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ORIGINAL ARTICLE

Retrospective Study

Influence of proton pump inhibitors on gastritis diagnosis and pathologic gastric changes

Soumana C Nasser, Mahmoud Slim, Jeanette G Nassif, Selim M Nasser

Soumana C Nasser, Jeanette G Nassif, School of Pharmacy, Lebanese American University, P.O. Box 36, Byblos, Lebanon
Mahmoud Slim, Institute of Neuroscience, University of Granada, 18012 Granada, Spain
Selim M Nasser, Department of Pathology, School of Medicine, Lebanese American University, Blat 36, Lebanon
Author contributions: Nasser SC and Nasser SM were involved in the conception and design of the study; Slim M participated in the data collection of the study; Nasser SM conducted the immunohistochemical analysis and evaluation; Nasser SC, Slim M, Nassif JG and Nasser SM participated in data analysis, interpretation and evaluation, drafting and final approval of the article.
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Data sharing: Technical appendix, statistical code, and dataset are available from the corresponding author at selim.nasser@lau.edu.lb.

Correspondence to: Selim M Nasser, MD, Associate Professor, Chief, Department of Pathology, School of Medicine, Lebanese American University, Blat 36,
Lebanon. selim.nasser@lau.edu.lb
Telephone: +961-3-259806
Fax: +961-9-547256
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Abstract

AIM: To investigate the influence of proton pump inhibitors (PPIs) exposure on the diagnosis of *Helicobacter pylori* (*H. pylori*) gastritis and intestinal metaplasia.

METHODS: Chronic PPI use is associated with masking of *H. pylori* infection. Patients with *H. pylori* infection are predisposed to gastric and duodenal ulcers, and long-term infection with this organism has been associated with gastric mucosal atrophy and serious long-term complications, such as gastric lymphoma and adenocarcinoma. Three hundred patients diagnosed with gastritis between January 2008 and April 2010 were included in our study. The computerized medical database of these patients was reviewed retrospectively in order to assess whether the type of gastritis diagnosed (*H. pylori vs* non-*H. pylori* gastritis) is influenced by PPI exposure. *H. pylori* density was graded as low, if corresponding to mild density following the Updated Sydney System, or high, if corresponding to moderate or severe densities in the Updated Sydney System.

RESULTS: Patients were equally distributed between males and females with a median age at the time of diagnosis of 50 years old (range: 20-87). The histological types of gastritis were classified as *H. pylori* gastritis (n = 156, 52%) and non-*H. pylori* gastritis (n = 144, 48%). All patients with non-*H. pylori* gastritis had inactive chronic gastritis. Patients with no previous PPI exposure were more likely to be diagnosed with *H. pylori* gastritis than those with previous PPI exposure (71% *vs* 34.2%, $P < 0.001$). Intestinal metaplasia

was more likely to be detected in the latter patients (1.4% *vs* 6.5%, P = 0.023). Multivariate analysis has also demonstrated that in the presence of previous PPI exposure (OR = 0.217, 95%CI: 0.123-0.385), GERD (OR = 0.317, 95%CI: 0.132-0.763, P = 0.01), alcohol intake (OR = 0.396, 95%CI: 0.195-0.804, P = 0.01), the detection of *H. pylori* was less likely. Chronic use of PPIs may mask *H. pylori* infections promoting the diagnosis of non-*H. pylori* gastritis and leads to a significant drop in *H. pylori* densities and to an increased risk of intestinal metaplasia.

CONCLUSION: The use of PPIs masks *H. pylori* infection, promotes the diagnosis of non-*H. pylori* inactive chronic gastritis diagnosis, and increases the incidence of intestinal metaplasia.

Key words: Gastritis; Diagnosis; *Helicobacter pylori*; Proton pump inhibitors; Social factors

Core tip: This study investigates the influence of proton pump inhibitors (PPIs) exposure on the diagnosis of *Helicobacter pylori* (*H. pylori*) gastritis in patients undergoing endoscopic gastric biopsies. The study findings revealed that in patients undergoing gastric biopsies, the use of PPIs promotes the diagnosis of non-*H. pylori* gastritis, is associated with lower *H. pylori* densities and to increased risk of intestinal metaplasia as compared with subjects with no PPI exposure. These findings should urge health-care professionals to consider the possibility of underdiagnosed *H. pylori* gastritis in patients exposed to PPI.

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INTRODUCTION

Proton pump inhibitors (PPIs) are widely used among patients experiencing symptoms of dyspepsia or gastroesophageal reflux disease (GERD), which is a common disorder affecting around one-third of adults and requiring long-term maintenance therapy. PPIs are also indicated in the treatment of peptic ulcer disease (PUD) in combination with suitable antibiotics for the eradication of *Helicobacter pylori* (*H. pylori*) infection. In addition, this class of medications is used for the treatment and prevention of NSAIDs-induced gastroduodenal ulcers and hypersecretory conditions such as Zollinger-Ellison Syndrome[1]. The risk of inadequate use of PPIs is not only attributed to their wide spectrum of indications, but mainly to the common practice of self-medication with these agents especially in developing countries. Profound acid suppression by PPIs was shown to be associated with masking *H. pylori* infections, the main cause of chronic active gastritis and peptic ulcer disease[2]. In this context, it was reported that the use of a PPI over an average of 6.5 days has turned Urea Breath Test (UBT) negative in *H. pylori* positive subjects[3,4], and that a minimum of a two-week period off the drug was needed to avoid false negative UBT results[5]. These observations implicate serious consequences as undetected *H. pylori* infection or persistent *H. pylori* gastritis may lead to atrophic gastritis with the development of intestinal metaplasia, dysplasia, and increased risk of gastric adenocarcinoma as well as gastric Mucosa-Associated-Lymphoid-Tissue (MALT) lymphoma[6]. Also, the use of PPIs among patients with *H. pylori* gastritis was shown to cause a change in the gastritis pattern, which shifted from antral- to corpus-predominant gastritis[7], as well as to an increased epithelial cell proliferation[8]. *H. pylori* eradication is therefore recommended to prevent many of the complications associated with the long-term use of PPIs in patients harboring *H. pylori* organisms[9,10]. However, lack of adherence to national and international guidelines for *H. pylori* infection treatment is not uncommon, and long-term PPI use can contribute to under-diagnosis of *H. pylori* gastritis. The long-term use of PPIs has also been linked to a wide range of complications such as small intestinal bacterial overgrowth (SIBO)[11], enterochromaffin-like cells hyperplasia[12], and gastrin-cell tumors[13]. However, atrophic gastritis, a prominent risk factor for gastric cancer, remains the most serious complication. The current evidence concerning this complication is contradictory. While PPIs were shown to be linked to an accelerated onset of atrophic gastritis in the study conducted by Kuipers *et al*[14], Lundell *et al*[15] reported the lack of effect of acid suppression therapy on gastric atrophy.

The primary objective of our study is to determine the effect of PPI exposure on the diagnosis of the type of gastritis (*H. pylori vs* non-*H. pylori* gastritis), *H. pylori* density, and intestinal metaplasia in patients with gastritis documented by gastroscopic biopsy. On the other hand, the effects of social habits on gastritis type were also evaluated.

MATERIALS AND METHODS

Three hundred and eleven patients with a pathologic diagnosis of gastritis received between January 2008 and April 2010 were identified in the archives of the pathology department in a Medical Center in Beirut, Lebanon. Patients were then stratified based on PPI exposure. Patients' electronic charts were reviewed. Demographic data, clinical presentation, and pathologic findings were collected using appropriated

data collection sheets. The type of gastritis, intestinal metaplasia, and *H. pylori* density were then correlated with PPI use. Gastritis type was defined as *H. pylori* gastritis or non-*H. pylori* gastritis, when *H. pylori* organisms were not detected. *H. pylori* density was graded as low, if corresponding to mild density following the Updated Sydney System or high, if corresponding to moderate or severe densities in the Updated Sydney System. To avoid confounders, all gastritis cases associated with specific etiologies other than *H. pylori*, such as reactive gastropathy or autoimmune gastritis, were excluded from the study. As such, 11 cases of reactive gastropathy (chemical gastritis) were excluded, and 300 cases of either *H. pylori* gastritis or non-*H. pylori* gastritis were included. All cases of non-*H. pylori* gastritis showed inactive chronic gastritis. Knowing that long-term PPI therapy is the mainstay treatment of GERD patients and is often justifiable, analysis was performed on a subgroup of patients after excluding those with GERD to control for possible bias.

Data collection forms included patient's demographic information, past medical history, medication use, social habits including alcohol intake, smoking, and exercise, history of PPI or other acid- suppressive treatment with emphasis on the specific PPI used, pathologic findings, and clo test results.

Immunohistochemical detection of H. pylori gastritis

All *H. pylori* negative cases showing inactive chronic inflammation were selected for Immunohistochemical (IHC) staining with *H. pylori* antibodies. 5-μm-thick tissue sections from formalin fixed paraffin embedded gastric biopsy samples were mounted onto charged glass slides. IHC staining was performed after microwave antigen retrieval using citrate buffer (Biogenex). Endogenous peroxidase activity was blocked by incubating the slides in a solution of hydrogen peroxide block (Biogenex). Slides were incubated for 60 min at room temperature with ready-to-use anti *H. pylori* monoclonal antibody (rabbit, clone y236, Biogenex). Antibody binding was detected by a Biotin-Strepatavidin detection system with Diaminobenzidine as chromogen (Super-sensitive link-label, Biogenex). Harris hematoxylin was used as counterstain. Sections of gastric biopsy with *H. pylori* organisms were run simultaneously as external positive controls.

Statistical analysis

Variables were summarized using frequencies and percentages with the exception of age where the median was used. The association between categorical variables was evaluated using Pearson χ^2 test or Fisher's exact test where the expected cell count was less than 5. The contribution of PPI use and social factors on the detection of *H. pylori* was evaluated using binary logistic regression and using a multivariate model when controlling for age, gender, exercise, smoking, alcohol intake, and GERD. A 0.25 *P* value of the Wald test from logistic regression was assumed as the cut-off point for selecting the covariates for the multivariate analysis. Possible interactions between covariates of the regression model were also evaluated. Hosmer-Leme show statistic was calculated to evaluate the model's goodness-of-fit. Statistical analyses were performed using SPSS version 18 software. *P* values below 0.05 were considered to be statistically significant.

The statistical methods of this study were reviewed by the biostatistician, Dr. Hani Dimassi, Associate Professor from the School of Pharmacy at the Lebanese American University.

RESULTS

Three hundred patients, diagnosed with *H. pylori* gastritis or non-*H. pylori* inactive chronic gastritis, were equally distributed between males and females with a median age of 50 years old (range: 20-87) at the time of diagnosis. The most common symptoms reported by patients upon presentation for endoscopy were abdominal pain (50.7%), heartburn (12.30%), and dyspepsia (11%). History of smoking, alcohol intake, and exercise were identified in 42%, 20.70%, and 32.70% of patients respectively (Table 1). The most common medical problem identified among all patients was hypertension 81 (27%) (Table 1). PPI use was documented in 155 (52%) of the patients, 47% of which were on rabeprazole. Of those on PPIs, 51% had clear indications such as GERD (31%), gastritis (13.5%), and peptic ulcer disease (6.5%), while 49% of the PPI users had an undocumented diagnosis (Table 1).

Effects of PPI exposure on H. pylori detection and density, gastritis type, and intestinal metaplasia

Out of the 300 patients reviewed, *H. pylori* gastritis was diagnosed in 156 patients (52%) and non-*H. pylori* inactive chronic gastritis in 144 patients (48%). Patients with previous PPI exposure were less likely to have *H. pylori* gastritis compared to non-users (34.2% *vs* 71%, $P < 0.001$). Therefore, the diagnosis of non-*H. pylori* inactive chronic gastritis was significantly more frequently established in patients with previous PPI exposure (65.8% *vs* 29%, $P < 0.001$) (Table 2). Moreover, patients diagnosed with *H. pylori* gastritis with PPI use had significantly lower *H. pylori* densities than those patients with *H. pylori* gastritis not using PPIs (25.8% *vs* 35.9%, $P < 0.001$). Indeed, low-density *H. pylori* colonies were seen in 75.5% (40 out of 53) of PPI users diagnosed with *H. pylori* gastritis; thus high-density colonies were detected in only one fourth of PPI users who were diagnosed with *H. pylori* gastritis (Table 2). Also of significance, the presence of intestinal metaplasia was higher among PPI users (6.5% *vs* 1.4%, $P = 0.023$) (Table 2).

We considered the possibility that the high prevalence

Table 1 Baseline patient characteristics *n* (%)

Characteristics	Value
Age, median (range), yr	50 (20-87)
Gender	
Male	150 (50)
Female	150 (50)
Symptoms	
Abdominal burn	152 (50.70)
Heart burn	37 (12.30)
Dyspepsia	33 (11)
Past medical history	
Hypertension	81 (27)
Dyslipidemia	53 (17.7)
Diabetes mellitus	36 (12)
Hypothyroidism	9 (3)
Social habits	
Smoking	126 (42)
Exercise	98 (32.7)
Alcohol intake	62 (20.7)
Medication history	
Anti hypertensives	86 (28.7)
Anti dyslipidemics	54 (18)
Oral hypoglycemics	28 (9.3)
Sedatives	15 (5)
Anti-depressants	16 (5.3)
PPIs[1]	155 (51.7)
Indications for PPI use	
Gastritis	21 (13.5)
GERD	48 (31)
GI ulcer	10 (6.5)
Undocumented diagnosis	76 (49)

[1]Proton pump inhibitors used: Rabeprazole (47%), esomeprazole (33%), omeprazole (17%), others (3%). GERD: Gastroesophageal reflux disease; PPIs: Proton pump inhibitors; GI: Gastrointestinal.

of non-*H. pylori* gastritis patients in the group of PPI users may be due to the fact that many of these patients were taking PPI due to associated GERD and that gastritis in those cases was an incidental finding. However, even after the exclusion of patients with GERD diagnosis, there was still a significant difference between the two groups for the incidence of *H. pylori* detection ($P < 0.0001$), intestinal metaplasia ($P = 0.042$), and *H. pylori* densities ($P = 0.01$) as shown in Table 3.

Results of IHC staining with H. pylori antibodies

Microscopic analysis of the immunostained slides identified rare *H. pylori* organisms in only 1 of 144 cases previously diagnosed with non-*H. pylori* gastritis.

Effect of social habits, gender, age, and on the detection of H. pylori gastritis

Univariate analysis demonstrated significant association between previous PPI exposure, age and alcohol intake and detecting of *H. pylori* (results shown in Table 4). Although the effect of exercise didn't reach statistical significance, it successfully fulfilled the condition for its inclusion in the multivariate logistic regression (Wald test *P*-value < 0.25). On the other hand, gender and smoking were excluded from the multivariate analysis.

Table 2 Effect of proton pump inhibitors exposure on *Helicobacter pylori* detection, density and intestinal metaplasia *n* (%)

	Previous PPI exposure *n* = 155	No PPI exposure *n* = 145	*P* value
H. pylori gastritis	53 (34.20)	103 (71)	< 0.001
Inactive chronic gastritis	102 (65.80)	42 (29)	< 0.001
H. pylori density			
Low density	40 (25.80)	52 (35.90)	< 0.001
High density	13 (8.38)	51 (35.17)	< 0.001
Intestinal metaplasia	10 (6.50)	2 (1.40)	0.023

PPI: Proton pump inhibitor; *H. pylori*: *Helicobacter pylori*.

Table 3 Effect of proton pump inhibitors exposure on *Helicobacter pylori* detection, density and intestinal metaplasia following gastroesophageal reflux disease patients exclusion *n* (%)

	Previous PPI exposure *n* = 109	No PPI exposure *n* =143	*P* value
Gastritis			
H. pylori gastritis	44 (40.40)	101 (70.60)	
Inactive chronic gastritis	65 (59.60)	42 (29.40)	< 0.0001
H. pylori density			
Low density	33 (75.0)	52 (51.50)	
High density	11 (25.0)	49 (48.50)	0.010
Intestinal metaplasia	7 (6.40)	2 (1.40)	0.042

PPI: Proton pump inhibitor; *H. pylori*: *Helicobacter pylori*.

Table 4 Univariate analysis to determine the association between age, gender, exercise, smoking, alcohol intake, gastroesophageal reflux disease and previous proton pump inhibitors exposure with the detection of *Helicobacter pylori*

	OR	95%CI	*P* value
Age	1.019	1.002-1.036	0.028
Gender	1.256	0.76-2.07	0.373
Exercise	0.664	0.389-1.136	0.135
Smoking	0.789	0.476-1.308	0.358
Alcohol intake	0.505	0.27-0.944	0.032
GERD	0.165	0.077-0.355	< 0.01
Previous PPI exposure	0.281	0.166-0.476	< 0.01

GERD: Gastroesophageal reflux disease; PPI: Proton pump inhibitor.

Results of the multivariate regression analysis, shown in Table 5, demonstrate that increasing age was linked to an increased likelihood of successful *H. pylori* detection (OR = 1.022, 95%CI: 1.004-1.041). On the other hand, the detection of *H. pylori* was less likely in patients with previous PPI exposure (OR = 0.217, 95%CI: 0.123-0.385, $P < 0.01$), GERD (OR = 0.317, 95%CI: 0.132-0.763, $P = 0.01$), alcohol intake (OR = 0.396, 95%CI: 0.195-0.804, $P = 0.01$) or exercise (OR = 0.721, 95%CI: 0.393-1.321).

The evaluation of the potential interactions between the different independent variables revealed

Table 5 Multivariate analysis to evaluate the effect of age, exercise, alcohol intake, gastroesophageal reflux disease and previous proton pump inhibitors exposure on the detection of *Helicobacter pylori*

	OR	95%CI	*P* value
Age	1.022	1.004-1.041	0.017
Alcohol intake	0.396	0.195-0.804	0.010
Exercise	0.721	0.393-1.321	0.289
GERD	0.317	0.132-0.763	0.010
Previous PPI exposure	0.217	0.123-0.385	< 0.01

GERD: Gastroesophageal reflux disease; PPI: Proton pump inhibitor.

the presence of significant interaction between GERD and previous PPI exposure (OR = 0.165, 95%CI: 0.077-0.355, $P < 0.01$).

DISCUSSION

Our study demonstrated an inverse relationship between PPI therapy and *H. pylori* detection. PPI exposure seems to suppress the growth of *H. pylori* leading to decreased likelihood of *H. pylori* gastritis diagnosis. This finding is consistent with previous studies[3-5,16]. *H. pylori* detection in our study was based on histological and immunostaining methods. Other studies utilizing UBT as the main method of detecting *H. pylori* revealed false UBT-negative results in around one-third of patients[4,5,17,18]. Dickey *et al*[19] concluded in their study that PPI use before endoscopy was associated with lower sensitivity of antral and corpus biopsies for the detection of *H. pylori* using both urease testing and histological examination. Although the exact mechanism is still unclear, several hypotheses explaining this observation have been postulated. One hypothesis attributes this observation to a number of "characteristic PPI effects", where PPIs promote focally dilated oxyntic glands with flattened or hypertrophic parietal cells protruding into their lumen, in addition to the masking of organisms at the gastric surface and promoting their presence in somewhat obscured locations making the detection of *H. pylori* difficult and thus causing false-negative results[2]. Another hypothesis is related to the elevation of the intragastric pH caused by PPIs, making it an unfavorable environment to *H. pylori* on one hand and promoting the closure of urea channels on the other hand[20-22]. In addition, a direct antimicrobial effect of PPIs causing a further decrease in the *H. pylori* load and thus making it more difficult to detect their presence has been proposed[23,24].

In our non-*H. pylori* gastritis group, the proportions of true *H. pylori* negative gastritis and masked *H. pylori* gastritis remain to be determined. Nordenstedt *et al*[25] have addressed the prevalence of true *H. pylori*-negative gastritis. They required for their diagnosis of *H. pylori* negative gastritis negative triple staining, negative *H. pylori* culture, negative IgG *H. pylori* serology, and no previous treatment for *H. pylori*. They reported that *H. pylori* negative gastritis was found in 21% of their patients. In our study, using routine diagnostic procedures and therefore reflecting usual clinical practice, the rate of *H. pylori* negative gastritis was 48%, which is much higher than that reported in the aforementioned study. We, therefore, suggest that a large proportion of gastritis cases with undetected *H. pylori* organisms on routine histologic examination may represent masked *H. pylori* gastritis, especially given that our geographic location probably carries a higher risk of *H. pylori* infection than that of the above mentioned study. In our study, using an IHC detection method, *H. pylori* organisms were detected in only 1 of 144 cases of *H. pylori* negative gastritis. This low detection rate is in agreement with other studies reporting that the use of ancillary staining techniques does not improve significantly the detection of *H. pylori* organisms over HE stain in gastric biopsies, even if *H. pylori* infection was documented by other means[26,27]. Nonetheless, while acknowledging this low-yield, recent recommendations from the Rodger C. Haggitt Gastrointestinal Pathology Society endorsed the use of special stains including immunohistochemistry for the detection of *H. pylori* gastritis in subsets of chronic inactive gastritis[28].

Our study also determined that PPI exposure led to a significant drop in *H. pylori* densities. This finding was consistent with the investigations conducted by Graham *et al*[29] and Gudlaugsdottir *et al*[30] which was seen as early as one week after omeprazole administration[4,29]. Similarly, in the cross-sectional study conducted by Gudlaugsdottir *et al*[30], patients using PPIs had significantly less *H. pylori* density detected histologically in the antrum region compared to non- users ($P = 0.014$).

The use of PPI was also associated with higher occurrence of intestinal metaplasia in our patient population. Such observation is consistent with the outcomes of an experimental trial in Mongolian gerbils, where long-term administration of PPI (6 mo) promoted significant development of intestinal metaplasia in 93% of the sample taking PPI and who in turn significantly developed adenocarcinoma (60% in the PPI group *vs* 7% in the non-exposed group)[31]. Moreover, Hirschowitz *et al*[32] also observed intestinal metaplasia in 1% of total isolated biopsies and 5% of the 60 patients who were on long-term lansoprazole therapy.

The association between inactive chronic gastritis and PPI exposure is expected in a population residing in a developing country where self-medication is commonly observed especially for common conditions as dyspepsia for a prolonged unnecessary period of time[33]. This was further revealed in data presented in Table 1, where around half of patients were receiving PPIs for an undocumented diagnosis.

We considered the possibility that the higher rate of

inactive chronic gastritis in PPI exposed patients might be due to the inclusion in our study of patients with GERD, whose gastritis may be an incidental finding. However, after excluding 48 GERD patients from the analysis, significant differences were maintained between PPI users and non-users in terms of gastritis type, *H. pylori* densities, and intestinal metaplasia. Besides the chronic use of PPI, we assessed other factors that might be associated with inactive chronic gastritis. Thus, the effect of previous PPI exposure on the masking of *H. pylori* diagnosis has been evaluated in a multivariate logistic regression while controlling for other possible confounding factors such as age, gender, exercise, smoking, alcohol intake and GERD. As a result, our model confirmed the significant association between previous PPI exposure and *H. pylori* masking (OR = 0.217, 95%CI: 0.123-0.385) even after controlling for the possible confounding factors (age, alcohol intake, exercise and GERD).

The increased likelihood of detection of *H. pylori* with increasing age observed in our study (OR = 1.022, 95%CI: 1.004-1.041) is consistent with the outcomes of the study conducted by Zevit *et al*[34], unlike the study conducted by Chen *et al*[35] where age and gender were not correlated with the detection of *H. pylori* using UBT. Our study revealed the absence of any significant correlation between gender and the detection of *H. pylori* contrary to Zevit *et al*[34] who showed increased positive outcomes in the female gender. Our OR for the association between age and *H. pylori* detection is approximately equivalent to what was reported in the study conducted by Zhang *et al*[36] (OR = 1.03, 95%CI: 1.01-1.06).

A history of alcohol intake was also significantly linked to a less likely detection of *H. pylori*. In a cross-sectional study conducted by Murray *et al*[37] the OR for *H. pylori* infection among consumers of 7–13 units of alcohol/week was 0.83 (95%CI: 0.70–0.98). The role of exercise has not been seen to significantly affect the detection of *H. pylori* (OR = 0.721, 95%CI: 0.393-1.321). To our knowledge, there are no published data concerning the potential effect of exercise on the detection of *H. pylori*.

Our study was limited by the lack of access to the accurate duration of previous PPI exposure in patients known to have a positive history of PPI intake. This, however, reflects the actual parameters under which gastric biopsies are evaluated by pathologists in our population. Additional limitations may include the retrospective nature of our study. However, the random selection of patients, the large sample size and the wide time range during which the patients conducted their gastroscopy may have offset some of these limitations. Moreover, the effect of PPIs on gastritis type, *H. pylori* density, and intestinal metaplasia maintained a statistically significant difference despite excluding 48 patients diagnosed with GERD.

In conclusion, our study suggests that the use of PPIs masks *H. pylori* infection, promotes the diagnosis of non-*H. pylori* inactive chronic gastritis diagnosis, and increases the incidence of intestinal metaplasia. IHC stains using *H. pylori* antibodies do not appear to significantly improve the detection of *H. pylori* organisms in these patients. This highlights the need for multidisciplinary health care intervention, where increasing patient awareness regarding the unfavorable outcomes associated with unmonitored long-term use of PPIs should be widely addressed. An additional approach would be considering switching the OTC-available PPIs to prescription dispensed medications.

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COMMENTS

Background

Proton pump inhibitors (PPIs) are widely used among patients with gastrointestinal disorders, and due to common practice of self-medication with these agents, especially in developing countries. Many studies showed that undetected *Helicobacter pylori (H. pylori)* infection or persistent *H. pylori* gastritis may lead to atrophic gastritis, increased risk of gastric adenocarcinoma and that long-term PPI use can contribute to under-diagnosis of *H. pylori* gastritis.

Research frontiers

Profound acid suppression by PPIs was shown to be associated with masking *H. pylori* infections, the main cause of chronic active gastritis, peptic ulcer disease and atrophic gastritis.

Innovations and breakthroughs

This study suggests that the use of PPIs masks *H. pylori* infection, promotes the diagnosis of non-*H. pylori* inactive chronic gastritis diagnosis, and increases the incidence of intestinal metaplasia. Immunohistochemical (IHC) stains using *H. pylori* antibodies do not appear to significantly improve the detection of *H. pylori* organisms in these patients.

Applications

This study highlights the need for multidisciplinary health care intervention, where increasing patient awareness regarding the unfavorable outcomes associated with unmonitored long-term use of PPIs should be widely addressed.

Terminology

PPIs are potent inhibitors of acid secretion for the treatment of acid-related diseases such as gastroesophageal reflux disease, peptic ulcer disease and chronic gastritis. Inactive chronic gastritis is defined as chronic inflammation of the gastric mucosa without neutrophils. IHC testing is a method of detecting the presence of antigens in histologic tissue section.

Peer-review

The study adds further support to the growing volume of the literature data indicating that the use of PPIs masks *H. pylori* infection, and increases the chance of diagnosis of non- *H. pylori* inactive gastritis and the incidence of intestinal metaplasia.

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