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Original Research Article

Evaluating the combination of amoxicillin, gemifloxacin and rabeprazole therapy for *Helicobacter pylori* eradication in young and older adult patients

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Abstract

Purpose: *To assess the effectiveness, safety and adverse effects of treatment regimen combining amoxicillin, gemifloxacin and rabeprazole for eradicating Helicobacter pylori in adult population.*
Methods: *A total of 211 patients comprising 33 patients (15.6 %) from the older adult group and 178 patients (84.4 %) from the younger adult group who visited Van Training and Research Hospital, Turkey were included in this study. Treatment, made up of amoxicillin (1000 mg) and rabeprazole (20 mg), was administered 12 hourly and gemifloxacin (320 mg) once daily to all patients for 7 days. Thereafter, patients were evaluated for H. pylori eradication by examining antigens in feces (immunochromatographically based, qualitatively), drug compliance and treatment tolerance.*
Results: *Post-treatment investigations showed that H. pylori was completely eradicated in 187 patients (88.6 %), while eradication was not achieved in 24 patients (11.4 %). In the older adult group, H. pylori was successfully eradicated in 27 of 33 patients (81.8 %). Excluding a total of 9 patients who did not complete treatment due to side effects, H. pylori eradication was achieved in 184 of 202 patients (91 %).*
Conclusion: *This combination of three antibiotics exhibits a high rate of eradication of H. pylori among adult patients, even when administered for a short period (one week). This investigation should be carried out using a larger and more diverse patient population to validate the outcomes reported in this study*

Keywords: *Helicobacter pylori, Gemifloxacin, Amoxicillin, Rabeprazole, Adult patients*

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INTRODUCTION

Helicobacter pylori (HP) is a gram-negative bacterium that colonizes the gastric mucosa. It was first isolated in 1982 and continues to pose a significant public health challenge [1]. It is known that approximately 50 % of the world's population is exposed to *H. pylori* and it is observed more frequently in developing countries compared to developed ones [2].

With the aging of the world population, early detection and treatment of cancer has become important. In 1994, the World Health Organization (WHO) identified *H. pylori* as a group 1 cancer agent for gastric cancer, increasing the importance of this bacterium, especially in elderly patients [3]. *Helicobacter pylori* is frequently seen in individuals aged 60 years and above. In a study in Shanghai, Chen *et al*. isolated *H. pylori* in 74 % of older adult population [4]. Another study in Italy reported that the infection rate was 40 – 60 % in asymptomatic older adults and > 70 % in those with gastrointestinal disease [5].

While various agents have been explored for eradicating *H. pylori* in older adults, research specifically examining the use of amoxicillin, gemifloxacin and rabeprazole in this age group is lacking [6]. The current study aimed to evaluate the effectiveness, safety and side effects of this treatment protocol for eradication of *H. pylori* in elderly individuals.

METHODS

Patients

This retrospective study involved 211 patients who visited Van Training and Research Hospital, Turkey with dyspeptic symptoms from February to October 2022. Patients were categorized into two age groups: those over 65 years (older adult group) and those under 65 years (younger adult group).

Inclusion criteria

Patients who underwent upper gastrointestinal system (GIS) endoscopy and stomach tissue biopsy in the Gastroenterology Department were identified as *H. pylori-positive* and treated accordingly. Patients aged between 18 – 78 years who were admitted to the clinic with dyspeptic complaints, who had not previously received *H. pylori* treatment and who consented to undergo endoscopy were included in the study. Duly completed and signed informed consent forms were obtained from the patients.

Exclusion criteria

Patients with a history of antibiotics, proton pump inhibitor (PPI), histamine-2 (H2) receptor blocker or antacid use in the month before the start of study were excluded. Additionally, those who were pregnant or breastfeeding had chronic illnesses such as liver cirrhosis or cancer or were unwilling to participate, were also excluded. For each patient, data was collected on age, gender, height, weight, body mass index (BMI; kg/m²), education level, marital status, employment status, smoking and alcohol consumption as well as details of any comorbidities.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Van Training and Research Hospital, Van, Turkey (no. 2022/21-01). All procedures performed in this study involving human participants 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 [7].

Endoscopic evaluation

Before the endoscopic procedure, patients were informed and their informed consent was obtained both verbally and in writing. All endoscopic examinations were performed in the Endoscopy Unit of Van Training and Research Hospital, using a Fujinon EG5300WR endoscope. After 8 hours of fasting, local pharyngeal anesthesia was performed with xylocaine followed by sedation with 1 mg/kg ketamine and 0.1 mg/kg midazolam. During the procedure, the entire gastrointestinal system was examined in detail, starting from the esophagus to the intestines and biopsies were taken from the corpus and antrum sections of the stomach to test for the presence of *H. pylori.*

Histopathological evaluation

Biopsies obtained during endoscopy were preserved in 10 %. After standard tissue processing, samples were embedded in paraffin blocks and 5-micron thick sections were taken. These sections were stained with hematoxylin and eosin (HE) for evaluation under a light microscope. Additionally, the modified Giemsa staining was performed to assess the presence of *H. pylori*. Biopsy results were evaluated using the updated Sydney classification, which includes parameters such as atrophy, inflammation, dysplasia, intestinal metaplasia, activation and *H. pylori* density [8].

Treatment regimens and post-treatment assessment

All patients received treatment consisting of rabeprazole (20 mg) and amoxicillin (1.0 g), twice daily and 320 mg of gemifloxacin once daily for 7 days. They were advised not to use any other medications that could interfere with *H. pylori*

treatment. One month after completion of treatment, the presence of *H. pylori* was assessed by testing stool samples [5]. Following the treatment, patients were also evaluated for medication adherence and treatment tolerance.

Statistical analysis

Data were analyzed using SPSS version 24.0 (Statistical Package for the Social Sciences). The normality of the data was evaluated with the Kolmogorov-Smirnov test, histograms and standard deviation values. Continuous variables were reported as mean ± standard deviation (SD), while categorical variables were presented as frequency (n) and percentage (%). Parametric data were compared between groups using the Student's *t*-test while the Chi-square test was employed for categorical data. *P*-value < 0.05 was considered statistically significant.

RESULTS

Basic characteristics of patients

The current study evaluated 211 patients who were diagnosed with *H. pylori* infection through endoscopy and histopathology and received appropriate treatment. This cohort consisted of 126 females (59.7 %) and 85 males (40.3 %). The mean age of patients included in the study was 40.7 ± 14.7 years (18 – 68 years). Thirty-three (33) patients (15.6 %) were in the older adult group (> 65 years), while 178 patients (84.4 %) were in the younger adult group (< 65 years). Post-treatment evaluations showed that *H. pylori* eradication was successful in 187 patients (88.6 %), while 24 patients (11.4 %) did not achieve eradication. In the older adult group, successful eradication was seen in 27 out of 33 patients (81.8 %). After excluding 3 patients from this group who did not complete treatment, 26 out of 30 patients (86.6 %) who finished the regimen achieved eradication.

There was no significant difference (p > 0.05) between both groups in terms of alcohol consumption and gender distribution.

Table 1: The demographic data and presence of comorbidities patients (mean ± SD; n (%))

Parameter	Patients (≥65 years)	Patients (<65 years)	Total	*P*-value
Age (years)	66.4±7.6	35.9±10.6	40.7±11.7	<0.001
Gender (female)	24 (72.7%)	102 (57.3%)	126 (59.7%)	0.097
Height (cm)	163.1±7.5	167.1±8.8	166.5±8.7	0.015
Weight (kg)	77.1±11.9	70.1±13.6	71.1±13.6	0.006
BMI	29.1±4.3	25.1±4.2	25.6±4.6	<0.001
Education level				<0.001
-Illiterate	12 (36.4%)	9 (5.1%)	21 (10.0%)	
-Primary school	12 (36.4%)	42 (23.6%)	54 (25.6%)	
-High school	9 (27.3%)	98 (55.1%)	107 (50.7%)	
-University	0 (0.0%)	29 (16.3%)	29 (13.7%)	
Employment status				<0.001
-Employed	0 (0.0%)	73 (41.0%)	73 (34.6%)	
-Not employed	33 (100%)	105 (59.0%)	138 (65.4%)	
Marital status				0.005
-Married	33 (100%)	142 (79.8%)	175 (82.9%)	
-Single	0 (0.0%)	36(20.2%)	36 (17.1%)	
Smoking status				0.007
-Smoker	3 (9.1%)	57 (30.2%)	60 (28.4%)	
-Non-smoker	30 (90.9%)	121 (68.0%)	151 (71.6%)	
Alcohol consumption				
-Yes	0 (0%)	0 (0%)	0 (0%)	-
-No	33 (100%)	178 (100%)	211 (100%)	
Comorbidities (present)				
-DM	26 (78.8%)	24 (13.5%)	50 (23.7%)	<0.001
-HT	12 (36.4%)	3(1.7%)	15 (7.1%)	<0.001
-HL	15 (45.5%)	9 (5.1%)	24 (11.4%)	<0.001
-IHD	3 (9.1%)	3 (1.7%)	6 (2.8%)	0.019
-Congestive heart failure	9 (27.3%)	6 (3.4%)	15 (7.1%)	<0.001
-CRF	3 (9.1%)	0 (0%)	3 (1.4%)	<0.001
-Asthma/COPD	5 (15.2%)	3 (1.7%)	8 (3.8%)	<0.001
-CVE	5 (15.2%)	12 (6.7%)	17 (8.1%)	0.103
-Malignancy	3 (9.1%)	0 (0%)	3 (1.4%)	<0.001
-Others	1 (3.0%)	1 (0.6%)	2 (0.9%)	0.179

Table 2: The relationships between treatment tolerance, the development of side effects, drug compliance and the eradication of *H. pylori* (mean ± SD; n (%))

Variable	Patients (≥65 year)	Patients (<65 years)	Total	*P*-value
Drug compliance				0.037
- Good	28 (84.8%)	170 (95.5%)	198 (93.8%)	
- Moderate	3 (9.1%)	3 (1.7%)	6 (2.8%)	
- Poor	2 (6.1%)	5 (2.8%)	7 (3.3%)	
Treatment tolerance				0.014
- Good	26 (78.8%)	162 (91.0%)	188 (89.1%)	
- Moderate	6 (18.2%)	8 (45.0%)	14 (6.6%)	
- Poor	1 (3.0%)	8 (45.0%)	9 (4.3%)	
Completion of treatment				0.135
- Yes	30 (90.9%)	172 (96.6%)	202 (95.7%)	
- No	3 (9.1%)	6 (3.4%)	9 (4.3%)	
Presence of side-effects	6 (18.2%)	22 (12.4%)	28 (13.3%)	0.365
Diarrhea	2 (6.1%)	8 (4.5%)	10 (4.7%)	0.697
Reflux	3 (9.1%)	0 (0%)	3 (1.4%)	<0.001
Bloating	2 (6.1%)	9 (5.1%)	11 (5.2%)	0.812
Abdominal pain	2 (6.1%)	3(1.7%)	5 (2.4%)	0.129
Nausea-vomiting	4 (12.1%)	5 (2.8%)	9 (4.3%)	0.015
Constipation	0 (0%)	0 (0%)	0 (0%)	-
Skin rash	1 (3.0%)	0 (0%)	1 (0.5%)	0.020
Lethargy- fatigue	2 (6.1%)	0 (0%)	2 (0.9%)	0.001
Headache	0 (0%)	0 (0%)	0 (0%)	-
Dizziness	0 (0%)	0 (0%)	0 (0%)	-
Palpitations	0 (0%)	0 (0%)	0 (0%)	-
Dry mouth	0 (0%)	0 (0%)	0 (0%)	-
Weight loss	0 (0%)	0 (0%)	0 (0%)	-

In the older adult group, the rates of literacy and smoking were seen to be lower and the rates of being married and not working were higher ($p < 0.05$). The older age group patients were observed to be shorter, heavier and had higher BMI values compared to the younger adult group. With respect to comorbid diseases, older adult group showed a significantly higher percentage of DM (78.8 vs 13.5 %), HL (45.5 vs 5.1 %), HT (36.4 vs 1.7 %), congestive heart failure (27.3 vs 3.4 %), IHD (9.1 vs 1.7 %), CRF (9.1 vs 0.0 %) and asthma/COPD (15.2 vs 1.7 %; $p < 0.05$; Table 1).

Drug compliance was determined to be good in 198 (93.8 %) patients, moderate in 6 (2.8 %), and poor in 7 (3.3 %), with significantly better drug compliance seen in the younger age group than in the older population (95.5 vs 84.8 %; $p = 0.037$). The ability to tolerate the treatment protocol was determined to be good in 188 (89.1 %) patients, moderate in 14 (6.6 %) and poor in 9 (4.3 %), with significantly better tolerance seen in the younger age group than in the older population (91.0 vs 78.8 %; $p = 0.014$). The 7-day treatment period was completed by 202 (95.7 %) patients of the whole sample and in the older age group but 3 (9.1 %) patients did not complete the treatment (Table 2). Although more side effects were reported in the elderly population, the difference between the two age groups was not statistically significant (18.2 vs 12.4 %; $p < 0.365$). In total, side effects were observed in 28 patients (13.3 %). Symptoms such as diarrhea, bloating, abdominal pain, nausea and vomiting, drowsiness and fatigue, skin rash and reflux were reported by patients, while no cases of constipation, headache, dizziness, palpitations, dry mouth or weight loss were recorded. In the older age group, there were significantly higher rates of reflux (9.1 vs 0.0 %), nausea and vomiting (12.1 vs 2.8 %), skin rash (3.0 vs 0.0 %) as well as lethargy and fatigue (6.1 vs. 0.0 %). However, there was no significant difference between both groups in terms of the occurrence of other side effects (Table 2).

DISCUSSION

Helicobacter pylori is positive in 40 – 60 % of asymptomatic individuals and 70 % of older adults with gastroduodenal diseases according to reports published two decades ago. However, studies in the last decade have shown that the rate of *H. pylori* prevalence in older adults has risen to 70 – 85 % and there has been a significant decrease in individuals above > 85 years of age [9]. The reason for decreased prevalence at an advanced age has been thought to be associated with chronic atrophic gastritis [10]. However, some studies reported that the development of atrophy at older ages is associated with *H. pylori* infection rather than being an age-related physiologic condition [5]. *Helicobacter pylori* infection and non-steroidal

anti-inflammatory drug (NSAID) use are independent risk factors for peptic ulcer and duodenal bleeding in the elderly. It has been shown that *H. pylori* eradication in HP-positive elderly patients starting long-term NSAID treatment significantly reduces the 6-month risk of peptic ulcer [11].

It is known that HP infection induces a sequence of events that leads to gastric neoplasia in genetically predisposed individuals [12]. To prevent the development of gastric cancer, it has been emphasized that eradication treatment should ideally be applied early to premalignant lesions, in other words, before the development of atrophy [13]. In a prospective, observational study of 1526 patients in Japan, it was reported that 2.9 % of patients infected with *H. pylori* developed gastric cancer after 7.8 years, while none of the uninfected individuals developed gastric cancer [14]. In addition to the gastric effects of HP infection in elderly patients, extra-gastric effects have been examined in several studies. Coronary artery disease, cognitive disorders, iron deficiency anemia and B12 deficiency are associated with *H. pylori* [15,16]. When all these effects of *H. pylori* are taken into consideration, eradication in the elderly becomes more important. However, there is no specific recommendation for HP eradication in older patients in the Kyoto Agreement. In previous studies, several treatments have been used in combination for the eradication of *H. pylori*, but it has also been reported that the older population could not complete drug treatments because of the development of side effects and drug interactions due to multidrug use.

There is a higher probability of older patients experiencing adverse drug reactions because of severe comorbidities and renal dysfunction. Therefore, to eradicate *H. pylori* in older patients, a comprehensive risk-benefit evaluation must be made and personalized treatment should be administered [17]. In this study, the treatment administered was gemifloxacin, amoxicillin and rabeprazole, and evaluations were made of an older and younger population with respect to the efficacy of treatment in eradicating *H. pylori*, treatment tolerance, drug compliance and development of side effects. The results showed that eradication rates, drug compliance and treatment tolerance were significantly better in younger age group than in older population. Although more side effects were seen in older patients, the difference between age groups was not statistically significant. Tanaka and co-workers also investigated the effect of HP eradication on dyspepsia symptoms in an older adult population and no significant side effects were seen [18]. There may be disadvantages to administering HP eradication treatment to older patients. However, in the current study, only 3 patients in the older adult group could not complete the treatment because of side effects and non-compliance.

Study limitations

The retrospective design of the study and small number of patients in the advanced age group are the limitations of this study.

CONCLUSION

This study shows that combination of three antibiotics is effective in the eradication of *H. pylori* in adult population. Even with short-term use, the combination of amoxicillin, rabeprazole and gemifloxacin is suitable for use as first-line treatment for *H. pylori* because of the high eradication rate and the low side-effect profile. This investigation should be carried out using a larger and more diverse patient population to validate the outcomes reported in this study.

DECLARATIONS

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None provided.

Ethical approval

The study was approved by the Ethics Committee of Van Training and Research Hospital, Van, Turkey (no. 2022/21-01).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Data collection was performed by Guner Kilic.

Statistical analysis was performed by Yusuf Kayar and Adnan Ozkahraman. Gulce Ecem Kilic, Ozan Durmaz, Nukhet Bayram Kayar and Guner Kilic conducted the literature search, wrote the article and confirmed the authenticity of all the raw data. Yusuf Kayar, Guner Kilic and Sevki Konur analyzed the results and contributed to the final manuscript. The original draft was written by Yusuf Kayar and Guner Kilic, All authors read and approved the final version of the manuscript.

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