Original Article

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The Efficacy of Combination Regime in *Helicobacter Pylori* Eradication: A Cross-Sectional Study from an Experienced Endoscopy Center

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Abstract

Aim: The success of antibiotics used for eradication in the treatment of *Helicobacter pylori* (Hp)-positive gastritis is controversial. This study aims to evaluate the post-treatment eradication success/failure of Hp-positive gastritis cases, discuss antibiotic resistance, and what we can do additionally.

Methods: The data of 1,471 patients who underwent upper gastrointestinal endoscopy between January 1 and December 31, 2019, were retrospectively evaluated through the hospital digital recording system. Of these, data of 126 patients who have been diagnosed with HP-positive gastritis and treated with a trio of clarithromycin, amoxicillin, and omeprazole were analyzed. Initial and control endoscopic pathologies and Hp-positivity were compared.

Results: In the control of 126 patients, 87 (69%) patients had a normal endoscopic appearance, but only 46 (36.5%) patients were normal in the histopathological examinations of biopsies. Regardless of the severity, complete eradication of Hp was possible in 31 (24.6%) patients. There was no statistically significant difference in Hp detection rates after treatment (p=0.719 for 1+, p=0.583 for 2+, p for 3+)=0.980).

Conclusion: In gastritis cases, Hp positivity continues despite the treatment, although the pathological severity changes. It is appropriate to discuss the effectiveness of routine treatments and to take culture/antibiogram, even bismuth including preparations to the forefront.

Keywords: *Helicobacter pylori*, gastritis, antibiogram

Introduction

Helicobacter pylori (Hp) is a gram-negative, spiral-shaped flagellated bacterium that causes gastroduodenal inflammation. Carriers are observed in half of the world population and 80% in developing countries (1,2). In Turkey, in 2013, the national prevalence study with the urea breath test, the ratio was determined as 81.6% (3). It is most commonly transmitted by oral-oral or fecal-oral route; In societies with low socioeconomic status and crowded families, it has been reported that it can be transmitted by Hp contaminated water and foods, even kissing and droplet infection (4).

The stomach was considered sterile due to its acidic environment. However, the detection of Campylobacter-like microorganisms in the stomach by Mashall et al. (5) in 1983, and then proving that this bacterium causes gastritis when taken orally by Marshall et al.(5) in 1985, the use of antibiotics in treatments came to the fore.

Inflammation and superficial epithelial damage are the main pathological mechanisms in gastritis; depending on the degree and duration, edema, hyperemia, erosion, regeneration, ulcer, cicatrix, and atrophy can be seen-acute or chronic gastritis patients present with epigastric pain, burning, dyspepsia, nausea, and vomiting. The definitive diagnosis can be made by showing the bacteria by endoscopy and biopsy and by breath urea test, antibody tests, and stool antigen tests (6).

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Standardized treatment in gastritis is antibiotics against Hp and acid-reducing proton pump inhibitors. Hp eradication is the basis of the treatment. Many people are asymptomatic carriers; changes in Hp intensity in lesions, antibiotic resistance, and frequent recurrence of the disease point to the difficulty in eradication and studies carried out on these handicaps and how to treat which patients.

This study aims to evaluate the post-treatment eradication success/failure of Hp positive gastritis cases, discuss antibiotic resistance, and what we can do additionally.

Methods

This study was conducted with approval from the Ethics Committee of the University of Health Sciences, Haseki Training and Research Hospital (ref no: 2020/294 date: 29.07.2020). Informed consent forms were obtained from all patients.

The study was conducted at the Surgical Endoscopy unit of Haseki Training and Research Hospital with patients diagnosed with antral gastritis, pangastritis, erosive gastritis, gastric ulcers between January 1 and December 31, 2019. One thousand four hundred seventy-one patients were retrospectively evaluated through the hospital digital recording system. Those diagnosed with bulbitis, duodenitis, alkaline reflux, gastric polyp, and gastric cancer were excluded from the study. Patients with a diagnosis of bulbitis, duodenitis, and alkaline reflux were not included in the study, as it would impair the study group's homogenization due to the bile effect. One hundred twenty-six patients were Hp positive and were treated with combined drugs containing clarithromycin, amoxicillin, and omeprazole for 14 days and then used omeprazole for 28 days, and whose pathological samples were collected with control endoscopies within the first three months after the end of treatment, were studied. The patients received triple clarithromycin therapy, which was recommended as the first-line treatment of Hp infection by the American College of Gastroenterology (7). Hp severity was evaluated with the updated Sydney classification in endoscopic biopsies, and it was expressed as "+" mild, "++" moderate, and "+++" severe Hp infection (8).

Statistical Analysis

Data analysis was performed by the SPSS 15.0 for Windows program. Categorical variables were presented as numbers and percentages, while numerical variables were presented as mean, standard deviation, minimum and maximum values. The chi-square test and McNemar test were used in dependent groups and independent groups, respectively. Analysis results with a $p<0.05$ were accepted as significant.

Results

In 2019, 1,471 patients with gastritis and related diagnoses were scanned, and 126 (8.6%) patients were included in the study. Seventy-seven (61.1%) were female, and 49 (38.9%) were male. The mean age was 45.2 years, ranging from 21 to 80 years.

Hp positivity change in endoscopic and pathological diagnoses before and after the treatment is in Table 1. In 87 (69%) of 126 patients diagnosed with antral gastritis, erosive gastritis, pangastritis, and ulcer, endoscopic appearance was normal after treatment. However, pathologically, only 46 (36.5%) patients were regular; the other patients had acute gastritis, chronic gastritis, erosion, and ulceration. Complete eradication of Hp regardless of the severity was possible in 31 (24.6%) patients.

Although 87% of the patients had a regular appearance in the endoscopic evaluation after the treatment, only 46% of the patients were evaluated as regular in the pathological examination. On the other hand, success in Hp eradication remained at 24.6%.

Endoscopic diagnoses, pathological diagnoses, and the severity of Hp are in Table 2-4, compared with post-treatment in the context of the same variables. The statistical relationship of Hp detection before and after treatment according to the diagnosis groups is shown in Table 5.

Although Hp eradication was achieved in 31 patients after treatment and was statistically significant, Hp positivity continues in 95 patients.

There was no statistically significant difference in Hp eradication rates according to pre-treatment diagnosis groups (Table 6) (0.719 p=0.583 p=0.980).

Table 1. Pre and post-treatment diagnoses results

		Before treatment	After treatment
		n (%)	n (%)
Endoscopic diagnosis	Normal view	0 (0.0)	87 (69.0)
	Antral gastritis	84 (66.7)	34 (27.0)
	Erosive gastritis	14 (11.1)	1 (0.8)
	Pangastritis	17 (13.5)	4 (3.2)
	Ulceration	11 (8.7)	0 (0.0)
Pathological diagnosis	Normal mucosa	0 (0.0)	46 (36.5)
	Acute gastritis	42 (33.3)	34 (27.0)
	Chronic gastritis	59 (46.8)	45 (35.7)
	Chronic gastritis with erosion and ulceration	25 (19.8)	1 (0.8)
Pathological *Helicobacter pylori* intensity	Hp negative	-	31 (24.6)
	1 +	37 (29.4)	55 (43.7)
	2 +	51 (40.5)	31 (24.6)
	3 +	38 (30.2)	9 (7.1)

Table 2. Comparative evaluation of endoscopic diagnoses before and after treatment

		Before treatment			
		Antral gastritis	Erosive gastritis	Pangastritis	Ulceration
		n (%)	n (%)	n (%)	n (%)
After treatment	Normal view	73 (86.9)	6 (42.9)	4 (23.5)	4 (36.4)
	Antral gastritis	11 (13.1)	7 (50.0)	11 (64.7)	5 (45.5)
	Erosive gastritis	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)
	Pangastritis	0 (0.0)	1 (7.1)	2 (11.8)	1 (9.1)

Table 3. Comparative evaluation of pathological diagnoses before and after treatment

		Before treatment		
		Acute gastritis	Chronic gastritis	Chronic gastritis with erosion and ulceration
		n (%)	n (%)	n (%)
After treatment	Normal mucosa	26 (61.9)	20 (33.9)	0 (0.0)
	Acute gastritis	14 (33.3)	20 (33.9)	0 (0.0)
	Chronic gastritis	2 (4.8)	19 (32.2)	24 (96.0)
	Chronic gastritis with erosion and ulceration	0 (0.0)	0 (0.0)	1 (4.0)

Table 4. Comparative evaluation of *Helicobacter pylori* intensity before and after treatment

		Before treatment		
		+	++	+++
		n (%)	n (%)	n (%)
After treatment	No colonization	9 (24.3)	13 (25.5)	9 (23.7)
	+	24 (64.9)	25 (49.0)	6 (15.8)
	+ +	4 (10.8)	11 (21.6)	16 (42.1)
	+++	0 (0.0)	2 (3.9)	7 (18.4)

When we evaluated which group was more successful in Hp eradication, it was seen that there was no significant difference between the groups.

Discussion

Even if Hp is asymptomatic, it can cause gastritis, gastric ulcer, gastric cancer, mucosa-related lymphoid tissue lymphomas (9,10). It is also associated with extra-gastric neurological, hematological, dermatological, cardiovascular, ocular, hepatobiliary, metabolic, and allergic diseases and is studied in the literature (11). Treatment is important. There are problems in its eradication due to antibiotic resistance globally and in our country (6,12-14).

Table 5. Post-treatment Hp positivity rates

		Before treatment Hp positivity	After treatment Hp		
			Negative	Positive	
		n=126	n (%)	n (%)	p
Total		n=126	31 (24.6)	95 (75.4)	<0.001*
Endoscopic diagnoses before treatment	Antral gastritis	n=84	22 (26.2)	62 (73.8)	<0.001*
	Erosive gastritis	n=14	4 (28.6)	10 (71.4)	0.125
	Pangastrit	n=17	4 (23.5)	13 (76.5)	0.125
	Ulceration	n=11	1 (9.1)	10 (90.9)	1.000
Pathological diagnoses before treatment	Acute gastritis	n=42	9 (21.4)	33 (78.6)	0.002*
	Chronic gastritis	n=59	17 (28.8)	42 (71.2)	<0.001*
	Chronic gastritis with erosion and ulceration	n=25	5 (20.0)	20 (80.0)	0.063
Hp intensity Before treatment	+	n=37	9 (24.3)	28 (75.7)	0.004*
	+ +	n=51	13 (25.5)	38 (74.5)	<0.001*
	+ + +	n=38	9 (23.7)	29 (76.3)	0.004*

*McNemar test, Hp: *Helicobacter pylori*

Table 6. Hp eradication rates after treatment in pre-treatment diagnosis groups

		Post-treatment Hp eradication	
		n (%)	p*
Endoscopic diagnoses before treatment	Antral gastritis Erosive gastritis Pangastrit	22 (26.2) 4 (28.6) 4 (23.5)	0.719
	Ulceration	1 (9.1)	
Pathological diagnoses before treatment	Acute gastritis Chronic gastritis	9 (21.4) 17 (28.8)	0.583
	Chronic gastritis with erosion and ulceration	5 (20.0)	
Hp intensity before treatment	+ + +	9 (24.3) 13 (25.5)	0.980
	+ + +	9 (23.7)	

*chi-square test, Hp: *Helicobacter pylori*

In our study, Hp was detected in 95 (75.4%) patients in control endoscopy and biopsies performed within the first three months after treatment of 126 patients treated for Hp positivity. Although the normal endoscopic appearance was obtained in 87 (69%) patients, the presence of Hp continued with a decrease in its severity. Our results were

found to be + in 55 (43.7%) patients, + + in 31 (24.6%) patients, and in 9 (7.1%) + + + is reflected in the form of detection. In all patients before treatment (p<0.001), patients with antral gastritis before treatment (p<0.001), patients with a pathological diagnosis of acute (p=0.001) and chronic (p<0.001) gastritis, in all groups regarding Hp severity (1+ for p=0.004, for 2+ p<0.001, for 3+ p=0.004) Hp eradication was found to be statistically significant in terms of its increase and decrease (McNemar test). There was no statistically significant difference in Hp eradication rates in the endoscopic diagnosis, pathological diagnosis and pathological Hp intensity groups before treatment (Table 6) (p=0.719 p=0.583 p=0.980).

Our results show the failure of the trio of clarithromycin, amoxicillin, and omeprazole which are widely used in Turkey. Most patients stop treatment when they become asymptomatic and do not come for control. Asymptomatic, untreated Hp infection continues. The success of eradication with these handicaps is controversial.

Although antibiotic resistance varies from country to country, in Hp eradication, treatment regimens are changing considering resistance, and new protocols are recommended. Culture and antibiogram stand out as the gold standard. To give an example of regimen changes suggested in the literature; the addition of bismuth to triple therapy was included in the Maastricht consensus in 1997, in regions where clarithromycin resistance is above 15-20%, and quinolone resistance is below 10%, levofloxacin instead of clarithromycin in triple therapy, adding metronidazole to triple therapy or hybrid therapies are recommended (7,15,16).

In a study conducted in Turkey, 18.2% clarithromycin, 45.5% metronidazole, 18.2% levofloxacin resistance were detected, while amoxicillin resistance was not observed (14).

Methods such as the detection of Hp in endoscopic sampling, rapid urease test, polymerase chain reaction, urea breath test, specific antigen detection in stool samples are used to diagnose Hp. However, none of these methods provide information about the antibiotic resistance that determines the treatment result. Since the culture antibiogram is now considered the gold standard, it is appropriate to shift the investigations in this direction (17). In the literature, culture positivity is around 30%, sensitivity is 45-89%, and specificity is 97-100%. Utku et al. (18) in a study conducted in Turkey they reported the culture positivity was 38.3%, sensitivity 60.3%, and specificity 100%. The aim of this article, which we wrote as a surgical team, is not to discuss the sensitivity and specificity of various tests or the effective methods of culture/antibiogram but to raise awareness. The difficulty of eradication of Hp, which can be isolated even from 6000-year-old mummies since ancient times should also be understood (19). The addition of bismuth salts to classical treatment is on the agenda again with successful results in resistant cases (20).

Study Limitations

The study was conducted by surgeons based on the data of the surgical endoscopy unit, and it does not include detailed gastroenterological evaluations. One of the limitations of the study is that it is retrospective. Our study once again reveals the failure of the triple regimen, which is widely used in our country in primary care. The data of our study can contribute to the literature in terms of reviewing traditional treatment regimens and using antibiotic susceptibility tests more widely.

Conclusion

In cases of gastritis, Hp positivity continues despite treatment, although the pathological severity changes. It would be appropriate to discuss the effectiveness of routine treatments and to emphasize the culture/antibiogram. In fact, it would be appropriate to use preparations containing bismuth more prominently into account.

Authorship Contributions

Concept: M.A., A.K.K., M.C., Design: A.H., A.K., Data Collection or Processing: M.S.D., O.M.A., Analysis or Interpretation: D.Y., M.S.D., O.M.A., Literature Search: M.C., D.Y., Writing: M.C., M.A.

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