



Levofloxacin-Based Regimen Versus Bismuth Quadruple Regimen for *Helicobacter pylori* Eradication in Kurdistan Region, Iraq

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Abstract

Background: *Helicobacter pylori* infection is associated with peptic ulcer diseases and gastric adenocarcinoma. Accordingly, the aim of this study was to assess the efficiency of tetracycline quadruple therapy versus levofloxacin-based regimen (LBR) for the eradication of *H. pylori*.

Methods: To this end, 197 subjects with *H. pylori* infection were recruited in this randomized clinical study in Kurdistan region, Iraq between October 2018 and May 2019 and randomly divided into 2 groups. The LBR group received levofloxacin 500 mg one time per day, amoxicillin 1000 mg two times per day, and omeprazole 20 mg two times per day for two weeks. In addition, the tetracycline-metronidazole-bismuth (TMB) group received bismuth subcitrate 140 mg, metronidazole 125 mg, and tetracycline 125 mg plus omeprazole 20 mg twice per day for 10 days. Finally, 28 days after the completion of the treatment course, the eradication of *H. pylori* was evaluated by the ¹⁴C urease breath test.

Results: The total eradication rate of *H. pylori* infection was 149/197 (75.6%). Although the success eradication rate in the LBR regimen was 70/112 (62.5%), the eradication success rate was 79/85 (92.9%) in the TMB regimen ($P = 0.001$, odds ratio = 7.9, confidence interval = 3.17-19.7). Finally, gender and age represented on the effect of the eradication rate.

Conclusions: In general, the bismuth-based regimen could eradicate a high rate of *H. pylori* infection. Therefore, this regimen can be used to overcome treatment failure in areas with a high prevalence of antibiotics resistance.

Keywords: *Helicobacter pylori*, Levofloxacin, Iraq, Bismuth, Ampicillin

Background

Helicobacter pylori is a gram-negative bacterium that infects half of the populations worldwide (1). In addition, it can cause gastric and duodenal ulcer and predispose to individuals gastric adenocarcinoma (2). Further, *H. pylori* infection is persistent while asymptomatic in most individuals. However, whenever the microorganism is diagnosed, it should be eradicated with the administration of antibiotics and the proton pump inhibitor (3). The determinants of the successful eradication of this microorganism include drug efficacy, bacterial resistance, and the patient's compliance. However, antibiotic resistance is considered as the most common cause of eradication failure and varies in different countries and within different regions of the same country (3), challenging *H. pylori* eradication and *H. pylori*-related complication treatment (3). Different variables may play an important role in the treatment failure of *H. pylori*, including patient characteristics, underlying disease

presence, and environmental factors.

The recommended course of the treatment includes the combination of amoxicillin plus clarithromycin with a proton pump inhibitor in the majority of international guidelines for the eradication of *H. pylori* (4, 5). The bismuth-containing quadruple or levofloxacin-based regimen (LBR) is advised for *H. pylori* eradication if the clarithromycin resistance rate is more than 20%. According to previous research, the clarithromycin resistance rate is 20% in Iraq (6). Nonetheless, no clinical trial study, to the best of our knowledge, has so far investigated the eradication success rates of bismuth-containing quadruple or LBR in this country.

Objectives

The aim of our project was to evaluate the effectiveness of levofloxacin versus bismuth-based courses for the eradication of *H. pylori*.

Materials and Methods**Study Design**

This randomized clinical trial was conducted recruiting patients visiting the gastroenterology and infectious disease unit in Kurdistan Region, Iraq from October 2018 to May 2019. The status of infection was proven by performing a slide urease reaction during endoscopy or by the urea breath test (UBT). The inclusion criteria for recruiting subjects were *H. pylori* positivity, adults older than 18 years, and agreement for recruitment. On the contrary, patients with prior history of antibiotics use and those showing reluctance were excluded from the study.

Intervention

The recruited patients were randomly divided into two groups and received the following medication;

1. LBR: This regimen included levofloxacin 500 mg (Zynova) once daily and amoxicillin 1 g (Atabay ilaç) twice daily. Both medications were advised to be taken after the meal. Furthermore, omeprazole 20 mg (Zynova) was given twice daily before the meal, and the regimen was given for 14 days.
2. Tetracycline-metronidazole-bismuth (TMB): PYLERA capsules (Allergan Pharmaceuticals International Ltd.) consisting of bismuth subcitrate 140 mg, metronidazole 125 mg, and tetracycline 125 mg were used and given with omeprazole 20 mg (Zynova) twice per day.

Four weeks after the completion of the treatment course, patients were requested to conduct a ¹⁴C-UBT.

Statistical Analysis

The statistical analysis was performed using the Minitab 17 statistical software. The eradication rate was calculated in each group as the percentage of subjects with a negative UBT among subjects who completed the course of treatment regimens. A chi-square test was applied to compare dichotomous variable data, and binomial regression analyses were used for numerical data. A $P < 0.05$ was considered statistically significant.

Results**Patients**

In general, the present clinical trial study included 197 subjects who visited the Gastrointestinal Disease Center at Azadi Teaching Hospital. Based on the obtained data, 89% of patients presented epigastric pain. In addition, 4 of the patients showed symptoms such as nausea and vomiting. Moreover, 12 and 3 patients had postprandial distress and melena, respectively. Additionally, the average age of the participants was 32.4 ± 13.7 years old and 118/197 (59.9%) of patients were females. The status of infection was proven by performing a slide urease reaction during endoscopy or by UBT. All subjects then were evaluated using the 14 carbon UBT after treatment

conclusion.

***Helicobacter pylori* Eradication**

In total, the *H. pylori* eradication rate was 149/197 (75.6%). Based on the results, the eradication success rate was 70/112 (62.5%) and 79/85 (92.9%) in LBR and TMB regimens, respectively, with an odds ratio (OR) of 7.9 and a confidence interval (CI) of 3.17-19.7 ($P = 0.001$). Then, age and gender were studied in terms of their effect on eradication. The overall efficiency of the regimens was statistically not significant in terms of age (success: 45.5 ± 12.6 vs. failure: 34.2 ± 11.4 , $P = 0.19$, OR = 0.981-1.01). The results indicated that gender has no effect on the eradication rate (males: 37/94, 39.36% vs. females: 22/48, 45.83%, $P = 0.35$, OR = 0.732, CI = 0.38-1.412). Conversely, a significant association was found between the age and the eradication success rate within the TMB group (success: 38.8 ± 13.1 vs. 47.7 ± 13.1 , $P = 0.017$, OR = 0.92, CI = 0.856-0.987). However, no association was observed between the eradication success rate and gender (success: males = 30/79, 37.97% vs. failure: 3/6, 50%, $P = 0.5$, OR = 0.61, CI = 0.0116-3.231). Moreover, there was no significant association between the eradication success rate and age within the LBR group (45.5 ± 12.5 vs. 34.2 ± 11.4 , $P = 0.26$, OR = 0.98, CI = 0.95-1.01). Eventually, no relationship was reported between the eradication success rate and gender (males: 28/71 (39.4%) vs. females: 19/42, 45.2%, $P = 0.48$, OR = 0.76, IC = 0.35-1.65).

Discussion

Several studies have thoroughly evaluated *H. pylori* infection in Iraq and reported it as a common infection (7-10). The eradication of *H. pylori* significantly improves the clinical outcome of the infected subjects. However, the eradication failure rate has been increasing progressively in developing countries such as in Iraq because of the increased resistance to antimicrobial agents. Therefore, choosing the correct antibiotics regimen for the eradication of *H. pylori* is challenging, and antibiotic sensitivity and eradication success rates should be updated continuously. To the best of our knowledge, no clinical trial study has so far focused on the eradication successful rate in our region. Therefore, the present study evaluated the success rate of two antibiotics regimens. The results showed that the eradication success rate of TMB was 92.9%, which was higher than that of the LBR regimen (62.5%). Previous studies performed in Iraq used molecular techniques and conventional methods to investigate *H. pylori* sensitivity to antibiotics and reported that clarithromycin and levofloxacin resistance rates were 20% and 4%, respectively (6, 11).

In our clinical trial, the *H. pylori* eradication success rate of the TMB regimen was 92.9%, which is in line with the results of previous trials (12, 13). In contrast,

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Luther et al showed a lower eradication rate (78%) with the TMB course (14). In a study recruiting patients from Egypt and Saudi, the eradication rate of LBR was 90.6% (15). In another study conducted in Iran, the eradication success rate of the LBR was 75% (16). In addition, the *H. pylori* eradication rate associated with the LBR was 83% in a similar study conducted in China (17). Based on the findings of another study recruiting patients with peptic ulcer perforation, the levofloxacin-containing regimen was successful in the eradication of the microorganism in 87% of the recruited subjects (18).

Different factors may play a role in *H. pylori* eradication including age and gender. In our clinical study, these two parameters did not influence overall treatment outcomes. The findings of one study demonstrated significant differences between treatment failure and age group (19). In another study performed in Korea, female gender was found to be a significant factor associated with treatment failure (20) while age had no effect on *H. pylori* eradication rates. The results of a similar study conducted in China represented that age and gender exerted no significant effect on treatment success rates (21). In Greece, gender, age, smoking, and gastric ulcer disease showed no significant effect on the eradication rate of *H. pylori* (22). In this study and within the TMB group, the eradication rate was higher in younger subjects, which is difficult to explain and thus more studies are required to discover this issue.

In conclusion, our study is important because it helps choosing the correct antibiotics regimen for the eradication of *H. pylori*. Based on the obtained data, the TMB regimen achieved a high rate of *H. pylori* infection eradication and was not influenced by patients' age and gender. Therefore, this regimen can be used to overcome treatment failure in areas with a high prevalence of antibiotics resistance.

Conflict of Interests

The authors declare that there is no conflict of interests.

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Ethical Statement

The study proposal was approved by the Ethics Committee of the College of Medicine, University of Zakho, Kurdistan Region of Iraq and the Kurdistan Board for Medical Specialties. Furthermore, the consent of the agreement was taken from all participants before study initiation. The clinical trial was registered under number IRCT20191010045053N1 in the Iranian Registry of Clinical Trials website.

Authors' Contribution

All authors equally contributed to designing the study, analyzing data, and writing the paper. Further, all authors approved the final draft and the authors' order.

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