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Main Article

Seroprevalence of *Helicobacter pylori* infection in patients with chronic nonspecific pharyngitis: preliminary study

İ Aladag, Y Bulut*, M Guven, A Eyibilen, K Yelken

Abstract

Background and objectives: Chronic nonspecific pharyngitis is a chronic inflammation of the pharynx. It is found worldwide, and treatment is difficult. The underlying aetiopathogenesis is still controversial. The aim of this study was to investigate *Helicobacter pylori* seroprevalence in chronic nonspecific pharyngitis patients without other possible causative factors for chronic pharyngeal irritation and without *H pylori* gastric mucosal infection.

Materials and methods: Forty-one patients with symptoms of chronic nonspecific pharyngitis and 30 healthy control subjects were enrolled in this prospective, controlled, clinical study. In both study and control groups, selected patients were shown to have gastric mucosa uninfected by *H pylori*, as demonstrated by the 14C-urea breath test. Comprehensive otorhinolaryngological examination did not elicit any factor contributing to the chronic pharyngeal complaint. Serum *H pylori* immunoglobulin G antibody titres were assayed using serum enzyme-linked immunosorbent assay. The difference between the study and control groups was analysed by the chi-square test (the likelihood ratio was used).

Results: Thirty-two of the 41 patients (78 per cent) and 14 of the 30 control subjects (46.7 per cent) were found to be *H pylori* positive. Patients with chronic nonspecific pharyngitis were found to have a significantly higher rate of *H pylori* seropositivity than the control group ($p = 0.016$).

Conclusion: These data may be important in developing future treatment strategies for chronic nonspecific pharyngitis.

Key words: Pharyngitis; Helicobacter Pylori

Introduction

Chronic nonspecific pharyngitis is a common complaint among patients seeking medical treatment. Frequently, these patients present with symptoms such as chronic throat irritation, sore throat, chronic cough, globus sensation, cervical dysphagia and intermittent hoarseness. Chronic nonspecific pharyngitis has been related to a wide variety of processes, such as nasal obstruction and mouth breathing, laryngopharyngeal reflux, and acute or chronic upper respiratory tract infection. Treatment of patients with chronic nonspecific pharyngitis must focus on the primary disorders. However, these remain unclear in many cases.

In patients with chronic nonspecific pharyngitis, the oropharyngeal mucosa may appear hypertrophic and granular, dry and atrophic, hyperaemic and oedematous, or sometimes normal. Diagnosis is often based on the patient's history and the clinical examination. Treatment is usually based on reducing the symptoms by medical or behavioural methods.

Helicobacter pylori is well known as a pathogenic micro-organism responsible for chronic inflammation of gastric mucosa.[1] It has been estimated to infect approximately half the world's population, the majority with no gastric ailments.[2] However, epidemiological studies have focused only on the gastric manifestations of this micro-organism; there are few data on symptoms and findings associated with other organ systems.

In the past few years, a variety of extradigestive disorders have been associated with *H pylori* infection.[3] *Helicobacter pylori* has been isolated from the oral cavity, dental plaques, salivary secretions,[4,5] adenotonsillar tissues[6] and tracheo-bronchial secretions.[7] Recently, *H pylori* seropositivity has been found in many cases of chronic inflammatory respiratory disease.[8–10]

The aim of this study was to investigate *H pylori* seroprevalence in adult patients with chronic nonspecific pharyngitis.

Materials and methods

The study was conducted from March 2003 to December 2004 within our otolaryngology

From the Departments of ORL and *Microbiology, Faculty of Medicine, Gaziosmanpasa University, Tokat, Turkey.
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out-patient department. We prospectively evaluated a total of 257 consecutive subjects with one or more symptoms of chronic nonspecific pharyngitis, and 74 subjects with no pharyngeal complaint (for at least three months). The chronic nonspecific pharyngitis symptoms included were sore throat, chronic throat irritation, chronic cough, globus sensation, cervical dysphagia and intermittent hoarseness, persisting for three months or more.

An initial questionnaire was conducted to evaluate any other conditions that might contribute to pharyngeal irritation. Then, a comprehensive otorhinolaryngological examination was performed, including nasal, pharyngeal and laryngeal endoscopic evaluations. Any subject (from both groups) found to have suspicious questionnaire results or examination findings was excluded from the study (Table I). A 14C-urea breath test (Helicap, Noster System AB, Stockholm, Sweden) was used in the remaining subjects in order to detect *H pylori* infection of the gastric mucosa. Subjects with positive or suspicious results for this test were also excluded. Thus, the study was conducted on 41 patients in the study group (21 women and 20 men; age range 38–67 years, mean age 51.5 years) and 30 subjects in the control group (16 women and 14 men; age range 40–64 years, mean age 49.1 years).

All symptoms and oropharyngeal appearances were documented, and patients and control subjects were followed for three months. Venous blood samples from the two groups were obtained and stored at −70°C before analysis. *Helicobacter pylori* immunoglobulin (Ig) G antibody titres were measured using a serum enzyme-linked immunosorbent assay (lot number 050325, Vidas, bioMérieux® SA, Marcy l'Etoile, France). Results for *H pylori* IgG were recorded as positive, equivocal and negative when the serum concentration was >20, 12.5–20 and <12.5 U/ml, respectively.

The difference between the study and control groups was analysed by chi-square test, with $p < 0.05$ accepted as significant.

TABLE I

FACTORS CONTRIBUTING TO CHRONIC PHARYNGEAL SYMPTOMS

Nasal obstruction & mouth breathing
Chronic upper respiratory infections
Laryngopharyngeal reflux
Chronic periodontal infections
Chronic exposure to irritating inhaled substances (e.g. tobacco; excessively hot, dry or polluted air; industrial fumes)
Excessively hot or cold foods
Alcohol intake
Pharyngeal neurosis
Angiotensin-converting enzyme inhibitors
Long-term use of antiseptic lozenges
Neoplasm & vasculitis

Results

There were no significant differences in the age or sex distribution of the two groups. In the control group, no patient reported any of the index symptoms for longer than 10 days. The predominant symptoms on presentation in the 41 chronic nonspecific pharyngitis patients were chronic throat irritation (56 per cent), sore throat (54 per cent), chronic cough (32 per cent), intermittent hoarseness (20 per cent), globus sensation (7 per cent) and cervical dysphagia (5 per cent). Most of the subjects in the control group had a normal oropharyngeal examination. Table II lists the oropharyngeal appearances seen in the study and control subjects.

Table III shows the analysis of serological parameters. Rates of *H pylori* seropositivity were significantly higher in patients with chronic nonspecific pharyngitis than in controls ($p = 0.016$). The mean serum concentration of *H pylori* IgG antibodies was also significantly higher in the chronic nonspecific pharyngitis patients than in the controls ($p = 0.012$).

Discussion

Chronic pharyngitis is a chronic inflammation of the pharyngeal mucosa. Occasionally, pharyngeal mucosa infection is secondary to a primary infection by specific micro-organisms such as *Treponema pallidum*, *Mycobacterium tuberculosis*, *Mycobacterium leprae* and *Klebsiella rhinoscleromatis*; this is termed chronic specific pharyngitis. These micro-organisms are generally associated with multiple organ effects. However, in most chronic pharyngitis patients, localised complaints are the only presenting symptoms.

Acute pharyngitis is considered to be a separate condition to chronic pharyngitis, as it has a different history, different findings and different disease course. Acute pharyngitis may be caused by a wide variety of microbial agents, but the majority of disease originates from viral agents. Group A beta-haemolytic streptococci are dangerous micro-organisms which are responsible for approximately 5–17 per cent of sore throats in adults. However, the causative micro-organism in many cases of streptococcal pharyngitis remains unclear.[11]

Generally, in patients with chronic pharyngeal complaints, an active, pathogenic micro-organism is not looked for or cannot be found. After such

TABLE II

OROPHARYNGEAL APPEARANCE IN CHRONIC NONSPECIFIC PHARYNGITIS PATIENTS AND CONTROLS

Group	Normal	Hypertrophic & granular	Dry & atrophic	Hyperaemic & oedematous
CNP (%)	4.9	12.2	29.3	53.7
Controls (%)	73.3	–	23.3	3.3

CNP = chronic nonspecific pharyngitis

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TABLE III

SEROLOGIC PARAMETERS IN CHRONIC NONSPECIFIC PHARYNGITIS PATIENTS AND CONTROLS

Group	*H pylori* IgG (%(*n*))			χ^2	*p*
	Positive	Negative	Borderline		
CNP*	78 (32)	19.5 (8)	2.4 (1)	8.4	<0.05
Controls†	46.7 (14)	40 (12)	13.3 (4)		

*$n = 41$; †$n = 30$. Ig = immunoglobulin; CNP = chronic nonspecific pharyngitis

causative factors as nasal obstruction, chronic sinonasal infection, allergy, laryngopharyngeal reflux and smoking are eliminated, the symptoms of pharyngeal irritation generally diminish or completely disappear.

However, in cases in which an obvious pharyngeal irritant does not exist, physicians struggle to reduce patients' complaints, using various topical anti-inflammatory agents or behavioural methods. Although no findings indicate acute bacterial infection, patients with chronic pharyngeal complaints are frequently treated with antibiotics by primary care physicians and sometimes by otolaryngologists. However, some patients do benefit from such treatment, and this fact suggests that bacteria may be responsible for the condition. There are a limited number of studies in the literature related to chronic pharyngitis. As yet, no published studies have assessed rehabilitation of chronic pharyngeal complaints using antibiotic therapy.

In the present study, *H pylori* was studied as a potential cause for nonspecific pharyngeal symptoms and pharyngeal inflammation in patients with chronic nonspecific pharyngitis. We suggest that antibiotics may be a useful therapeutic tool in some (but not all) patients with chronic nonspecific pharyngitis. Further investigation of the condition is needed.

Helicobacter pylori infection of the gastric mucosa affects approximately half the world's population. In Turkey, the incidence is reported to be about 60 per cent.[12] In the present study, rates of *H pylori* seropositivity in control subjects were 46.7 per cent. However, in the study group, the *H pylori* prevalence was significantly higher compared with rates both worldwide and in Turkey. Zhang *et al.* detected *H pylori* in 38 per cent of chronic nonspecific pharyngitis cases but in no control subjects, using a polymerase chain reaction assay.[13] In contrast, the present study excluded any patients with disorders which might potentially contribute to pharyngeal irritation. After elimination of such causative factors as nasal obstruction and smoking, patients' symptoms dramatically decreased. Since *H pylori* usually colonises gastric mucosa, we also excluded patients with acute *H pylori* infection of gastric mucosa. The results of our study strongly confirm the serologic evidence for *H pylori* in patients with chronic nonspecific pharyngitis.

In gastric mucosa, it is evident that *H pylori* stimulates the release of various proinflammatory substances, cytokines, eicosanoids and acute phase proteins.[14] Therefore, a pathogenic link between *H pylori* infection and diseases characterised by activation of inflammatory mediators may exist. These proinflammatory substances are also thought to be involved in the pathogenesis of a variety of respiratory diseases, including chronic bronchitis[15] and bronchiectasis.[16] Moreover, recent studies have shown an increased *H pylori* seroprevalence in patients with these inflammatory diseases.[8,9] Therefore, *H pylori* infection may play a proinflammatory role and act as a co-trigger in these diseases. It may also initiate and promote other chronic inflammatory disease processes, such as chronic nonspecific pharyngitis. In recent studies, *H pylori* has been isolated from adjacent tissues, such as oral cavity epithelium, dental plaque and salivary secretions.[4,5] Unver *et al.*[6] found *H pylori* to be present in 57.9 per cent of adenoid and tonsillar tissues. This result suggests that the oral cavity and pharynx may the initial site of *H pylori* colonisation and may act as a reservoir for systemic infection.

- **Chronic nonspecific pharyngitis is a chronic inflammation of the pharynx. Its treatment is controversial. The underlying aetiopathogenesis is still not completely understood**
- **This study aimed to investigate *Helicobacter pylori* seroprevalence in chronic nonspecific pharyngitis patients**
- ***Helicobactyer pylori* seropositivity rates were found to be significantly higher in chronic nonspecific pharyngitis patients than in controls**
- **Further investigations are needed to clarify the mechanism of mucosal inflammation in chronic nonspecific pharyngitis. *Helicobacter pylori* may be a causative factor in this condition**

We used two different tests to diagnose *H pylori*. The 14C-urea breath test measures urease activity and only detects gastric *H pylori*. This test was used to determine whether subjects' gastric mucosa was infected with *H pylori*. Then, serological investigation determined subjects' *H pylori* seropositivity. Although biopsy-based methods (including culture, polymerase chain reaction and histopathology) have been accepted as the gold standard by many authors, they are technically difficult and expensive.

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Furthermore, biopsy-based methods may be susceptible to sampling error (because of discontinuous *H pylori* colonisation of mucosa), thus requiring multiple biopsy specimens.[17] However, it is difficult to take oropharyngeal biopsies in the out-patient department, because of proximity of deep cervical fascia, thin mucosa, and severe, persistent pain following the procedure. Therefore, we preferred serological investigation for *H pylori*. The sensitivity and specificity for *H pylori* antibody tests are about 95 per cent.[2] In addition, such serological tests are non-invasive, relatively inexpensive and easily performed. Furthermore, results are not affected by prior treatment with antibiotics or proton pump inhibitors.

Further investigations are needed to clarify the mechanism of mucosal inflammation in patients with chronic nonspecific pharyngitis. *Helicobacter pylori* may be one of the causative factors in the initiation of chronic nonspecific pharyngitis.

Conclusion

This study found a high rate of *H pylori* seroprevalence (78 per cent) in patients with chronic nonspecific pharyngitis; this is significantly higher than in subjects without chronic pharyngeal symptoms (46.7 per cent). Chronic nonspecific pharyngitis is a common disease. We believe that these results may be important in understanding the pathophysiology of this disease and in developing future treatment strategies.

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Address for correspondence:
Professor İbrahim Aladag,
Department of Otorhinolaryngology,
Medical Faculty,
Gaziosmanpasa University,
Tokat, Turkey.

Fax: 90 356 213 31 79
E-mail: ibrahimal@hotmail.com

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