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Efficacy of *Helicobacter pylori* Eradication Based on Rabeprazole–Bismuth–Tetracycline–Tinidazole Regimen in Vietnamese Patients with Duodenal Ulcers

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Abstract: (1) Background: In Vietnam, *H. pylori* bacteria has a resistance rate of 63% to the antibiotic clarithromycin. The initial therapy of *H. pylori* eradication with a standard three-drug regimen has low efficacy. Objective: Assess the efficacy of *H. pylori* eradication therapy which uses a four-drug regimen of rabeprazole–bismuth–tetracycline–tinidazole in patients with duodenal ulcers. (2) Methods: We performed gastrointestinal endoscopy on patients with a diagnosis of duodenal ulcers, gastric mucosa biopsy for a rapid urease test, and histopathology to diagnose *H. pylori* bacteria before and after treatment. Treatment for eradication of *H. pylori* bacteria using a rabeprazole–bismuth–tetracycline–tinidazole regimen was prescribed for 14 days. (3) Results: The rate of successful *H. pylori* eradication treatment according to per protocol (PP) and intention to treat (ITT) was 91.3% (95%CI: 84.8–96.7) and 82.4% (95%CI: 74.5–89.2) respectively. The success rate of *H. pylori* eradication therapy in males was 96.0% (95%CI: 92–100), higher than in females, which was 70.6% (95%CI: 47.1–88.2), $p < 0.01$. (4) Conclusions: Treatment of *H. pylori* with rabeprazole–bismuth–tetracycline–tinidazole regimen is highly effective. Men had higher *H. pylori* eradication results than women.

Keywords: eradication therapy; *Helicobacter pylori*; RBTT; Vietnamese

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1. Introduction

Helicobacter pylori (H. pylori) infection is associated with upper gastrointestinal diseases, such as duodenal ulcers, stomach ulcers, stomach cancer, etc., in which duodenal ulcers are a more common disease [1]. The overall prevalence of *H. pylori* is 44.3% worldwide, ranging from 34.7% in developed countries to 50.8% in developing countries. The global prevalence of *H. pylori* infection is 46.3% in men compared with 42.7% in women. The prevalence in adults (≥18 years) of 48.6% is significantly higher than in children at 32.6% [2]. There are indications for treatment of *H. pylori* in gastritis, peptic ulcer, etc. Medication for treating H. *pylori* includes proton pump inhibitors (PPIs), antibiotics, and bismuth [3].

Several worldwide studies reviewed in Vietnam also illustrate that the first-time eradication of *H. pylori* with a four-drug regimen including bismuth is more effective than the standard three-drug regimen [4,5]. According to the Maastricht VI consensus recommendation, H. pylori eradication therapy is essential when the strain of H. pylori has a resistance rate of more than 15% to clarithromycin, uses a combination of four drugs including bismuth, which is the most succesful treatment [6]. The prevalence of *H. pylori* strains resistant to clarithromycin in countries in southeast Asia, such as Malaysia,

Indonesia, Laos, Singapore, and Thailand, are 5%, 9%, 13%, 16%, and 19%, respectively. In Vietnam, however, *H. pylori* bacteria has a high rate of resistance to clarithromycin, specifically 63% [7]. t The Vietnam Association of Gastroenterology Sciences recommends that the standard regimen of three drugs for *H. pylori* treatment should not be used as the first treatment, but rather the regimen of four drugs including bismuth (PPI, bismuth, tetracycline, metronidazole or tinidazole between 7 and 14 days) should be used [8]. Tinidazole and metronidazole, the same group of antibiotics as nitroimidazole, have similar sterile effects and side effects.

However, some studies show that using tinidazole in *H. pylori* eradication therapy has some advantages over metronidazole. When cultivating *H. pylori* bacteria and making antibiograms, *H. pylori* bacteria are more sensitive to combining tinidazole and clarithromycin than metronidazole and clarithromycin [9]. *H. pylori* eradication therapy with a three-drug regimen containing tinidazole is more effective than metronidazole [10]. Three out of 91 patients who were given the three-drug regimen containing metronidazole discontinued it due to side effects, however all 80 patients who were given the three-drug regimen including tinidazole finished the course of treatment [11]. 86% of patients finished the second eradication therapy using the regimen of ranitidine, bismuth, citrates, doxycycline, and tinidazole [12].

We conducted this study to assess the efficacy of *H. pylori* eradication in patients with duodenal ulcers using a four-drug regimen including rabeprazole, bismuth, tetracycline, and tinidazole (RBTT) for 14 days, and to assess the related factors that improve the efficacy of *H. pylori* eradication therapy.

2. Materials and Methods

2.1. Study Materials

There were 102 patients diagnosed with duodenal ulcers to be examined and treated at Can Tho University of Medicine and Pharmacy Hospital from January 2015 to December 2016.

2.1.1. Selection criteria

Only patients being treated for *H. pylori* for the first time were included in the study. Clinical symptoms were related to upper gastrointestinal pathologies (pain, epigastric burning, belching, etc.). Endoscopy detected large duodenal ulcers more than 5 mm (measured by the distance between the jaws of biopsy pliers). A positive *H. pylori* test was indicated by a rapid urease test and histopathology. Patients were required to be over the age of 18. All participants gave informed consent to participate in the study.

2.1.2. Exclusion Criteria

Pre-treatment exclusion criteria included patients with a history of a gastrectomy. Those with duodenal ulcers with complications, including perforation and gastrointestinal hemorrhage were not included. Patients with a combination of severe diseases, such as cirrhosis, cancer, and Crohn's disease, or had contraindication of gastric-duodenal endoscopy were also excluded. This study did not include women who were pregnant or breastfeeding. Patients who took antibiotics and bismuth for four weeks prior to the endoscopy were not included. Patients using proton pump inhibitors (omeprazole, lansoprazole, dexlansoprazole, pantoprazole, esomeprazole, or rabeprazole) and/or H_2 antihistamines (cimetidine, ranitidine, famotidine, or nizatidine) within two weeks before the endoscopy were excluded. Patients who were taking nonsteroidal anti-inflammatory drugs and aspirin were also excluded. Patients with a history of drug allergies included in the study regimen were not included.

Criteria of exclusion during the course of treatment included patients who changed the treatment drugs or took additional drugs other than the treatment regimen on their own (such as nonsteroidal anti-inflammatory drugs, aspirin, etc.).

2.2. Study Methods

2.2.1. Study Design

Type of research: interventional research.

2.2.2. Sample Size

Sample size calculated by the formula:

$$n = \frac{Z^2_{1-\alpha/2} \times P \times (1-P)}{d^2}$$

$Z^2_{1-\alpha/2}$: confidence coefficient with 95% reliability (1.96).
d: absolute error (5–10%).
P: the rate of first successful *H. pylori* eradication therapy.

According to the results of the study by Kou C.H., the rate of first-time treatment of *H. pylori* with RBTM regimen following the research outline (PP) was 85.1% ($p = 0.85$) [13] with an absolute error of 7.5% (d = 0.075), confidence coefficient of 95% (1.96). The study's sample size was 87.1 (rounded to 88 patients). When analyzed in PP, the sample loss rate was 7/97 (7.4%). We took 8% of the sample loss rate, therefore we studied 95.04 patients (rounded to 96 patients).

2.2.3. Study Facilities

The Olympus GIF 180 duodenal gastroscopy machine from Olympus, Japan was used. The solution jar contained 10% neutral formol to fix the biopsy sample of the stomach lining. A rapid urease test (NK-H. pylori test) sample was provided by Nam Khoa Service Trading Limited Company, Ho Chi Minh City.

Drugs for treating duodenal ulcers and eradicating *H. pylori* at Can Tho University of Medicine and Pharmacy Hospital pharmacy included: rabeprazole sodium 20 mg: Pariet specialty 20 mg, of Eisai Company, Tokyo, Japan; colloidal bismuth subcitrate 120 mg: Trymo specialty 120 mg, by Raptakos Brett Company, Maharashtra, India; tetracycline hydrochloride 500 mg: tetracyclin specialty 500 mg, by Domesco Company, Cao Lanh City, Vietnam; and tinidazole 500 mg: tinidazole specialty 500 mg by Domesco Company, Cao Lanh City, Vietnam.

2.2.4. Implementation Steps

(1) Patient reception and clinical examination: The doctor examined the patient, noted the clinical signs, and prescribed an endoscopy. Clinical symptoms: epigastric pain, epigastric burning, hunger pain, burping, nausea, vomiting. The severity of clinical symptoms was assessed using the GSRS scale (Gastrointestinal Symptoms Rating Scale) [14]. Smoking habits were assessed according to the U.S. Centers for Disease Control and Prevention in 2009 [15]. Alcohol consumption was rated according to the AUDIT-C alcohol use disorder screening questionnaire (The Alcohol Use Disorders Identification Test Consumption) by Bradley K.A [16].

(2) Duodenal gastroscopy

The patients fasted 6–8 h before the endoscopy. The duodenal ulcers survey revealed the number of ulcers and their sizes (measured through biopsy pliers, in mm).

We performed a biopsy of the stomach lining via two samples of the pyloric antrum 3 cm from the pylorus and two samples of the stomach body from the greater curvature. Two biopsy samples (one in the stomach body, the other in the pyloric antrum) were obtained for the rapid urease test, and two additional samples from these areas were obtained for histopathology to diagnose infection with *H. pylori* bacteria.

(3) Urease test diagnosed *Helicobacter pylori*

We took two biopsy samples (one from the stomach body, one from the pyloric antrum) to utilize in the rapid urease test and read the results within 60 min.

Identification of the results: rapid urease tested positive when the reagent switched from yellow to pink 60 min after inserting the biopsy sample. After that time, all colorless samples were considered negative.

(4) Gastric mucosal histopathology test diagnosed *Helicobacter pylori*

In the endoscopic room, after performing the biopsy of the stomach lining, we took two samples from the biopsy (one from the stomach body, one from the pyloric antrum), put them in 2 jars of formol solution 10%, wrote the full name and code on the jars, then sent them to the Anatomy Department of Can Tho University of Medicine and Pharmacy Hospital.

A diagnosis of *H. pylori* infection was made on Giemsa and Hematoxylin-eosin dyed specimens. We assessed the *H. pylori* infection density on histopathology (light, medium, and heavy according to the classification standards of the updated Sydney Classification System [17]).

(5) Treatment of duodenal ulcers contaminated with *Helicobacter pylori* (Table 1).

Table 1. Four-drug regimen with bismuth.

Rabeprazole (Pariet) 20 mg			
Breakfast: a.c/ 1 tablet	Lunch: a.c 30–60 mins/ 1 tablet	Dinner: none	Bedtime: none
Bismuth (Trymo) 120 mg			
Breakfast: a.c 30 mins/ 1 tablet	Lunch: a.c 30 mins/ 1 tablet	Dinner: a.c 30 mins/ 1 tablet	Bedtime: a.c 15 mins/ 1 tablet
Tetracycline 500 mg			
Breakfast: p.c 30 mins/ 1 tablet	Lunch: p.c 30 mins/ 1 tablet	Dinner: p.c 30 mins/ 1 tablet	Bedtime: a.c 15 mins/ 1 tablet
Tinidazole 500 mg			
Breakfast: p.c/ 1 tablet	Lunch: p.c 30 mins/ 1 tablet	Dinner: none	Bedtime: none

Continually using for 14 days, a.c: before meal, p.c: after meal.

After finishing the *H. pylori* eradication therapy, continued treatment with rabeprazole (Pariet) 20 mg was prescribed with the recommendation to take one tablet at a time, two times a day (before breakfast andbefore lunch 30–60 mins), continuously for 14 days to heal the scars of the duodenal ulcer (Table 1).

Post-treatment re-examination: all patients were scheduled for a second visit four weeks after finishing the RBTT regimen (two weeks after discontinuing rabeprazole). The doctors examined and assessed the improvement of the clinical signs and side effects of the treatment drugs; endoscopy assessed ulcers and biopsies of the stomach lining were obtained for rapid urease test and histopathology diagnosis of *H. pylori*.

(6) Assessment of the efficacy of treating duodenal ulcers with *H. pylori* infection

Assessment of the efficacy of treating duodenal ulcers infected with *H. pylori* was made using the rapid urease test and histopathology and found to successfully eradicate *H. pylori* (*H. pylori* was negative on both the rapid urease test and histopathology). Ulcers were also found to be in recovery.

Patients for whom the treatment had not been effective:

For results indicating *H. pylori* eradication therapy failed, it was considered that change to the treatment according to the new regimen as recommended by the Vietnam Society of Gastroenterology in 2013 may be beneficial [8]. If treatment continues to fail, we will culture *H. pylori* and make antibiograms.

Non-recovered ulcers scars: it was recommended to continue to take PPIs for another four weeks and determine causes of the failure of reducing ulcer scarring, such as drinking

alcohol, smoking, NSAIDs and/or aspirin use, etc. If the ulcer is still not recovered, surgical treatment will be considered.

(7) Processing and analyzing data

All data was processed on the computer using SPSS 20.0 software. Continuous variables had a standard distribution and were described as mean numbers and standard deviations, and the taxonomic variables were described as frequencies and percentages. We compared the efficacy of the interventional measures before and after the treatment using the paired and non-parameter comparison methods (Wilcoxon Signed Ranks Test). In comparing two ratios, we calculated Odds Ratio (OR) and verified using Pearson Chi-Square Test for one side to assess the difference in the ratio of a parameter between the two groups. We used Fisher's Exact Test when more than 20% of the expected counts were less than 5. In comparing more than two ratios, we used the Chi-Square Test for both sides. The Logistic Regression Test determined the association between the independent and dependent variables. The test results were assessed as statistically significant when $p < 0.05$.

3. Results

3.1. Patients' Characteristics in the Study

Among 102 patients recruited in this study, 92 qualified patients were selected for treatment and assessed for the efficacy of the RBTT regimen. Ten patients were excluded from the analysis because these patients did not return for re-examination and undergo an endoscopy to assess duodenal ulcer scars and *H. pylori* diagnosis (Figure 1).

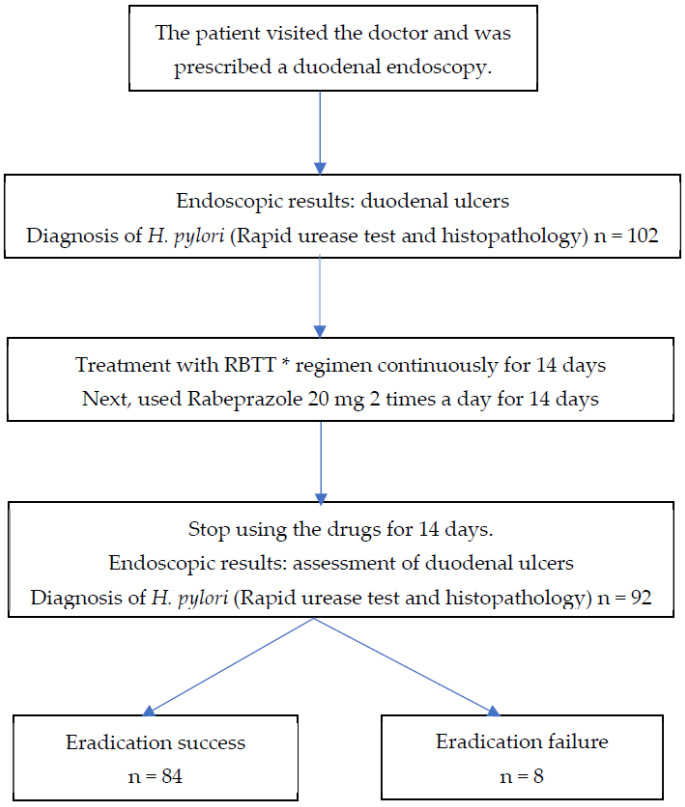

Figure 1. Diagnosis and *H. pylori* eradication therapy. (*) RBTT: rabeprazole, bismuth, tetracycline, tinidazole.

Among 102 patients with duodenal ulcers infected with *H. pylori* bacteria and recruited in the study, males accounted for 77.5% and females for 22.5%. The mean age was 43.8 ± 13.9, the youngest was 19, and the oldest was 84. The mean weight was

59.7 ± 8.5 kg, the lightest was 39 kg, and the heaviest was 80 kg. Patients who had smoking habits accounted for 49% and those with drinking habits accounted for 57.8% (Table 2).

Table 2. Patients' characteristics.

Demographic Characteristics	Frequency (n = 102)	Rate (%)
Sex		
Male	79	77.5
Female	23	22.5
Age		
Mean age	43.8 ± 13.9	
<30 years	16	15.7
30-59 years	73	71.6
Weight (kg)		
Mean weight	59.7 ± 8.5	
Smoking		
Yes	40	49
No	52	51
Alcohol		
Yes	59	57.8
No	43	42.2
Symptoms		
Epigastric pain	96	94.1
Epigastric burning	61	59.8
Burping	63	61.8
Hunger pain	93	91.2
Nausea, vomiting	21	20.6
At least one symptom	102	100
Quantity of ulcers		
1	86	84.3
≥2	16	15.7
Size of ulcers		
<10mm	66	64.7
≥10mm	36	35.3
H. pylori bacterial density		
Mild	57	55.9
Medium	34	33.3
Severe	11	10.8

The study's 102 duodenal ulcer patients had at least one of five clinical signs: epigastric pain, epigastric burning, burping, hunger pain, or nausea, and vomiting. In particular, the most common signs were epigastric pain, 94.2% (96/102), burning and hunger pain, 91.2% (93/102). Less common symptoms were epigastric burning, accounting for 59.8% (61/102); heartburn, accounting for 61.8% (63/102); and nausea and vomiting, accounting for 20.6% (21/102) (Table 2).

Endoscopic imaging revealed that most patients had one duodenal ulcer, which accounted for 84.3% (86/102), with two or more ulcers accounting for 15.7% (16/102). In terms of ulcer size, duodenal ulcers <10 mm in size accounted for a high proportion of 64.7% (66/102), and ulcers ≥10 mm in size accounted for 35.3% (36/102). The density of *H. pylori* bacteria in the stomach lining (stomach and mouth) was assessed and mild *H. pylori* infection accounted for the highest rate of 55.9% (57/102). The mean level was found to be 33.3% (34/102), and the most severe density accounted for 10.8% (11/102) (Table 2).

3.2. Results of Helicobacter pylori Eradication Therapy

After the therapy of *H. pylori* eradication cessation of antibiotics and bismuth for at least four weeks, and rabeprazole for at least two weeks), 92 patients were assessed for clinical signs, endoscopic examination, and the presence of *H. pylori* bacteria. We noticed that 75 (81.5%) patients no longer had clinical symptoms, and 17 (18.5%) patients had mild symptoms and a significant decrease in GSRS mean score (7.7 ± 2.73/before treatment about 2.0 ± 1.73/after treatment, $p < 0.01$, CI: 4.3–7.11). There were 89 (96.7%) patients with duodenal ulcer recovery. The rate of successful *H. pylori* eradication treatment according to per protocol (PP) and intention to treat ITT) were 91.3% and 82.4%, respectively (Table 3).

Table 3. Treatment results.

Factor	Result			
	Success		Failure	
	n	%	n	%
H. pylori (PP)	84	91.3	8	8.7
H. pylori (ITT)	84	82.4	18	17.6
H. pylori in males	72	96.0	3	4.0
H. pylori in females	12	70.6	5	29.4
Duodenal ulcers	89	96.7	3	3.3
Clinical signs	75	81.5	17	18.5

Regarding the factors that impacted the efficacy of *H. pylori* eradication therapy, among 92 patients treated, treatment efficacy in female patients was 70.6%, lower than the male patients, which was 96% ($p < 0.01$, OR = 10.0, 95%CI: 2.10–47.41). There were no statistically significant differences in the efficacy of *H. pylori* eradication therapy by age group, *H. pylori* bacterial density, alcohol consumption, or smoking habits ($p > 0.05$) (Table 4).

Table 4. *Helicobacter pylori* eradication rate of tailored therapy and associated factors ($n = 92$).

Factor	*n*	Eradication		*p*	OR, 95% CI
		Success	Failure		
Age group					
<60	82	75 (91.5)	7 (8.5)	1.00	1.19, 0.13–10.81
≥60	10	9 (90.0)	1 (9.0)		
Gender					
Male	75	72 (96.0)	3 (4.0)	<0.01	10.00, 2.10–47.41
Female	17	12 (70.6)	5 (29.4)		
Density of *H. pylori*					
Mild	51	48 (94.1)	3 (5.9)	0.45	2.22, 0.49–9.11
Medium, severe	41	36 (87.8)	5 (12.2)		
Alcohol					
Yes	57	52 (91.2)	5 (8.8)	1.00	0.97, 0.21–4.35
No	35	33 (91.4)	3 (8.6)		
Smoking					
Yes	49	44 (89.8)	5 (10.2)	0.71	0.66, 0.14–2.94
No	43	40 (93.0)	3 (7.0)		

When analyzing multivariate regression, factors related to the results of *H. pylori* eradication therapy include age group (≥60 vs. <60), sex (male vs. female), the density of *H. pylori* bacteria (mild vs. medium to severe), alcohol consumption (yes vs. no), and smoking (yes vs. no). The results illustrate that only sex is associated with the results of *H. pylori* eradication therapy ($p < 0.01$, OR = 19.12, 95%CI: 2.83–128.93) (Table 5).

Table 5. Multivariate regression analysis of factors related to *Helicobacter pylori* eradication therapy results (n = 92).

Factor	OR	95% CI	p
Age: ≥60	3.05	0.20–46.14	0.41
Sex: female	19.12	2.83–128.93	<0.01
Density of *H. pylori*: medium and severe	3.19	0.58–19.77	0.17
Alcohol: yes	1.68	0.12–22.56	0.69
Smoking: yes	2.0	0.15–26.82	0.59

3.3. Side Effects

Side effects of the drugs included in the regimen of *H. pylori* eradication among 92 patients treated were noted in 23.9% (95%CI: 15.2–33.7) of patients (22/92). Most side effects were mild and medium; there were no cases of hospitalizations for side effects of the drugs. The most common side effects were nausea, accounting for 11.9% (11/92); headaches, accounting for 4.3% (4/92); and other rare manifestations, including vomiting, diarrhea, constipation, etc. Moreover, there were no complications due to gastroduodenoscopy.

4. Discussion

In our study, the rate of successful *H. pylori* eradication treatment according to PP and ITT was 91.3% and 82.4%, respectively. Compared with other studies of *H. pylori* eradication treatment with a regimen of four drugs including bismuth, our study was most consistent with the study of Xie Y. in China on 107 patients with duodenal ulcer infected by *H. pylori*, treated with an RBAT regimen (rabeprazole, bismuth, amoxicillin, tetracycline), and including high-dose rabeprazole for 10 days. Xie Y. determined the successful *H. pylori* eradication rate in PP was 91.9%, according to ITT 86.0% [18].

The proportion of RBTM regimen treatment (rabeprazole, bismuth, tetracycline, metronidazole) in this study was higher than in the study of Sapmaz F. in Turkey on 98 patients with non-ulcerative functional indigestion infection of *H. pylori* after 14 days of treatment. The successful *H. pylori* eradication rate in PP was 88.8%, according to ITT 87.8% [19]. Wu M.C.'s study in Taiwan on 81 patients with functional indigestion or epigastric discomfort were infected with *H. pylori* and treated with an RBAC regimen (rabeprazole, bismuth, amoxicillin, clarithromycin) containing high-dose rabeprazole for 7 days, and the successful *H. pylori* eradication rate in PP was 81.8%, according to ITT 77.8% [20].

The proportion of RBTM regimen treatment in this study was lower than in the study of Kefeli A. in Turkey on 130 patients with gastritis, gastric ulcer, and/or duodenal ulcer infection of *H. pylori*, who were treated with an RBTM regimen (rabeprazole, bismuth, tetracycline, metronidazole) for 10 days., The successful *H. pylori* eradication rate in PP was 94.2%, according to ITT 87.7% [21]. Xie Y. performed a study in China on 106 patients with duodenal ulcer infected with *H. pylori*, and treated with the RBAC regimen (rabeprazole, bismuth, amoxicillin, clarithromycin) with 10-day high-dose rabeprazole. The successful *H. pylori* eradication rate in PP was 94.8%, according to ITT 87.7% [18]. The study by Gu L. in China on 118 patients with peptic ulcer, non-ulcerative indigestion, or apparent etiology with *H. pylori* infection treated with an RBAD regimen (rabeprazole, bismuth, amoxicillin, doxycycline) for 14 days. The successful *H. pylori* eradication rate in PP was 93.8%, according to ITT 89.8% [22]. Bang C.S.'s study in South Korea in patients with gastritis, gastric ulcer, duodenal ulcer, and *H. pylori* infection treated 116 patients with RBTM regimen (rabeprazole, bismuth, tetracycline, metronidazole) over 14 days. The successful *H. pylori* eradication rate in PP was 96.9%, according to ITT 82.8%; Bang C.S. also prescribed the PBMA regimen (pantoprazole, bismuth, metronidazole, amoxicillin) in 117 patients over 14 days, and the efficacy of *H. pylori* eradication treatment in PP was 96.2%, according to ITT 87.2% [23].

Studies worldwide show that the treatment of *H. pylori* eradication with a four-drug regimen containing bismuth is highly effective at more than 80%.

Our study results are consistent with *H. pylori* eradication including a bismuth four-drug regimen in other studies in Vietnam. According to a study by Hue N.Q.D., *H. pylori* eradication was attempted in 122 patients with chronic gastritis for the first time with an EBTM regimen (esomeprazole, bismuth, tetracycline, metronidazole) in 10 days. The successful *H. pylori* eradication rate in PP was 90.65% and according to ITT was 79.51% [24]. In the study by Huy V.T., initial treatment for *H. pylori* eradication in patients with chronic gastritis using the RBMA regimen (rabeprazole, bismuth, metronidazole, amoxicillin) in 60 patients over 14 days resulted in the successful rate of *H. pylori* eradication in PP of 91.2% and according to ITT was 86.7%; with RBTM regimen (rabeprazole, bismuth, tetracycline, metronidazole) in 60 patients over 14 days, the success rate of *H. pylori* eradication in PP was 90% and according to ITT was 75% [25]. According to Tuong T.K.T.'s study, the research of 89 patients diagnosed with *H. pylori* infection indicated treatment with the RBAL regimen (rabeprazole, bismuth, amoxicillin, levofloxacin) for 14 days, and the successful *H. pylori* eradication rate in PP was 92.7% and according to ITT was 89.9% [26].

The treatment results in our study were higher than Nam C.B.'s study, which prescribed treatment of *H. pylori* eradication in 306 patients with inflammation and/or peptic ulcers using PBTM regimen (pantoprazole, bismuth, tetracycline, metronidazole). The successful rate of *H. pylori* eradication was 88.56% [5]. This difference may be due to differences in the use of PPI drugs in the *H. pylori* eradication regimen.

Concerning the factors impacting the treatment efficacy, we found that the bactericidal rate in the male patient group was 96%, higher than that of the female patient group, which was 70.6%. In females, there was a 10-fold higher rate of *H. pylori* eradication treatment failure than in males; this difference was statistically significant with $p < 0.05$ (95%CI: 2.10–47.41). The study's results are consistent with Oh J.H.'s study of eradication treatment of *H. pylori* in 210 patients with gastric ulcers, duodenal ulcers, and gastritis using a PAC regimen (pantoprazole, amoxicillin, clarithromycin) for 7 days. In the successful *H. pylori* eradication group, males accounted for 57% and females for 43%; in other words, males had a higher rate of successful *H. pylori* eradication than females (OR = 2.64, $p = 0.01$) [27]. However, according to the study by Kang J.M, results of *H. pylori* eradication treatment in 327 patients with chronic gastritis, gastric ulcers, duodenal ulcers, dysplasia, or cancer using PAC regimen (pantoprazole, amoxicillin, clarithromycin) on 190 patients and EAC (esomeprazole, amoxicillin, clarithromycin) on 137 patients for 7 days, the successful *H. pylori* eradication group had a male/female ratio of 173/105. In the failed *H. pylori* eradication group, the male/female ratio was 33/16 (there was no difference in the male/female ratio between the 2 groups, with $p > 0.05$) [28]. According to the study by Furuta T., the eradication treatment of *H. pylori* in 350 patients with gastritis, gastric ulcers, and duodenal ulcers using the OAC regimen (omeprazole, amoxicillin, clarithromycin) on 175 patients and LAC (lansoprazole, amoxicillin, clarithromycin) on 175 patients for 7 days, the successful rate of *H. pylori* eradication in males was 87% and in females was 89% (there was no difference in treatment ratio between the 2 sexes, with $p > 0.05$) [29]. According to Furuta T.'s study, *H. pylori* eradication was treated in 313 patients with gastritis, gastric ulcers, and duodenal ulcers using the LAC regimen (lansoprazole, amoxicillin, clarithromycin) for 7 days. The successful eradication rate of *H. pylori* in males was 78% and in females was 76% (there was no difference in treatment results between male and female, with $p > 0.05$) [30]. According to the study by Kuo C.H., 190 patients with gastritis, peptic ulcers, and polyps, including *H. pylori* infection, were treated with the EBTM regimen (esomeprazole, bismuth, tetracycline, metronidazole), and RBTM (rabeprazole, bismuth, tetracycline, metronidazole), for 7 days, and the successful eradication rate of *H. pylori* in men was 75.9%; in women it was 75.7% (there was no difference in treatment results between the 2 sexes, with $p > 0.05$) [13]. According to Kuo C.H., the study treated *H. pylori* in 150 patients with gastritis, peptic ulcers, polyps, and *H. pylori* infection using the EBTL regimen (esomeprazole, bismuth, tetracycline, levofloxacin) andEBTM regimen (esomeprazole, bismuth, tetracycline, metronidazole) for 10 days. The successful rate of *H. pylori* eradication in males was 84.9%, and in females it was 91.1% (there was no difference in treatment results between the 2 sexes,

with RR = 0.516) [31]. According to the study by Zhang Y.W., the eradication treatment of *H. pylori* in 992 patients with functional indigestion, gastritis, peptic ulcers, gastric tumors, and gastritis included a PPI regimen (rabeprazole, esomeprazole, pantoprazole, lansoprazole, omeprazole), bismuth, furazolidone, and amoxicillin for 10–14 days. The eradication rate of *H. pylori* in males was 93.6%, and for females was 95.3% (there was no difference in the rate of eradication of *H. pylori* between the 2 sexes, with $p > 0.05$) [32]. Mohammed S.A.'s study treated *H. pylori* eradication in 124 patients (29 with peptic ulcers and 95 without peptic ulcers) using the OAC regimen (omeprazole, amoxicillin, clarithromycin) and OAL (omeprazole, amoxicillin, levofloxacin) and the OAL regimen (omeprazole, amoxicillin, levofloxacin) for 14 days. The eradication rate of *H. pylori* in men was 87.5% and in women was 77.6% (there was no difference in *H. pylori* eradication rate between the two sexes, with $p > 0.05$) [33]. The results of our study are inconsistent with the referenced studies, possibly due to differences in patient subjects and some drugs in the four-drug regimen, including bismuths.

Most studies show that gender does not affect the results of *H. pylori* eradication treatment, however, some studies do indicate that men have better treatment results than women. Results of *H. pylori* treatment might be affected by *CYP2C19* gene polymorphisms. According to the study by Ghazvini K., the eradication rate of *H. pylori* in the CYP2C19 phenotype of HomEM, HetEM, and PM groups were 77%, 82.7%, and 85.4%, respectively. The outcome of first-line *H. pylori* eradication with PPIs, such as omeprazole, lansoprazole, and esomeprazole, significantly depend on *CYP2C19* genotype status. In contrast, PPIs such as pantoprazole and rabeprazole are not affected by this gene polymorphism [34].

The benefits of our study were the assessment of patients with duodenal ulcers using the two diagnostic methods of *H. pylori*, rapid urease test, and histopathology; using only one PPI drug (rabeprazole), which was less metabolized by the *CYP2C19* gene; and all of the patients were evaluated for the efficacy of treatment by the *H. pylori* test and histopathology. These tests were highly specific, which allows for assessment of the efficacy. The unique element of our study was in using tinidazole instead of metronidazole. The results show that the female sex had a lower therapeutic efficacy than the male. We also ensured that a specialist carefully consulted all of the patients and followed up with the treatment and procedures. The limitation of our study was the design of a non-group clinical trial, whose subjects' age and weight fluctuated.

5. Conclusions

Due to the increase in antibiotic-resistant strains of *H. pylori*, successful eradication treatment is challenging. The therapy prescribed in our study to eradicate *H. pylori* has been very successful, achieving over 90%, but for female patients, it does not demonstrate eradication above 80%. Side effects of the regimen are mainly mild, and 100% of patients completed the course of treatment. We recommend that in countries with high rates of antibiotic-resistant *H. pylori* strains, the RBTT regimen should be implemented. More research with a larger sample size is needed to determine the causes affecting the results of *H. Pylori* eradication treatment in female patients.

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