Scholars Academic Journal of Pharmacy
Abbreviated Key Title: Sch Acad J Pharm
ISSN 2347-9531 (Print) | ISSN 2320-4206 (Online)
Journal homepage: http://saspublishers.com

OPEN ACCESS
Medicine

Evaluation of the Efficacy of *Helicobacter pylori* Eradication Regimens

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DOI: https://doi.org/10.36347/sajp.2024.v13i07.005 | **Received:** 28.08.2024 | **Accepted:** 15.09.2024 | **Published:** 19.09.2024

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Abstract | **Original Research Article**

Background*:** Several studies have been carried out to assess the effectiveness of current combination therapies for H. pylori infection. Usually, a PPI is combined with two antibiotics (triple therapy) or bismuth salts are added to these three medication agents (quadruple therapy). Antibiotic selection ought to be region-specific, taking into account local H. pylori resistance to those drugs. ***Aim of the Study: The objective is to evaluate and compare the efficacy of treatment regimens for *H. pylori* infection. ***Methods*:** A retrospective cohort study will be conducted at the Gastroenterology department at King Hussein Medical Centre in The Royal Medical Services, Amman, Jordan. Electronic health records (Hakeem) will be accessed for data extraction. Inclusion criteria will be patients who were diagnosed with H. pylori infection and received one of the two prescribed eradication regimens. Regimen A consists of two doses of 1 g amoxicillin capsules and 40 mg esomeprazole capsules twice a day for 14 days, in addition to a 500 mg levofloxacin tablet once a day while regimen B consists of 500 mg clarithromycin tablets, 500 mg metronidazole tablets, and 40 mg esomeprazole capsules taken twice daily. Exclusion Criteria include patients with incomplete medical records or those with contraindications to standard eradication therapies. Version 24 of the Statistical Package for the Social Sciences (SPSS) will be used to code and analyse the data. ***Results*:** We enrolled 62 patients in the levofloxacin-based regimen and in the clarithromycin-based therapy distributed equally among the two study groups. The former was successful in 27 patients (43.5%) and the latter in 20 patients (32.3%), using chi-square test ($P < .05$). Regimen A had greater eradication rates than regimen B in the current investigation, with 87% and 64.5% eradication rates, respectively. ***Conclusion*:** A levofloxacin–amoxycillin-based triple therapy has been proved to be acceptably effective as second- or even third-line therapy.

Keywords: *H. pylori* eradication, Treatment regimens, Levofloxacin, Clarithromycin.

INTRODUCTION

Helicobacter pylori (H. pylori) is a stomach-infecting bacterium linked to several gastrointestinal illnesses like peptic ulcers and gastric cancer [1]. Eliminating H. pylori is critical in managing these conditions, and multiple eradication approaches have been developed over time [2]. Common infections worldwide include *Helicobacter pylori*, with an estimated 50% of the global population infected, rising to 80% in developing countries. H. pylori infection is linked to the development of gastritis, peptic ulcer diseases, and gastric cancer [3].

New research indicates that *Helicobacter pylori* infection affects an estimated 4.4 billion people globally, comprising more than half of the world's population. Significantly, H. pylori is believed to contribute to 89% of noncardia gastric adenocarcinomas (GCs), a particularly deadly form of cancer characterized by a mere 5-year relative survival rate of 32% [4].

Since its discovery in 1983 as a bacterium capable of colonizing the stomach, mounting evidence has linked H. pylori to various gastric ailments. These span from benign conditions like chronic gastritis, duodenal peptic ulcers, and gastric peptic ulcers, to more serious afflictions such as gastric cancer and gastric mucosa-associated lymphoid tissue (MALT) lymphoma. Over the past three decades, researchers have documented over 50 extragastric effects of H. pylori infection across multiple medical fields including cardiology, dermatology, endocrinology, gynecology and obstetrics, pneumology, neurology, odontology, ophthalmology, otorhinolaryngology, pediatrics, and hematology. This review focuses specifically on hematological manifestations [6]. H. pylori is a minute

organism, measuring between 0.5 to 1.0 μm in width and 2.5 to 5.0 μm in length, characterized by its spiral shape, high motility, and gram-negative rod structure. It possesses 4-6 unipolar sheathed flagella for movement [7]. The bacterium grows slowly in laboratory settings and necessitates specific media and a microaerophilic environment (5% O2, 10% CO2, and 85% N2) for optimal growth [6]. Notably, it produces abundant urease, a key enzyme that breaks down urea into carbon dioxide and ammonia. This process generates ammonium hydroxide in the presence of water, enabling H. pylori to counteract the acidity in its immediate surroundings [8].

Eradication Regimens

The Maastricht 2-2000 Consensus Report, which addresses the management of H. pylori, advocates for a primary care approach utilizing proton pump inhibitors/ranitidine bismuth citrate (RBC) alongside clarithromycin and amoxicillin as the initial treatment regimen [9]. If this therapy proves ineffective, the recommended second-line approach involves proton pump inhibitors, bismuth, metronidazole, and tetracycline administered for at least 7 days. In cases where bismuth is unavailable, an extended course of proton pump inhibitor-based triple therapy is advised. Referral to specialists is recommended for subsequent treatment failures [10].

Efficacy of Eradication Regimens

Triple therapy used to be the standard treatment for eradication of H. pylori, but it's become less effective over time because of growing antibiotic resistance, especially to clarithromycin. Recent studies show that triple therapy now has eradication rates between 70% and 85% [11]. As a better alternative, sequential therapy has been suggested and has shown higher success rates, particularly in areas where there's a lot of resistance to clarithromycin. With sequential therapy, eradication rates are reported to be around 80% to 90%. Concomitant therapy has also shown high success rates, similar to sequential therapy, and might be preferred because it's simpler to take [12]. Quadruple therapy, especially when combined with bismuth, is recommended as a backup option for eradicating H. pylori, particularly in cases with multiple antibiotic resistances. The success rates for quadruple therapy range from 75% to 85% [13]. Triple therapy used to be the standard treatment, but its effectiveness has decreased due to rising antibiotic resistance, especially to clarithromycin. Sequential therapy has been suggested as a better alternative and has shown higher success rates, particularly in areas with high clarithromycin resistance [14].

Factors Affecting Efficacy

Several factors can impact how well H. pylori treatments work, including antibiotic resistance, how well patients follow their prescribed treatments, and the presence of other gastrointestinal issues [15]. Antibiotic resistance, especially to clarithromycin and metronidazole, is a major concern and can greatly reduce the effectiveness of these treatments. Patient compliance is also crucial, as not following the treatment plan can lead to failure. Additionally, having other gastrointestinal diseases, like GERD, can influence both the choice and success of the treatment regimen [16]. The goal is to assess and compare how effective different treatments are for H. pylori infection.

METHODS

Study Design and Site

A retrospective observational study design was used to investigate the efficacy of *Helicobacter pylori* eradication regimens at the Gastroenterology department at King Hussein Medical Centre in The Royal Medical Services, Amman, Jordan.

Data Collection

We accessed electronic health records (Hakeem) to extract data. We obtained a de-identified set of records for all adults 18 years or older who tested positive for H. pylori through stool antigen testing (SAT), urea breath test (UBT), or positive immunoglobulin G (IgG) serology between October 2022 and December 2022. We gathered information on age, gender, primary disease symptoms, and the initial diagnostic test. Additionally, we checked whether the exclusion criteria were met. Participants were then randomly assigned to one of two H. pylori eradication regimens. Regimen A consisted of 1 g amoxicillin capsules and 40 mg esomeprazole capsules, both taken twice a day for 14 days, along with a 500 mg levofloxacin tablet taken once a day. Regimen B consisted of 500 mg clarithromycin tablets, 500 mg metronidazole tablets, and 40 mg esomeprazole capsules, all taken twice daily. Patients were instructed to report any potential side effects during their therapy. A follow-up assessment was conducted after 4 weeks, where information on symptom relief and drug side effects was collected.

Inclusion and Exclusion Criteria

We included patients who were diagnosed with H. pylori infection and had received one of the two prescribed treatment regimens. We excluded those with incomplete medical records or who had contraindications to the standard treatments. Once these criteria were met, patients were examined and enrolled in the study.

Sample Size

The study enrolled a convenient sample of sixty-two patients who had a confirmed diagnosis of *H. pylori* infection either *H. pylori*.

Ethical Considerations

The protocol of this study was approved by the ethics committee in the Royal Medical Services.

Statistical Analysis

The data were coded and analysed using the Statistical Package for the Social Sciences (SPSS)

version 24. The numerical variables were described as mean and standard deviation, while the categorical data were represented as frequencies and percentages. Independent samples *t*-test was used to compare the means of two samples. The chi-square test was used to test the significance of the association between the categorical variables. *p*-value < 0.05 was the criterion of statistical significance.

RESULTS

At the beginning of the study and again following a 4-week follow-up period, sixty-two patients with H. pylori infection underwent evaluations. With a range of 20 to 72 years, the average age was 42.5 years. Of these, thirty-four (54%) were women and 28 (46%) were men. The gender and age group distributions of the research participants are displayed in Table 1. The table shows that the majority of participants (46.8%) were in the 20–39 age range, followed by 37.1% in the 40–59 age range, and 1.6% in the 60–80 age range. Sixty-six percent of the participants were between the ages of sixty and eighty, and thirty-seven percent were between the ages of forty and sixty.

Table 1: Age and gender distribution of the study sample

Gender	**Frequency**	**Percentage (%)**
Male	28	46
Female	34	54
Age Group (year)	Frequency	Percentage
20-39	25	40.3
40-59	33	53.2
60-80	4	6.5

The distribution of important clinical factors in patients with *Helicobacter pylori* was examined in detail in Table 2. Within the study sample, 38 (61.2%) individuals reported experiencing epigastric pain or discomfort, making it the most common symptom. Stool antigen testing was utilised in 13% of the patients' initial diagnostic procedures. Additionally, the identical number of patients (31 in each group) received Regimen A and Regimen B. Of the participants, 22 (35.5%) reported nausea as the most common side effect, while 14 (22.5%) reported diarrhoea.

Table 2: Clinical characteristics of the study sample

Variables	***n* (%)**
Main symptom	
Abdominal pain or discomfort	38 (61.2)
Nausea or vomiting	24 (38.7)
Bloating or belching	21 (33.8)
Heartburn	23 (37)
Others: Loss of appetite, Weight loss	5 (8)
Initial diagnostic test	
Urea Breath Test	54 (87)
Stool antigen	8 (13)
Eradication Regimen	
Regimen A	31 (50)
Regimen B	31 (50)
Side effects	
Nausea	22 (35)
Diarrhea	14 (22)
Headache	9 (14.5)
Abdominal pain	7 (11.2)
Vomiting	3 (4)
Metallic Taste in the mouth	2 (3)
Follow up Test	
Urea Breath Test	55 (88.7)
Stool antigen	7 (11.29)
Follow up test result	
Negative	51 (82.3)
Positive	11 (17.7)
Total	62 (100)

Out of 51 patients (82.2%) who took the follow-up test, the majority (i.e., the total eradication rate) tested negative. The percentage of patients who received treatment who tested positive, however, was only 17.7%. Both H. pylori eradication regimens were randomly assigned to patients who tested positive for the infection at the beginning of the study. A total of 31 patients were compared in two equal groups as a result. The regiment B group's mean age is 44.11±11.11 years, while the regiment A group's mean age is 45.12±10.21 years, according to Table 3. The mean age difference was not statistically significant (p>0.05), and the ages of the participants were similar in both groups. The results also showed the gender breakdown of the two groups, with females outnumbering males in both groups. There is no significant difference in gender between the two groups (*p*>0.05).

Table 3: Age and gender distribution of the two study groups

Group	***Regimen A***	***Regimen B***	***P value***
Age	Mean±SD		
	45.12±10.21	44.11±11.11	0.612*
Gender	N (%)	N (%)	
Male	13 (19.3)	15 (22.5)	
Female	18 (29)	16 (25.8)	0.287**
Total	31 (100%)	31 (100%)	

* Independent samples *t*-test is used.

** Chi-square test is used.

Table 4 presents the results of comparing the two regimens (Regimen A and Regimen B) based on clinical parameters. The two regimens differed statistically significantly (p<0.05) for both the initial diagnostic test and the follow-up test. Compared to Regimen B, slightly more patients (34.5% vs. 35.4%, respectively) reported side effects from Regimen A. Statistical significance was not achieved (p>0.05) in the difference.

Table 4: Comparison of two regimens according to different clinical parameters

Groups	**Regimen A**	**Regimen B *p*-value**	***p*-value***
Initial diagnostic test			
Urea Breath Test	27(43.5)	29(46.7)	0.023
Stool antigen	4(6.4)	2 (3.2)	
Side Effects			
Experienced Side effects	4	8	
No side effects	27 (43.5)	*22(35.4)*	0.081
Follow-up test			
Urea Breath Test	30 (48.3)	26 (41.9)	0.0421
Stool antigen	1 (1.7)	5 (8.1)	
Follow-up test result			
Negative	30 (48.3)	26 (41.9)	0.032
Positive	1(1.7)	5 (8.1)	
Symptoms after treatment			
Unchanged	1 (1.7)	6 (9.6)	0.0178
Improved	3 (4.8)	5 (8.1)	
Completely relieved	27 (43.5)	20 (32.3)	
Total	31(100)	31(100)	

* Chi-square test is used.

It was found from the results that Regimen A had a significantly (p<0.05) higher rate of successful H. pylori eradication than Regimen B. For example, 87% of patients in Regimen A had successful H. pylori eradication based on negative results from follow-up tests; in contrast, only 64.5% of patients in Regimen B experienced the same result. At last, there was a significant statistical difference (p<0.05) in the degree of symptom relief following therapy between the two regimens. The percentage of patients in Regimen B (9.6%) compared to Regimen A (1.7%) who reported no change in symptoms following therapy.

DISCUSSION

The treatment of peptic ulcer disease has been transformed by *Helicobacter pylori* eradication procedures. The challenge lies in selecting appropriate candidates for eradication therapy, since the goal of testing is to eliminate all potential beneficiaries [17]. The results of several upper gastrointestinal tract disorders are impacted by the inability to completely eradicate H.

pylori. Clinicians are therefore faced with a difficult situation when antibiotic resistance affects H. pylori eradication therapy. Safe, simple, affordable, and effective (eradication rate > 90%) would characterise the perfect H. pylori eradication therapy. Currently, the majority of the world's regions have eradication rates of less than 80% for triple antibiotic therapy, which is the gold standard. Since most of the study participants were drawn from an outpatient clinic and were seeking medical advice regarding their problems, the majority of them experienced symptoms even though the vast majority of H. pylori infections are asymptomatic [18]. 61.2% and 38.7% of the patients, respectively, reported having abdominal pain and nausea.

The most common complaints among participants in a Zha *et al.,* metanalysis were nausea and stomach pain, which further confirmed this. The stool antigen test and urea breath test were used as follow-up measures to determine successful eradication in our study sample in addition to serving as diagnostic tools [19]. Because of their high sensitivity and specificity (both over 90%), availability, and non-invasiveness, both procedures are advised in clinical practice. As follow-up and diagnosis tests, both are trustworthy.

Each of the several diagnostic techniques for identifying H. pylori infection has pros and cons of its own. None of them can be regarded as the gold standard because of their low sensitivity or specificity [20]. Nonetheless, multitest combinations, such as the urease enzyme production test, microscopy, bacterial isolation, and polymerase chain reaction (PCR), typically result in a diagnosis that is highly satisfactory. These techniques are costly, invasive, and limited to tertiary level laboratories [21]. Numerous non-invasive tests have been developed to diagnose H. pylori because of the drawbacks of invasive procedures. This study found that patients on regimen B experienced adverse effects more frequently, albeit not significantly. Because of the unbearable side effects of regimen B, two patients stopped their treatment. In another study, this was also noted, with 2.5% of the study population quitting treatment before the planned duration [22]. Both metronidazole and clarithromycin may have negative effects on the gastrointestinal tract, particularly when taken together. Additionally, they impart a metallic taste due to their elimination in saliva through diffusion or carrier-mediated transport. 90% success rate is considered to be the minimum for the optimal H. pylori therapy [23].

In this study, the results showed that the overall *H. pylori* eradication rate was 75.8%, which was somewhat lower than the anticipated aim. A triple therapy regimen consisting of levofloxacin and amoxycillin has been suggested in recent years as a first-line or rescue therapy to treat H. pylori infection [24]. Additionally, two large meta-analyses demonstrated that this therapy had a substantially higher success rate than the quadruple regimen and a lower frequency of side effects and adverse effects that required therapy discontinuation. Additionally, it has been demonstrated that this treatment plan is more effective than rifabutin plus amoxycillin. Nonetheless, there is a growing incidence of primary levofloxacin resistance [25]. The quinolone treatment of urinary or pulmonary infections is likely the cause of this rise in bacterial resistance to levofloxacin. Levofloxacin resistance was, in fact, considerably higher in elderly patients than in younger ones, as we recently discovered. Testing the effectiveness of alternative rescue regimens, such as a higher dose of levofloxacin, may be beneficial in light of these observations. Although the data do not appear promising, studies have used 500 mg of levofloxacin twice daily [26].

Resistance to metronidazole or clarithromycin is the reason for regimen B's lower eradication rates. To prevent the development of combined strain resistance and to "save" either metronidazole or clarithromycin for a later attempt, it is advised against combining these drugs in first-line eradication schemes. In fact, the Maastricht 2-2000 Consensus Report recommends the use of nitroimidazoles in second-line treatments, as well as the combination of metronidazole, amoxicillin, and a proton pump inhibitor in triple therapy or bismuth salt, tetracycline, and a proton pump inhibitor (or ranitidine) in quadruple regimen [27]. The utilisation of triple therapies in compliance with the Maastricht criteria and the homogeneity of the two treatment therapy lines employed were the study's strengths.

Study Limitations

Numerous limitations of the study include a small sample size, patients who do not adhere to their prescribed treatment plans, and a loss of follow-up following the initial diagnosis and course of treatment.

CONCLUSION

Levofloxacin based regimen (regimen A) is more effective than regimen B in eradicating *H-Pylori* infection.

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