 50 = no anxiety; score 50–59 = mild anxiety; score 60–69 = moderate anxiety; score 70–80 = severe anxiety. Changes in SAS score before and after treatment, as well as the difference between the two groups, were compared.

Statistical Analysis

SPSS17.0 software was used for statistical analysis. Countable data were expressed as a percentage and number of cases and analyzed using a χ^2 test. Measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm s$) and analyzed using a *t*-test. Spearman's rank correlation

analysis was used for correlation analysis. $P < 0.05$ was considered statistically significant.

Results

The Comparison of Clinical Data Between the Control Group and the Treatment Group Before Treatment

Before treatment, the differences between the control group and the treatment group in age, duration of disease, clinical symptom score, and SAS were not statistically significant (all $P > 0.05$). The differences in the general characteristics between the two groups were not statistically significant (see Table 1).

The Comparison of Clinical Data Between the High-Pressure Group and the Non-High-Pressure Group

In the control group, the clinical symptom score was 2.65 ± 0.81 before treatment and 2.50 ± 0.76 after treatment, and the difference was not statistically significant ($t = 1.83$, $P = 0.083$). The SAS score in the control group was 42.81 ± 10.95 before treatment and 42.38 ± 10.39 after treatment, and the difference was not statistically significant ($t = 1.80$, $P = 0.090$). In the treatment group, the clinical symptom score was 2.85 ± 0.75 before treatment and 1.4 ± 0.75 after treatment, and the difference was statistically significant ($t = 6.18$, $P < 0.001$). The SAS score in the treatment group was 43.69 ± 11.47 before treatment and 30.44 ± 5.04 after treatment, and the difference was statistically significant ($t = 6.39$, $P < 0.001$).

The difference between the control group and the treatment group in clinical symptom score was statistically significant after treatment ($t = 4.82$, $P < 0.001$), and the difference between the two groups in SAS score after treatment was statistically significant ($t = 4.812$, $P < 0.001$).

Table 1 The Comparison of Clinical Data Between the Control Group and the Treatment Group Before Treatment

Group	Age (Year)	Duration of Disease (Month)	Clinical Symptom Score	SAS Score
Control group	45.70 ± 10.38	14.10 ± 9.78	2.65 ± 0.81	42.81 ± 10.95
Treatment group	45.30 ± 10.98	13.60 ± 10.13	2.85 ± 0.75	46.69 ± 11.47
t value	1.12	0.16	0.81	0.25
P value	0.896	0.875	0.422	0.806

Note: Data are expressed as mean \pm standard deviation ($M \pm SD$).

Table 2 The Comparison of Clinical Data Between the High-Pressure Group and the Non-High-Pressure Group

Group	Age (Year)	Duration of Disease (Month)	Clinical Symptom Score	SAS Score
High-pressure group	44.14 ± 9.79	23.07 ± 8.66	3.50 ± 0.52	55.09 ± 5.54
Non-high-pressure group	46.23 ± 11.06	8.89 ± 6.20	2.35 ± 0.56	36.88 ± 7.40
t value	0.59	5.99	6.36	8.06
P value	0.557	< 0.001*	< 0.001*	< 0.001*

Notes: * $P < 0.05$, the difference is statistically significant. Data are expressed as mean ± standard deviation (M ± SD).

Clinical Treatment Efficacy

The control group had no cases in which treatment was scored as very effective, three cases in which it was scored as effective, and 17 cases in which it was scored as ineffective, with an overall efficacy rate of 15% (3/20). The treatment group had two cases in which treatment was scored as very effective, 14 cases in which treatment was scored as effective, and four cases in which treatment was scored as ineffective, with an overall efficacy rate of 80% (16/20). The difference between the two groups in efficacy rate was statistically significant ($\chi^2 = 16.94$, $P < 0.001$).

Results of Esophageal Solid-State HRM

The LES resting pressure, LES residual pressure, and DCI were all within the normal ranges in all 40 patients. Elevated UES resting pressure was present in 35% of the patients (14/40), and 30% of the patients (12/40) had elevated UES residual pressure. The enrolled patients were divided into two groups based on UES resting pressure: a high-pressure group (UES resting pressure > 104 mmHg) (n = 14) and a non-high-pressure group (UES resting pressure ≤ 104 mmHg) (n = 26).^{13,14} Comparisons of the age, duration of disease, clinical symptom score, and SAS score are shown in Table 2.

There was no significant difference in age between the high-pressure group and the non-high-pressure group ($P > 0.05$). The course of disease, clinical symptom score and SAS score of the two groups were statistically significant (all $P < 0.05$). The hypertension group had longer course of

disease, more severe clinical symptoms and higher SAS scores.

Correlation Between Esophageal Pressure Changes and Psychological Status

An SAS score of less than 50 was considered to indicate no anxiety, a score of 50–59 mild anxiety, and a score of 60–69 moderate anxiety. In the high-pressure group, there were two cases with no anxiety, eight cases with mild anxiety, and four cases with moderate anxiety. In the non-high-pressure group, there were 24 cases with no anxiety and two cases with mild anxiety. A comparison of SAS scores between the two groups is shown in Table 3.

There was a significant difference in Anxious state of the two groups ($\chi^2 = 21.04$, $P < 0.001$). The high-pressure group was more anxious than the non-high-pressure group.

The spearman rank correlation analysis of esophageal pressure and anxiety was used and gave a result of $R = 0.74$ and $P < 0.001$, indicating a statistically significant positive correlation between esophageal pressure and anxiety ($R = 0.69$, $P < 0.001$).

Discussion

The results of the comparison of clinical symptoms and SAS scores before and after treatment in the control group suggested no significant improvement in symptoms and psychological status after treatment, therefore indicating that the effect of using proton-pump inhibitors and prokinetic drugs in the treatment of globus sensation is unsatisfactory.¹⁵ The

Table 3 The Comparison of Anxious State Between the High-Pressure Group and the Non-High-Pressure Group

Anxiety State	High-Pressure Group n (%)	Non-High-Pressure Group n (%)	χ^2	P
Anxiety	12 (85.71%)	2 (7.69%)	21.04	< 0.001*
No anxiety	2 (14.29%)	24 (92.31%)		
Total	14	26		

Note: * $P < 0.05$, the difference is statistically significant.

efficacy rate in the treatment group, which was given flupentixol/melitracen in addition to the treatment given to the control group, was 80%—much higher than that of the control group (15%). Comparison of the efficacy rate between the two groups revealed that the difference was statistically significant ($\chi^2 = 16.94$, $P = 0.00$), which indicates that the therapeutic effect with the addition of flupentixol/melitracen was better than that of the treatment in the control group. Furthermore, the clinical symptom score and SAS score decreased in the treatment group after treatment ($P = 0.00$), indicating that clinical symptoms and anxiety status improved significantly after treatment. These results suggest that flupentixol/melitracen is effective in the treatment of globus sensation.¹⁶

Tang et al¹⁷ previously reported that the occurrence of globus sensation is closely correlated with psychosomatic factors. Flupentixol/melitracen, as a compound preparation, helps to regulate the level of various neurotransmitters in the synaptic gap, prompting the improvement of autonomic and central nervous system functions, with good anti-anxiety and antidepressant effects. Moreover, flupentixol/melitracen can effectively improve mental perception abnormalities and reduce visceral hypersensitivity, the mechanism of which might be correlated with the increased excitability of the vagus nerve in these patients.¹⁸ Flupentixol/melitracen could lower the anxiety of patients with globus sensation, reduce visceral hypersensitivity, and improve the symptoms of foreign-body sensation in the pharynx, which could be worthy of clinical application.

In the solid-state esophageal HRM results, elevated UES resting pressure was present in 35% of patients, while elevated UES residual pressure was present in 30% of patients, suggesting that elevated esophageal sphincter pressure might be present in patients with globus sensation.^{19,20} In the present study, the patients were divided into two groups based on UES resting pressure: a high-pressure group (UES resting pressure > 104 mmHg) (n = 14) and a non-high-pressure group (UES resting pressure ≤ 104 mmHg) (n = 26). Comparison of the duration of disease, clinical symptom score, and SAS score revealed that the differences between these two groups were statistically significant ($P < 0.001$). Patients in the high-pressure group were found to have a longer duration of disease, more severe clinical symptoms, and more significant anxiety than those in the non-high-pressure group.^{21,22} In the high-pressure group, there were two cases with no anxiety, eight cases with mild anxiety, and four cases with moderate anxiety, whereas

in the non-high-pressure group there were 24 cases with no anxiety and two cases with mild anxiety. The difference in the incidence of anxiety between the two groups was statistically significant ($P < 0.001$), indicating that patients in the high-pressure group were more prone to developing anxiety than those in the non-high-pressure group. The results of the correlation analysis of esophageal pressure and anxiety were $R = 0.74$ and $P < 0.001$, indicating that there is a positive correlation between esophageal pressure and anxiety.

The present study had some limitations: Firstly, the conclusions of the study lack novelty. Although a more advanced method of measuring esophageal pressure, the HRM method, was used, no esophageal dynamics factors related to the globus were found. Secondly, the number of cases was small and the clinical data was limited, so a larger sample size should be used in future studies.

Conclusion

The addition of flupentixol/melitracen in patients with globus sensation was clinically effective and is worth promoting. Some patients with globus sensation had elevated UES resting and residual pressure. Patients with globus sensation who develop anxiety were more likely to have high pressure in the upper esophageal sphincter.

Acknowledgements

We would like to acknowledge the hard and dedicated work of all staff that implemented the intervention and evaluation components of the study.

Funding

Science and Technology Bureau of Wenzhou City, Zhejiang Province (N0.Y2020297).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Gastroenterology group, behavioral medicine branch, Chinese Medical Association. Chinese experts' consensus on multidisciplinary diagnosis and treatment of globus sensation. *Chin Soc Behav Med.* 2020;8(4):217–222.
2. Liu Y, Jia L. The esophageal motility characteristics and levels of brain-gut peptide in patients with refractory globus. *Chin J Diagn.* 2016;4(3):149–152.
3. Bouchoucha M, Girault-Lidvan N, Hejnar M, Mary F, Airinei G, Benamouzig R. Clinical and psychological characteristics of patients with globus. *Clin Res Hepatol Gastroenterol.* 2019;43(5):614–622. doi:10.1016/j.clinre.2019.01.006

4. Rasmussen ER, Schnack DT, Ravn AT. A prospective cohort study of 122 adult patients presenting to an otolaryngologist's office with globus pharyngeus. *Clin Otolaryngol off J ENT-UK off J Netherlands Soc Oto-Rhino-Laryngol Cerv-Fac Surg.* 2018;43(3):854–860. doi:10.1111/coa.13065
5. Tawil J, Fass R. Globus: current concepts and dilemmas. *J Clin Gastroenterol.* 2018;52(10):845–852. doi:10.1097/MCG.0000000000001129
6. Fox MR, Bredenoord AJ. Oesophageal high-resolution manometry: moving from research into clinical practice. *Gut.* 2008;57(3):405–423. doi:10.1136/gut.2007.127993
7. Kahrilas PJ. Esophageal motor disorders in terms of high-resolution esophageal pressure topography: what has changed? *Am J Gastroenterol.* 2010;105(5):981–987. doi:10.1038/ajg.2010.43
8. Kwiatek MA, Mirza F, Kahrilas PJ, Pandolfino JE. Hyperdynamic upper esophageal sphincter pressure: a manometric observation in patients reporting globus sensation. *Am J Gastroenterol.* 2009;104(2):289–298. doi:10.1038/ajg.2008.150
9. Cook IJ, Dent J, Collins SM. Upper esophageal sphincter tone and reactivity to stress in patients with a history of globus sensation. *Dig Dis Sci.* 1989;34(5):672–676. doi:10.1007/BF01540336
10. Corso MJ, Pursnani KG, Mohiuddin MA, et al. Globus sensation is associated with hypertensive upper esophageal sphincter but not with gastroesophageal reflux. *Dig Dis Sci.* 1998;43(7):1513–1517. doi:10.1023/a:1018862814873
11. Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features and Rome IV. *Gastroenterology.* 2016;150:1262–1279.e2. doi:10.1053/j.gastro.2016.02.032
12. Sweis R, Anggiansah A, Wong T, Kaufman E, Obrecht S, Fox M. Normative values and inter-observer agreement for liquid and solid bolus swallows in upright and supine positions as assessed by esophageal high-resolution manometry. *Neurogastroenterol Motil off J Eur Gastrointest Motil Soc.* 2011;23(6):509–e198. doi:10.1111/j.1365-2982.2011.01682.x
13. Rogers BD, Gyawali CP. Enhancing high-resolution esophageal manometry: use of ancillary techniques and maneuvers. *Gastroenterol Clin North Am.* 2020;49(3):411–426. doi:10.1016/j.gtc.2020.04.001
14. Kuribayashi S, Iwakiri K, Shinozaki T, et al. Clinical impact of different cut-off values in high-resolution manometry systems on diagnosing esophageal motility disorders. *J Gastroenterol.* 2019;54(12):1078–1082. doi:10.1007/s00535-019-01608-3
15. Zhang W, Tang S, Wang Y, Bao W. Efficacy of TCM Qingre Sanjie therapy combined with pantoprazole sodium and mosapride citrate on chronic pharyngitis with gastroesophageal reflux. *Chin J Gen Pract.* 2017;15(10):1725–1727.
16. Tang Y, Liang J, Liang X, et al. Analysis of the efficacy of flupentixol and melitrazin combined with acid inhibitors and prokinetic drugs in the treatment of hysteria. *J North Pharm.* 2019;16(11):91–92.
17. Tang B, Cai HD, Xie HL, Chen DY, Jiang SM, Jia L. Epidemiology of globus symptoms and associated psychological factors in China. *J Dig Dis.* 2016;17(5):319–324. doi:10.1111/1751-2980.12354
18. Yu -Y-Y, Fang D-C, Fan -L-L, et al. Efficacy and safety of esomeprazole with flupentixol/melitracen in treating gastroesophageal reflux disease patients with emotional disorders. *J Gastroenterol Hepatol.* 2014;29(6):1200–1206. doi:10.1111/jgh.12552
19. Peng L, Patel A, Kushnir V, Gyawali CP. Assessment of upper esophageal sphincter function on high-resolution manometry: identification of predictors of globus symptoms. *J Clin Gastroenterol.* 2015;49(2):95–100. doi:10.1097/MCG.0000000000000078
20. Nevalainen P, Walamies M, Kruuna O, Arkkila P, Aaltonen L-M. Supragastric belch may be related to globus symptom - a prospective clinical study. *Neurogastroenterol Motil off J Eur Gastrointest Motil Soc.* 2016;28(5):680–686. doi:10.1111/nmo.12764
21. Sun J, Xu B, Yuan Y-Z, Xu J-Y. Study on the function of pharynx upper esophageal sphincter in globus hystericus. *World J Gastroenterol.* 2002;8(5):952–955. doi:10.3748/wjg.v8.i5.952
22. Zhou W-C, Jia L, Chen D-Y, et al. The effects of paroxetine and amitriptyline on the upper esophageal sphincter (UES) pressure and its natural history in globus pharyngeus. *Dig Liver Dis off J Ital Soc Gastroenterol Ital Assoc Study Liver.* 2017;49(7):757–763. doi:10.1016/j.dld.2017.02.008

International Journal of General Medicine

Dovepress

Publish your work in this journal

The International Journal of General Medicine is an international, peer-reviewed open-access journal that focuses on general and internal medicine, pathogenesis, epidemiology, diagnosis, monitoring and treatment protocols. The journal is characterized by the rapid reporting of reviews, original research and clinical studies

across all disease areas. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-journal-of-general-medicine-journal>