

Does *Helicobacter pylori* treatment improve the symptoms of globus hystericus?

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Background/aims: Globus hystericus is a feeling of tension in the throat, irrelevant of swallowing, persisting for at least 12 weeks. Since the cause of globus hystericus is not fully described, the treatment is controversial. We aimed in this study to determine the symptoms of gastroesophageal reflux disease, upper gastrointestinal endoscopic findings, prevalence of *Helicobacter pylori*, and post-treatment symptoms (symptoms of gastroesophageal reflux and/or *Helicobacter pylori*) in patients with a diagnosis of globus hystericus. **Materials and Methods:** One hundred twenty three patients were recruited from the archives of the Department of Gastroenterology and Endoscopy at Celal Bayar University Medical School between January 2009 and August 2010. **Results:** *Helicobacter pylori* was positive in 75 (60%) of 123 patients with globus hystericus. *Helicobacter pylori* (+) patients had significantly more heartburn, regurgitation, and inlet patch in upper esophagus than *Helicobacter pylori* (-) patients. Significantly more *Helicobacter pylori* (-) patients had normal endoscopy findings when compared to *Helicobacter pylori* (+) patients. While 27 (50%) of *Helicobacter pylori*-eradicated patients had regressing globus symptoms, 12 (17.3%) of them did not have any regression in globus symptoms. Improvement in symptoms showed a positive correlation with *Helicobacter pylori* eradication ($p=0.001$). **Conclusions:** *Helicobacter pylori* rate among cases with globus sensation was similar to values in the general population. *Helicobacter pylori* eradication was found to decrease globus symptoms.

Key words: Globus hystericus, *Helicobacter pylori*, eradication of *Helicobacter pylori*

Helikobakter pilori eradikasyonu globus histerikus semptomlarını geriletmekte mi?

Giriş ve Amaç: Globus histerikus, en az 12 haftadır devam eden, boğazda takılma hissi, yutmada zorlanma olarak tanımlanmaktadır. Globus histerikus sebebi net aolarak açıklanmadığı gibi tedavisinde de bir fikir birliği yoktur. Bu çalışmada amacımız endoskopi ünitesinde globus histerikus ön tanısı ile sevk edilen ve üst gastrointestinal endoskopisi yapılan olgularda; gastroözofageal reflü semptomları, üst gastrointestinal endoskopik bulguları, *Helikobakter pilori* prevalansını saptamak ve *Helikobakter pilori* eradikasyonu yapılan olgularda globus histerikus semptomlarının durumunu belirlemektir. **Gereç ve Yöntem:** Ocak 2009-Ağustos 2010 yılları arasında Celal Bayar Üniversitesi Tıp Fakültesi Gastroenteroloji kliniğinde boğazda takılma hissi (Globus histerikus?) ön tanısı ile endoskopi yapılan ve Gastroenteroloji polikliniğinde eradikasyon tedavisi verilen ve tekrar kontrole gelen 123 olgunun dosya bilgileri retrospektif olarak kaydedildi. **Bulgular:** Globus histerikuslu 123 olgunun 75'inde *Helikobakter pilori* (+) olarak bulunmuştur. *Helikobakter pilori* (+) olgularda göğüs arkasında yanma, ağza acı ekşi su gelme ve üst özofagus düzeyinde inlet patch *Helikobakter pilori* (-) olgulara göre anlamlı olarak daha yüksek bulundu. *Helikobakter pilori* (-) olgularda normal endoskopi *Helikobakter pilori* (+) olgulara göre anlamlı olarak daha yüksek idi. *Helikobakter pilori* eradike olan 27 (%50) olguda globus histerikus semptomlarının geçtiği 12 (%17.3) kişide ise herhangi bir değişiklik olmadığı bulunmuştur. *Helikobakter pilori* eradikasyonu ile semptomların gerilemesinde pozitif korelasyon bulunmuştur. **Sonuç:** *Helikobakter pilori* globus histerikus olan olgularda toplumda aynı düzeyde olmakla birlikte *Helikobakter pilori* tedavisinin globus histerikus şikayetlerini geriletmediği görülmüştür.

Anahtar kelimeler: Globus histerikus, *Helikobakter pilori*, *Helikobakter pilori* eradikasyonu

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INTRODUCTION

Globus sensation (GS) is a feeling of tension in the throat, irrelevant of swallowing, persisting for at least 12 weeks (1,2). The sensation can be described as if something is caught in the throat, a subjective sensation of a lump, felt between meals in the absence of dysphagia or odynophagia, pathological reflux, achalasia, or any other motility disorder with a recognized pathological basis (3). The cause of globus is unknown. Although many reasonable, pathogenetic mechanisms (cricopharyngeal spasm, temporomandibular joint dysfunction, pharyngeal dysmotility, and gastroesophageal reflux [GER]) have been suggested for globus, all remain unproven (3,4).

Helicobacter pylori (*Hp*) is a Gram-negative bacteria and is considered a causative agent of peptic ulcer disease, gastric lymphoma, and gastric carcinoma; it was also investigated in extra-digestive conditions (coronary artery disease, urticaria, diabetes mellitus, migraine, auto immune thyroiditis, etc.), which were associated somewhat with *Hp* infections, though the pathogenetic mechanism is mostly unknown (5,6).

Since the cause of GS is not fully described, the treatment is controversial. In this retrospective study, we aimed to determine the symptoms of gastroesophageal reflux disease (GERD), upper gastrointestinal (GI) endoscopic findings, prevalence of *Hp*, and post-treatment symptoms (symptoms of GER and/or *Hp*) in patients with a diagnosis of globus hystericus.

MATERIALS AND METHODS

Patients were recruited from the archives of the Department of Gastroenterology and Endoscopy at Celal Bayar University Medical School between January 2009 and August 2010. One hundred and twenty-three patients (36 males, 87 females; mean age: 43.2 years; age range: 18-76 years) were diagnosed as having GS and were enrolled in this study.

The study was carried out with the approval of the Institutional Ethical Review Board of the Celal Bayar University Medical Center. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki.

Patients who were on continuous treatment with acid suppression in the preceding four weeks before endoscopy, who were on continuous treatment with *Hp* eradication, who had refused upper gastrointestinal system (GIS) endoscopy, and those

who had accepted upper GIS endoscopy but rejected treatment or did not take their drugs regularly were excluded from the study. Those who had a history of previous laryngeal, pharyngeal, liver, lung, renal, or hematological disorders, history of GI surgery or history of connective tissue disorders were also excluded from the study.

All patients in our clinic had initially attended the psychiatric and ear, nose and throat (ENT) clinics and had normal results as reported from these clinics.

Upper GI endoscopy was performed in all patients, and two biopsy specimens were taken from the antrum and the gastric body for histological examination and detection of *Hp*. Biopsy specimens were fixed in formalin, embedded in paraffin, and stained with a modified toluidine blue for detection of *Hp*.

According to the endoscopic findings, patients were assessed in relation to esophagitis (according to the Los Angeles classification) (7), gastritis (antral and/or corpus), duodenal ulceration, and normal endoscopic findings. Patients were considered *Hp*-positive (+) if histology and/or rapid urease tests were positive.

After *Hp* eradication, the patients were checked with urea breath test.

Typical GERD symptoms were defined as at least three episodes per week of regurgitation and/or heartburn. Heartburn was defined as a burning pain or discomfort behind the breast bone in the chest. Regurgitation was defined as a bitter or sour-tasting fluid entering the throat or mouth.

Erosive esophagitis was defined as the presence of superficial esophageal erosions in patients with or without typical symptoms of GERD. Los Angeles classification uses the term "mucosal breaks" instead, to denote the presence of either esophageal erosions or ulcerations (7).

Heterotopic gastric mucosa was defined as patches covered with salmon-red mucosa distinguishable from the surrounding grayish-pearl-colored esophageal mucosa by well-defined margins.

Patients who had normal pathological and endoscopic evaluations were designated as normal.

Cigarette use was ascertained as a history of cigarette smoking (yes or no) and, for current smokers, the number of cigarettes per day. Alcohol use was defined in terms of average number of drinks per week in the previous year.

This study does not include an investigation on pharmaceutical agents; therefore, the names of products were kept confidential. The patients who had reflux symptoms or gastritis and were *Hp*-negative (-) were given proton pump inhibitor (PPI) treatment, those who were *Hp* (+) with or without reflux symptoms were given *Hp* eradication (2 weeks). Four weeks after treatment, *Hp* status was checked using the C14 urea breath test or upper GI endoscopy. All patients were then evaluated in terms of the improvement four weeks after treatment of globus symptoms.

Data were coded and entered in the Statistical Package for the Social Sciences (SPSS) program (SPSS version 15.0) for analysis. Chi-square or Fisher's exact test was used to compare discrete variables and the t-test for continuous variables. The level of significance was accepted as $p < 0.05$.

RESULTS

One hundred and twenty-three patients (36 males, 87 females) with globus hystericus who underwent endoscopic examination were recruited into this study. The mean age $\pm$ SD of the patients was 43.2 ± 15.7 years. *Hp* was positive in 75 (60%) of the 123 patients. Clinical endoscopic and characteristic data of the patients are summarized in Table 1.

Hp was positive in 61% of women and 58% of men of the 123 patients. There was no significant difference between genders regarding the presence or not of *Hp*. Reflux symptoms were positive in 32 (26%) patients. Twenty-seven (21.9%) patients had inlet patch.

In patients with globus hystericus, *Hp*(+) patients had significantly more heartburn, acid regurgitation, and inlet patch in the upper esophagus than *Hp* (-) patients. Furthermore, significantly more *Hp* (-) patients had normal endoscopy findings when compared to *Hp* (+) patients. There was no difference between tobacco and alcohol use between the two groups.

Improvement in globus symptom after *Hp* eradication and/or PPI treatment is summarized in Table 2. After the treatment (*Hp* eradication and/or PPI treatment), 54 (43.9%) patients reported improvement in the globus symptoms and 69 (56.1%) had no improvement in their globus symptoms. There was no significant difference between the two groups ($p = 0.239$).

Although 42 patients who had received *Hp* eradication treatment indicated improvement in the globus symptoms, 35 patients who had received *Hp* eradication treatment did not. There was no significant difference between the two groups.

Table 1. Clinical endoscopic and characteristic data of patients

	<i>Hp</i> (+) (n=75)	<i>Hp</i> (-) (n=48)	p value
Female, n (%)	54 (71.1)	33 (70.2)	0.539
Male, n (%)	21 (28.9)	15 (29.8)	0.539
Age (years)	45.2	41.3	0.568
Heartburn, n (%)	13 (17.1)	2 (4.3)	0.029
Regurgitation, n (%)	15 (19.7)	2 (4.3)	0.012
Inlet patch in upper esophagus, n (%)	21 (27.6)	6 (12.8)	0.041
Esophagitis, n (%)	8 (10.5)	4 (8.5)	0.487
Gastritis (antral and/or corpus), n (%)	34 (44.7)	17 (36.2)	0.227
Duodenal ulcer, n (%)	6 (7.9)	2 (4.3)	0.348
Alcohol, n (%)	13 (17.1)	5 (10.6)	0.237
Tobacco, n (%)	26 (34.2)	11 (23.4)	0.143
Normal endoscopy	15 (19.7)	17 (36.2)	0.036

Table 2. Improvement in globus symptoms after *Hp* eradication and/or PPI treatment

	Improvement in globus symptoms	No improvement in globus symptoms	P
All patients	54 (43.9)	69 (56.1)	0.249
<i>Hp</i> -eradicated patients	27 (50)	12 (17.3)	0.0001
Patients with failed eradication	15 (27.7)	23 (33.3)	0.478
Patients with PPI treatment only	14 (22.3)	34 (49.4)	0.462

Thirty-nine of the patients who had received *Hp* eradication treatment had successful *Hp* eradication, but *Hp* eradication failed in 38 patients.

While 27 (50%) of the *Hp*-eradicated patients had regressing globus symptoms, 12 (17.3%) of them had no regression in globus symptoms. Improvement in symptoms showed a positive correlation with *Hp* eradication ($p=0.000$).

Of the patients who underwent *Hp* eradication treatment but with eradication failure, 15 (27.7%) had improvement in globus symptoms and 23 (33.3%) had no improvement in globus symptoms. Furthermore, there was no significant difference between the two groups of patients.

There was no significant difference in the improvement in globus symptoms in patients who received only PPI treatment.

DISCUSSION

Globus sensation (GS) is primarily caused by cervical disturbances. The usual complaint in GS is sensation of a ball or lump in the throat, which is usually not accompanied by dysphagia. It is not a painful condition, and obstruction of food is not an issue (8-10). Studies on globus have shown a prevalence of up to 35% of men and over 50% of women (11,12).

In our study, 29.2% of the cases were men and 70.8% were women. The exact cause of globus is unknown. Published potential causes include cricopharyngeal spasm, psychogenic causes, lingual tonsillary hypertrophy, cervical osteophytes, and temporomandibular joint disorders (2).

To our knowledge, this is the first study to date about globus symptoms and *Hp*. Previous studies found an association between *Hp* and nonspecific pharyngitis but not an association with nasal polyps, larynx tissue and/or otitis media (13-15). In our study, *Hp* was found to be positive in 60% of globus hystericus patients. These results are in compliance with *Hp* prevalence studies conducted in Turkey (prevalence of *Hp* in Turkey is between 48% and 68%) (16,17). The correlation between globus hystericus and GERD was investigated in previous studies, but the exact cause was not fully explained (3,18). Sinn *et al.* (18) showed that GERD symptoms were positive in 64% of cases with symptoms of globus. However, the improvement in the typical reflux symptoms had no asso-

ciation with improvement in globus symptoms after two weeks of PPI treatment. In our study, the reflux symptoms were positive in 32 (26%) of the cases with symptoms of GS. This result was lower than in the study by Sinn *et al.* (18), but it complies with results of epidemiological reflux studies conducted in our country (16,17). In the present study, PPI (30 mg/day) was administered to *Hp*(-) cases with dyspepsia and/or reflux symptoms (endoscopic, clinic). Among cases who did not respond to *Hp* eradication and who only received PPI treatment (even though symptoms of pyrosis and regurgitation improved in 86%), treatment did not lead to any change in globus symptoms.

Previous studies did not demonstrate a positive correlation between PPI treatment and GS symptoms, as in our study (18,19).

To our knowledge, this is the first study about globus symptoms and *Hp* and the improvement in globus symptoms after treatment of *Hp*. *Hp* eradication treatment was provided to all cases for two weeks. *Hp* status was checked two weeks after discontinuation of eradication treatment with urea breath test. *Hp* eradication was observed in 51.3% of cases who received eradication treatment. We believe that drug resistance is a possible cause of the failed eradication treatment. In our study, symptoms were relieved in 53.9% (41) of patients who received eradication treatment. Among *Hp*-eradicated cases, globus symptoms improved significantly. Is the improvement in symptoms with treatment correlated with *Hp* located in the upper esophagus? Upon evaluating our cases in terms of a response to this question, inlet patch was found in 28 patients, all of whom were subjected to biopsy. *Hp* was positive in 21 cases, and 8 of these patients (38%) were eradicated. Among these 8 cases, globus symptoms improved in 4 cases; this result represents a negative response to the question stated above. In this study, is *Hp* one of the leading and unknown causes of GS? Further studies conducted on larger patient series are definitely required to clarify this issue.

In conclusion, the *Hp* rate among cases with GS was similar to values in the general population. *Hp* eradication was found to decrease symptoms of globus. Further prospective studies conducted on larger patient groups and drug-based trials, if needed, are required to confirm these results.

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