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*Original Research*

# The effect of Helicobacter pylori eradication treatment with amoxicillin, gemifloxacin and rabeprazole on inflammatory parameters

The effect on inflammatory parameters of Helicobacter pylori eradication

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**Abstract**

Aim: Inflammation of the gastric mucosa caused by H. pylori is usually chronic and lasts a lifetime. This permanent colonization results in the mucosal expression of chemotactic factors that attract neutrophils and mononuclear cells. Despite the known production of proinflammatory cytokines in stomach mucosa and infiltration of inflammatory cells, there are few studies in the literature related to the effects of these and changes after treatment. The aim of this study was to evaluate patients determined with H.pylori positivity endoscopically and histopathologically, and to investigate the change in inflammatory parameters after successful eradication treatment with gemifloxacin, amoxicillin and rabeprazole.

Material and Methods: This study included 126 patients who presented with dyspeptic complaints between April 2022 and September 2022, who were determined as HP-positive from stomach tissue biopsies taken under upper gastrointestinal system (GIS) endoscopy in the Gastroenterology Endoscopy Unit, and were then determined with successful eradication following the treatment given. Demographic data (age, gender) of all the patients were documented. Blood samples were taken for analysis before the treatment and after successful HP eradication treatment.

Results: The patients consisted of 72 (57.1%) females and 54 (42.9%) males with a mean age of 40.7±13.8 years (range, 18-65 years). Statistically significant differences were determined in the comparisons of the inflammatory parameters before and after treatment in patients with successful H.pylori eradication.

Discussion: Although H.pylori seems to be a local infection, persistent inflammation results in long-term gastric and extra-gastric effects. A reduction in inflammatory parameters with successful eradication reduces the long-term effects that can develop.

**Keywords**

H.Pylori, Eradication, Inflammatory, Parameters

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## Introduction

Helicobacter pylori (H.pylori) is a gram-negative bacteria that affects more than half of the world's population. These are pathogenic bacteria closely associated with chronic gastritis, stomach ulcers, stomach adenocancer and stomach lymphoma (mucosa-related lymphoid tissue lymphoma). H.pylori positivity has been shown to vary according to different factors such as age, geographic region, living conditions, and socioeconomic status [1, 2]. The prevalence of H.pylori infections has been estimated to be 85-95% in developing countries and approximately 30-50% in developed countries [3, 4].

The stomach mucosa inflammation caused by this bacteria is generally chronic and lasts throughout life [5]. This permanent colonization results in the mucosal expression of chemotactic factors that attract neutrophils and mononuclear cells [6, 7]. Cytokines produced from IL-8 play a role in the activation and uptake of neutrophils in the stomach mucosa, and extensive biological effects of IL-6 in mononuclear cells are known, including macrophage activation and lymphocyte differentiation [8, 9]. Despite the known production of proinflammatory cytokines in stomach mucosa and infiltration of inflammatory cells, there are few studies in the literature related to their effects and changes after treatment [8].

Although long-term gastric and extra-gastric effects of H.pylori has been shown, there are few studies showing a change in the inflammatory parameters of these effects. Therefore, the aim of this study was to evaluate patients determined with H.pylori positivity endoscopically and histopathologically, and to investigate the change in inflammatory parameters after successful eradication treatment with gemifloxacin, amoxicillin and rabeprazole.

## Material and Methods

### *Patient Selection*

This retrospective, observational study included 126 patients who presented with dyspeptic complaints between April 2022 and September 2022, who were determined as HP-positive from stomach tissue biopsies taken under upper gastrointestinal system (GIS) endoscopy in the Gastroenterology Endoscopy Unit, and were then determined with successful eradication following the treatment given. The patients were aged 18-65 years, presented with dyspeptic complaints, gave permission for upper GIS endoscopy to be performed, had not previously received any treatment for H.pylori eradication, and provided informed consent for voluntary participation in the study.

The study exclusion criteria were defined as use of antibiotics and/or proton pump inhibitors (PPI) up to one month before the study, irregular or incomplete use of the HP eradication treatment, failure of HP eradication, a history of acute or chronic disease that could affect inflammatory markers, or not willing to participate in the study. Demographic data (age, gender) of all the patients were documented. Blood samples were taken for analysis before the treatment and after successful HP eradication treatment.

### *Endoscopic evaluation*

The endoscopic examination of the patients was made in the Endoscopy Unit of our hospital using a Fujinon EG530WR endoscopy device. Verbal and written informed consent was obtained from the patient before the endoscopy procedure. After a 6-hour fasting period, local pharyngeal xylocaine anesthesia was administered, then sedation was applied with 0.1mg/kg midazolam and 1mg/kg ketamine. During the endoscopy procedure, first the oesophagus, and then the stomach together with the duodenum were examined in detail. Biopsies were taken from the antrum and corpus for examination of the presence of HP.

### *Histopathological evaluation*

The biopsies taken endoscopically from the antrum and corpus were sent to the pathology laboratory in 10% formaldehyde. Following routine tissue processing, the tissue samples were embedded in paraffin blocks. Sections were cut at a thickness of 5 microns, then routinely stained with hematoxylin-eosin (HE) and evaluated under light microscopy. To evaluate the presence of H.pylori, staining was applied with modified Giemsa. Biopsies were reported according to the updated Sydney classification (inflammation, activation, dysplasia, intestinal metaplasia, atrophy, and H.pylori density) [10].

### *Laboratory analysis*

Complete blood counts [neutrophil count, lymphocyte count, platelet counts] were analyzed using an XN-1000 analyzer (USA). CRP, ferritin, and fibrinogen levels were analyzed using a Roche Hitachi Cobas 501 analyzer (Switzerland). Erythrocyte sedimentation rates were measured automatically using the Biosed 100 (Italy) device in blood sample tubes. NLR was calculated by division of neutrophil counts to lymphocyte counts. PLR was calculated by dividing platelet counts to lymphocyte counts.

### *HP eradication treatment*

All the patients were administered Amoxicillin (1000 mg twice a day) + Gemifloxacin (320 mg once a day) + Esomeprazole (40 mg twice a day) treatment for 7 days. One month after the end of the treatment, HP eradication was evaluated in all patients by examining HP antigen in the faeces [11].

### *Statistical analysis*

The data obtained in the study were analyzed statistically using SPSS vn. 24.0 software (Statistical Package for the Social Sciences). Continuous variables were reported as mean ± standard deviation values and categorical variables as number (n) and percentage (%). Conformity of the data to the normal distribution was assessed with a histogram and the Kolmogorov-Smirnov test. Comparisons were made using the Paired Samples t-test and the Independent Samples t-test, as appropriate. A p- value $<0.05$ was accepted as statistically significant.

### *Ethical Approval*

Ethics Committee approval for the study was obtained.

## Results

We evaluated 126 patients who were endoscopically and histopathologically determined to be positive for H.pylori, who were treated, and obtained successful eradication. The patients consisted of 72 (57.1%) females and 54 (42.9%) males with a mean age of 40.7±13.8 years (range, 18-65 years).

Statistically significant differences were determined in the comparisons of the inflammatory parameters before and after treatment in patients with successful H.pylori eradication.

**Table 1.** Changes in the inflammatory parameters of the patients with HP eradication.

| Variables | Pre-treatment | Post-treatment | p value |
|---|---|---|---|
| Leukocytes | 7.40±1.68 | 6.42±1.59 | <0.001 |
| Neutrophils | 5.18±1.17 | 4.38±1.11 | <0.001 |
| Lymphocytes | 1.11±0.25 | 1.22±0.31 | <0.001 |
| NLR | 4.6±1.4 | 3.5±1.3 | <0.001 |
| PLR | 245.2±74.1 | 199.6±60.3 | <0.001 |
| Thrombocytes | 261.1±58.4 | 233.4±58.5 | <0.001 |
| CRP | 2.75±0.3 | 1.77±0.1 | <0.001 |
| Sedimentation | 12.6±5.2 | 8.9±3.1 | <0.001 |
| Ferritin | 40.7±21.6 | 30.9±16.7 | <0.001 |
| Fibrinogen | 359.7±72.7 | 297.6±52.2 | <0.001 |

Following treatment, a statistically significant decrease was determined in the leukocyte level (7.40±1.68 vs. 6.42±1.59), neutrophil level (5.18±1.17 vs. 4.38±1.11), NLR (4.6±1.4 vs. 3.5±1.3), PLR (245.2±74.1 vs. 199.6±60.3), thrombocyte level (261.1±58.4 vs. 233.4±58.5), CRP level (2.75±0.3 vs. 1.77±0.1), sedimentation level (12.6±5.2 vs. 8.9±3.1), ferritin level (40.7±21.6 vs. 30.9±16.7) and fibrinogen level (359.7±72.7 vs. 297.6±52.2), and a statistically significant increase was determined in the lymphocyte level (1.11±0.25 vs. 1.22±0.31) (p<0.001) (Table 1).

## Discussion

Although H.pylori infection can be seen in all regions of the world, colonization rates vary significantly according to geographical regions. Higher rates have been reported in developing countries than in developed countries [12]. In almost all infected individuals, chronic gastritis develops associated with long-term colonisation, but clinical findings occur in only a small proportion of colonized individuals. Variable outcomes of H. pylori infection from person-to-person are most probably due to factors such as strain-specific bacteria components, inflammatory responses that develop associated with the genetic variations of individuals or ultimately, environmental factors affecting the interaction between the pathogen and the host [13].

This infection, which affects more than half of the global population, is chronic and lives for decades in the stomach of the host, and can cause serious problems such as several changes in cells and subclinical inflammation lasting a lifetime. Pathogenesis has been associated with various virulence factors such as flagella, lipopolysaccharides (LPS), vacuolation toxin (VacA) and cytotoxin-associated gene pathogenicity island (cagPAI). In connection with these factors, changes are seen such as changes in the host gene expression, infection-related cell proliferation, loss of polarity in epithelial cells, deterioration of cell-cell links, and decreased stomach acid expression [14].

Extra-gastric findings associated with inflammation developing due to H.pylori infection have been determined in previous studies, and these findings have been shown to decrease with eradication treatment. In a study by Kohda et al., it was reported that following eradication treatment, thrombocyte counts increased significantly in patients with idiopathic thrombocytopenic purpura (ITP) [15]. Similarly, Zentilin et al. showed that with H.pylori eradication in rheumatoid arthritis patients, the disease activity significantly decreased over 2 years in the H.pylori -negative group [15]. The results of the current study showed that eradication treatment resulted in a regression of inflammation that had developed associated with H.pylori infection. Although this inflammation seems to be a local inflammation, previous studies have shown that there are extra-gastric effects [16]. Even if inflammatory parameters examined before H.pylori eradication treatment are in the normal range, reduction of long-term inflammation in the stomach prevents the development of diseases such as stomach/duodenal ulcer, adenocancer, and lymphoma.

This study had some strengths and limitations. Strong aspects of the study include that the study was prospective in design and therefore, the results were more accurate and reliable as all acute and chronic diseases which could affect inflammatory parameters were excluded, that the presence of H.pylori was investigated endoscopically and histopathologically, and a new treatment regimen was used of amoxicillin+gemifloxacin +esomeprazole. The relatively low number of patients can be considered a limitation of our study.

## *Conclusion*

Although H.pylori seems to be a local infection, persistent inflammation results in long-term gastric and extra-gastric effects. A reduction in inflammatory parameters with successful eradication reduces the long-term effects that can develop. The treatment of amoxicillin+gemifloxacin+esomeprazole used in the patients with indication in this study was seen to effectively reduce the inflammatory parameters.

***Scientific Responsibility Statement***

*The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.*

***Animal and human rights statement***

*All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.*

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***Conflict of interest***

*None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.*

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