Difference of Helicobacter pylori Colonization in Recurrent Inflammatory and Simple Hyperplastic Tonsil Tissues

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Objective: To investigate the difference in colonization by Helicobacter pylori between recurrent inflammatory and normal hyperplastic human palatine tonsil tissues.

Design: A retrospective review of a prospective data set.

Setting: Tertiary referral center.

Patients: Patients undergoing tonsillectomy for a variety of reasons had routine screening for H pylori. Medical records of all patients who underwent tonsillectomy were reviewed to identify (1) indications for surgery and (2) presence or absence of H pylori in the specimen. All medical records that had information on H pylori were included. Patients were divided into the following 2 groups: those having tonsillectomy for chronic recurrent tonsillitis and those having tonsillectomy for sleep-related breathing disorders (SRBDs) with no recent history of tonsillitis.

Results: There were 44 patients in the tonsillitis group (18 women and 26 men; mean age, 28.6 years) and 50 patients in the SRBD group (11 women and 39 men; mean age, 33.6 years). Of 94 patients the Pronto Dry test results were positive in 33 (35%) and negative in 61 (65%). The H pylori positive rates in the tonsillitis and SRBD groups were 48% (21 of 44) and 24% (12 of 50), respectively (P<.001).

Conclusions: Helicobacter pylori can colonize in human palatine tonsil tissues. A significantly higher positive H pylori rate was present in the tonsillitis group (48%) compared with the SRBD group (24%). Based on this finding, future studies should be performed to elucidate whether eradication therapy for H pylori is effective in decreasing recurrent inflammation of human palatine tonsils.


Tonsillectomy is one of the most common surgical procedures in the field of otolaryngology.1 Although there are a wide variety of tonsil diseases, recurrent inflammation causing chronic tonsillitis and obstructive hyperplasia causing sleep-related breathing disorders (SRBDs) are 2 common conditions indicating tonsillectomy. In the upper aerodigestive tract, the Waldeyer ring serves as the first line of mucosal defense against invading pathogens. Tonsillar tissue is a component of mucosa-associated lymphoid tissue (MALT) involving antigen processing and concerned with immune surveillance. Swollen tonsils may narrow breathing passages and cause SRBDs.

Helicobacter pylori, first acknowledged in 1983 by Marshall and Warren,2 is involved in duodenal ulcer, gastric ulcer, gastric adenocarcinoma, and MALT formation.3 The World Health Organization’s International Agency for Research on Cancer classified H pylori as a group I (definite) carcinogen.4 Although the stomach is the natural reservoir of H pylori, various tissues are proposed as potential reservoirs of infection such as dental plaque, gingiva, saliva, gallbladder, and coronary arteries.5 Results of several studies trying to detect H pylori in chronic tonsillitis tissue were controversial.6-11 Furthermore, most of these studies lacked a control group. Therefore, we performed the first study to investigate the difference of H pylori colonization in recurrent inflammatory and simple hyperplastic human palatine tonsil tissues.

Methods

Medical records of all patients who underwent tonsillectomy for chronic tonsillitis and uvulopalatopharyngoplasty for SRBD were reviewed to identify patients with available data on H pylori. Institutional review board approval for this study was obtained. All medical records with available data were included in the study. The records were reviewed to identify the following data: (1) patient demographics, (2) indications for surgery, and (3) result of the Pronto Dry test. Surgical indications were...
divided into 2 groups. Group 1 comprised patients with chronic recurrent tonsillitis (which occurred more than 3 times and had poor response to aggressive antibiotic therapy in 1 year) without SRBD. Group 2 comprised patients with SRBD without recent history of tonsillitis. The incidence of positive Pronto Dry test results (H pylori presence) was assessed in each group of patients.

The standard protocol included cutting a 2- to 3-mm-diameter piece from each tonsillectomy specimen with a sterile blade. To prevent contamination while obtaining the specimens, each specimen was cut with different blade and gloves were changed between each cutting. The tissue piece was placed in a Pronto Dry test kit (Medical Instruments Corp, Solothurn, Switzerland) that detects the urease enzyme of H pylori to detect the presence of H pylori. The Pronto Dry test findings were examined at intervals of 5, 30, and 60 minutes at room temperature. A pink–magenta color change in the external ring of the prepared kit indicates a positive reaction; if it stayed yellow, the result was recorded as a negative reaction.

RESULTS

There were 44 patients in the tonsillitis group (18 women and 26 men; mean age, 28.6 years) and 50 patients in the SRBD group (11 women and 39 men; mean age, 33.6 years). The male to female ratio in tonsillitis group was 1.4:1, and that of the SRBD group was 3.6:1.

Of the 94 patients, the Pronto Dry test results were positive for H pylori in 33 (35%) and negative in 61 (65%). Thirteen of the 33 H pylori–positive patients (39%) had positive reactions for both tonsil tissues, while 20 (61%) were positive on only 1 side. The H pylori positive rate was 31% among male patients and 45% among female patients, which showed no statistical significance (P = .19, χ² test; difference, 14% [95% confidence interval, −6% to 34%]). However, the H pylori–positive rate was significantly different (P = .02, χ² test; difference, 23.8% [95% confidence interval, 4% to 41%]) between the tonsillitis group (21 of 44 [48%]) and the SRBD group (12 of 50 [24%]) (Table).

COMMENT

Helicobacter (formerly known as Campylobacter) pylori are gram-negative microaerophilic spiral-shaped bacteria. Since the discovery of H pylori in 1983, its role in the pathogenesis of gastritis, peptic ulcer disease, and low-grade MALT lymphoma has been well established.² ³ ⁹ Helicobacter pylori is well adapted to life in the hostile acidic environment of the stomach. Several important factors are responsible for its ability to thrive in the stomach, such as its spiral shape, flagella that allow it to move rapidly through viscous mucus, production of urease, which produces ammonia from urea to buffer gastric acid, and its ability to adhere to gastric mucous cells.¹² Although H pylori is a common infection that has affected approximately half of the world’s population,¹³ to date the precise modes of transmission are not yet fully understood. Many confounding factors such as socioeconomic status of the patients, bacterial and patient genetic characteristics, presence of concomitant infections, and previous antibiotic therapies could all influence epidemiological and clinical studies of H pylori colonization.¹¹

In 1989, Krajden et al¹⁴ first reported the isolation of H pylori from the oral environment. They found that 3.4% of patients with H pylori gastritis had H pylori in their dental plaque. Since then, several investigators reported identifying H pylori in the oral cavity.¹⁵ However, most of these studies focused on only dental plaque and saliva. In 1997, Minoo et al¹⁶ reported the first study linking a history of tonsillectomy with gastric colonization of H pylori. They concluded that a history of tonsillectomy was associated with decreased prevalence of gastric colonization. This raised the question of whether H pylori colonized the tonsils. Unver et al¹⁷ conducted the first study investigating the colonization of H pylori in tonsillar and adenoid tissues by Campylobacter–like organism (CLO) test. Their results showed that 11 of 19 patients (58%) with chronic recurrent tonsillitis were H pylori positive. Compared with these data, our results showed a relatively lower H pylori–positive rate (48%) in the tonsillitis group. This difference could be due to the exclusion of the patients with obvious symptoms of gastroesophageal reflux or laryngopharyngeal reflux in our study. While most study findings of tonsils as reservoirs for H pylori were affirmative,¹⁸ all of the studies focused only on patients with chronic tonsillitis and lacked control groups. To our knowledge, this is the first study to investigate the colonization of H pylori in 2 different tonsillar diseases.

The palatine tonsils originating from the second pair of pharyngeal pouches are the lateral walls that compose the bulk of the Waldeyer ring of lymphoid tissue. They are coated by nonkeratinous stratified epithelium including approximately 30 deep crypts that invaginate into the parenchyma and bacteria can also be present in the crypts.¹⁹ The histological investigation of chronic inflammation of the palatine tonsils often shows hyperkeratosis of the crypt epithelium.¹⁷ This epithelial modification causes impaired antigen uptake and neutrophil chemotaxic function, which led to the recurrence of inflammatory processes, with increasingly severe hyperparakeratosis, triggering a vicious circle. Some immunohistochemical examination of chronic tonsillitis tissue revealed persistent hyperplasia of B lymphocytes and decreased T-cell compartment that could alter the host immunologic state. In our study, we observed that in recurrent inflammatory tonsillitis tissues, the positive rate for H pylori infection was significantly higher than that of tissue with simple hyperplasia. These results gave rise to the hypothesis that among patients in the chronic recurrent tonsillitis group, morphologic changes in the crypt epithelium and alteration of immune mechanisms could predispose patients to colonization with H pylori. Previ-
ous reports also suggested that *H pylori* activates macrophages and stimulates inducible nitric oxide synthase expression and activity in the forager. However, Skinner et al found that macrophage inducible nitric oxide synthase expression in tonsil samples was significantly higher in *H pylori* seropositive patients compared with seronegative patients. This finding made us believe that *H pylori* could prime the tonsils by inducing macrophage inducible nitric oxide synthase expression and more marked cytokine responses. Therefore, it is plausible that *H pylori* induced a proinflammatory reaction in the palatine tonsils, which are located at the port of entry into the upper aerodigestive tract, as with other MALT tissue. This could have explained the higher colonization rate of *H pylori* in the tonsillitis group than in the SRBD group in our study.

There are various methods available to detect *H pylori* infection. They include culturing for *H pylori*; determining the level of urease activity in the specimen; staining the specimen with hematoxylin-eosin stain, Giemsa stain, or Warthin-Starry silver stain; evaluating specimens by means of polymerase chain reaction; and using the enzyme-linked immunosorbent assay technique to identify specific immunoglobulin G antibodies against *H pylori* in the serum. Of these methods, culture is the most difficult to perform and requires the most time with the greatest meticulousness of technique. However, polymerase chain reaction, which is an important tool for detecting genetic material of *H pylori*, is more complicated than culture to perform. The accuracy of polymerase chain reaction can also be affected by several factors such as the choice of primers and the target DNA, bacterial density of the sample, preparation of the specimen, and variations in laboratory protocols. The urease test is the most frequently used for the diagnosis of *H pylori* in clinical practice. Said et al compared the accuracy and reaction time of the Pronto Dry and the CLO test. The Pronto Dry test had a faster positive reaction time compared with the CLO test, with 96.2% positive reaction by 30 minutes vs 70.8%, and 100% positive reaction by 55 minutes vs 83%.

The colorimetric changes were also more distinct with the Pronto Dry test compared with the CLO test. Other advantages of the Pronto Dry test include no refrigeration required, no incubation or liquids required, and color change showing the degree of infection. The Pronto Dry test was also cost-effective, simple, and convenient and had a high sensitivity with specificity for *H pylori*.

In conclusion, our study showed that *H pylori* colonizes human palatine tonsil tissue (positive results in 35%). Furthermore, we found a significantly higher positive rate for *H pylori* in the tonsillitis group (48%) than in the SRBD group (24%). Based on this finding, future studies should be performed to elucidate whether eradication therapy for *H pylori* is effective in decreasing recurrent inflammation of human palatine tonsils and may play an important role in treating patients with chronic recurrent tonsillitis.

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**Author Contributions:** Dr Lin had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Lin. Acquisition of data: Lin and Wu. Analysis and interpretation of data: Lin, Friedman, Chang, and Wilson. Drafting of the manuscript: Lin and Wu. Critical revision of the manuscript for important intellectual content: Friedman, Chang, and Wilson. Statistical analysis: Chang and Wilson. Administrative, technical, and material support: Lin and Wu. Study supervision: Friedman.

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**References**


