

Research Article

Is The Theoretical Knowledge Reflected in Current Practice: Histopathological *Helicobacter Pylori* Research?

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Abstract: Objective: *Helicobacter pylori* (*H. pylori*) is considered in the category of biological agent directly responsible for cancer. Guidelines recommend discontinuing suppressive conditions prior to histopathological *helicobacter pylori* testing, but there is little clinical trial data on how outcome is affected if this is not done. Optimal test recommendations in the guidelines are based on *in vitro* study results.

In present study, we aimed to observe whether there was a difference in the prevalence of *H. pylori* histopathologically in patients who met the necessary prerequisites before Esophago-Gastro-Duodenoscopy (EGD) compared to the subjects group who did not meet the PPI discontinuation condition.

Materials & Methods: This retrospective study was conducted between October 2015 and August 2016 in a reference hospital with 1.5 million hinterlands. Patients who underwent EGD by meeting all the prerequisites recommended by the guidelines for the *H. pylori* test were included in the study group (n=213), and those who discontinued other suppressive drugs except PPI were included in the control group (n=193).

Results: While *H. pylori* was found to be 74.6% positive in the study group that provided all the prerequisites for histopathological *H. pylori* detection, *H. pylori* was found to be 64.9% positive in the control group continuing to receive PPI treatment (p=0.02).

Conclusion: In conclusion, we suggest that it is necessary to proceed with the guidance of classical knowledge in determining the presence of *H. pylori*, which is a common public health problem that is up-to-date.

Keywords: *Helicobacter pylori*, Suppressive condition, Proton pump inhibitor, Histopathology, Cancer, Guideline.

INTRODUCTION

Helicobacter pylori (*H. pylori*) ranks first among cancer related infections that in a study based on 2018 Globocan data [1]. When not eradicated, it is blamed in the aetiology of many diseases, from chronic gastritis to gastric maltoma, as a result of progressive damage to the mucosa, and is considered in the category of biological agent directly responsible for cancer by the World Health Organization [2-4].

The socioeconomic status, infrastructure and sanitation conditions of the countries affect its prevalence [5]. Non-invasive and invasive methods are used for *H. pylori* detection and the sensitivity and specificity of these methods vary [6-8]. Biopsy samples taken during esophagogastroduodenoscopy (EGD) show the presence / absence of *H. pylori* as well as the information about the gastric mucosa. In order to determine *H. pylori* histopathological, certain prerequisites must be met before EGD procedure. It is known that upper Gastrointestinal System (GIS) bleeding, antibiotics, bismuth preparations and Proton Pump Inhibitors (PPI) affect *H. pylori* tests. It is a common advice that PPIs should be discontinued for *H. pylori* detection, and it has been put into the guidelines after preclinical studies [9-11]. There are many studies on the negative effects of suppressive states on *H. pylori* tests. There are a

limited number of clinical studies directly investigating the effect of PPI use on histopathological *H. pylori* prevalence [12, 13].

In present study, it was investigated whether there was a difference in the prevalence of *H. pylori* histopathological in patients who met the necessary prerequisites before EGD compared to the subjects group who did not meet the PPI discontinuation condition and continued to use PPI.

MATERIALS AND METHODS

This retrospective study includes individuals who admitted to a reference hospital gastroenterology clinic between October 2015 and August 2016. Local ethic board approved the study. Consecutive patients enrolled to the study who admitted to the gastroenterology clinic without gastrointestinal bleeding, and with intact stomach. The patients were evaluated for study criteria right after obtaining at least 4 biopsy specimens from large and lesser curvatures of antrum and corpus. Suppressive conditions were noted by patient history and confirmed from computerized database (national patient data registry system). According to the guidelines, patients without suppressive conditions were enrolled to the study group while other subjects with only used PPI as a suppressive condition were grouped into the control group. Design of the study was abstracted in Fig. (1).

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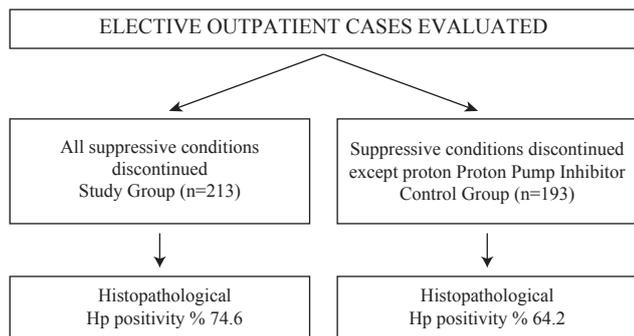


Fig. (1). Study Flowchart.

Exclusion criteria were as follows: unwilling to participate, inadequate data about medical history in last 1 month, conflicting medical history and national medical registry database.

Finally, 213 patients without a history of any suppressive conditions were enrolled in study group, while 193 patients with PPI use without antibiotic or bismuth usage were enrolled as controls. Endoscopic biopsy specimens were evaluated according to the Sydney classification after they have been transported in 10% formaldehyde solution to the pathology laboratory. Specimens were stained with Giemsa or hematoxylin eosin and *H. pylori* was evaluated with Toluidine dye [14].

STATISTICAL ANALYSES

SS 16.0 software was used in comparison of the data in study and control groups. Kolmogorov Smirnov test was used in evaluation of normality data. Data with normal distribution was compared with independent Samples T test and expressed as mean ± standard deviation. Nonparametric data were expressed as numbers and percentage and compared with X2 test. A P value lower than 0.05 was considered as statistically significant.

RESULTS

Total population consisted of 406 patients; 213 in the study group (134 women (63%), 79 men (37%)) and 193 subjects in the control group (106 women (55%), 87 men (45%)). Mean age of the study and control groups were 52 ±15 years and 54.6 ±15 years, respectively (p=0.360). In the study group, 159 cases (74.6%) were reported as positive for *H. pylori*, 54 cases (25.4%) were reported to be *H. pylori* negative. The effect of gender on *H. pylori* has not been determined (p=0.100). Table 1 shows the characteristics of the study population.

H. pylori was positive in 124 (64.2%) of 193 cases in the control group. There was no effect of gender on *H. pylori* positivity in patients in the control group (p=0.12).

Table 1. Effects of PPI use on *H. pylori* Positivity.

Group	<i>H. pylori</i> (+)	<i>H. pylori</i> (-)	n
PPI discontinued	159 (%74.6)*	54 (%25.4)*	213
PPI continued	124 (%64.2)	69 (%35.8)	193

H. pylori: *Helicobacter pylori*, PPI: Proton pump inhibitor.
*P=0.020.

While *H. pylori* was found to be 74.6% positive in the study group that provided all the prerequisites for histopathological *H. pylori* detection, *H. pylori* was found to be 64.2% positive in the control group continuing to receive PPI treatment. There is a statistically significant difference between the two groups in terms of *H. pylori* positivity (p=0.020).

DISCUSSION

The data underlying the guidelines for the detection of *H. pylori* are based on preclinical, *in vitro* studies. Our study is unique because it is a clinical study that aims to investigate the effect of PPI on histopathological *H. pylori* detection using real life data. While the prevalence of *H. pylori* was 74.6% in the study group performed under ideal conditions, the prevalence of *H. pylori* was found to be 64.2% lower in the control group whose PPI was not discontinued (p=0.02).

Contribution of *H. pylori* infection to gastric carcinogenesis; detection and treatment is important due to the importance of regression in *H. pylori* -associated premalignant lesions with eradication [15]. Biopsy samples taken during esophagogastroduodenoscopy provide information about the presence of *H. pylori* as well as the histopathological findings of the mucosa. By histopathological method, *H. pylori* test has 90% sensitivity and 97% specificity, 96% positive and 97% negative predictive value [16, 17]. Detection of *H. pylori* presence during the endoscopic biopsy procedure is affected by some factors. Therefore, it is recommended to stop antibiotic and bismuth preparations 1 month in advance and PPI group drugs 2 weeks before the procedure. In addition, the *H. pylori* test results of patients who had GIS bleeding in the last 2 weeks are affected by histopathological method [18]. It is difficult to provide optimal conditions in gastroenterology practice for various reasons.

The use of antibiotics and bismuth directly affects *H. pylori* with an antibacterial effect [19]. With the use of PPI, the colonization of *H. pylori* in the stomach changes, urease activity decreases and turns from spiral form to coccoid form [20, 21]. Therefore, the value of *H. pylori* tests decreases.

In a study conducted on *H. pylori* isolates, it was shown that omeprazole and lansoprazole exhibited a suppressive effect on *H. pylori* and urease activity, and these agents recovered the bacterial activity only 12-14 days after they were removed from the environment [22].

Knoop *et al.* found that 76% of the patients who underwent EGD in outpatients and inpatients were in suppressive condition and 70% of these cases were using PPI [13]. In the aforementioned study, *H. pylori* was investigated in half of the patients, and *H. pylori* was not indicated in the other half. In our study, due to the conditions of our country, a routine investigation of *H. pylori* was performed in all patients, and also in outpatient elective cases. Therefore, the cases are homogeneous in terms of *H. pylori* research. In the study of Knoop *et al.* *H. pylori* positivity was 17.3% in the group that was deemed appropriate to investigate *H. pylori*. 82.7% of the cases were *H. pylori* negative and the rate of PPI usage in this negative group was investigated. In our study design, the effect of PPI use on *H. pylori* is revealed more clearly since the cases are grouped in terms of PPI usage from the beginning.

In our study, while *H. pylori* negativity was 25.4% in the cases that met optimal conditions, it was found 35.8% negativity in the group using PPI. Therefore, the use of PPI has been shown to increase false negativity.

In the study conducted by Sirin *et al.* patients were recruited from 3 different centers and the areas where the biopsy were taken varied [12]. In our study, the patients were standardized by taking four biopsy samples from a single center and from 2 regions from all patients.

In a retrospective study conducted in Canada, the rate of standard biopsy from the antrum and corpus is 57% when the biopsied stomach segments of the cases undergoing *H. pylori* research are evaluated. The rate of taking biopsy only from the antrum is 47% and only from the corpus is 13% [23]. In this context, our study is a study in which both suppressive conditions and biopsy intake conditions are provided under optimal conditions. The lack of any method other than histopathology is the deficiency of our study. However, our clinical possibilities are limited with this method.

With this study, a result confirming the guideline information that PPI should be discontinued before EGD operation was reached. It has been shown that the false negativity rate of cases increases significantly when the procedure is performed without interrupting the PPI.

H. pylori infection is an issue that is up-to-date in gastroenterology practice, and eradication and vaccination efforts have not achieved the desired success. Despite the relative decrease in prevalence due to the interest of physicians and patients compared to the 90's when it came to the agenda, it still remains a public health problem for many countries.

CONCLUSION

In conclusion, we suggest that it is necessary to proceed with the guidance of classical knowledge in determining the

presence of *H. pylori*, which is a common public health problem that is up-to-date. It should be kept in mind that an invasive method with a sensitivity and specificity of more than 90% in detecting the presence of *H. pylori* results in a substantially false negative result when the necessary preconditions are not met.

CONFLICT OF INTEREST

Declared none.

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