OPEN ACCESS

Research Paper

Efficacy and Tolerability of Levofloxacin Versus Clarithromycin Based First Line Triple Therapy for Eradication of Helicobacter Pylori Infection: A Comparative Study

Zainab H. Ghafil [1], Nawal Mehdi Alkhalidi[2], Mustafa G. Alabbassi[3]

ABSTRACT:

BACKGROUND:

The increasing prevalence of antibiotic-resistant strains of Helicobacter pylori contributed to reduce the effectiveness of the first-line standard therapy. Consequently, it is necessary to identify alternative regimens that provide better or comparable efficacy and safety.

OBJECTIVE:

Compare the efficacy and tolerability of 10-days levofloxacin-based triple therapy versus clarithromycin-based triple therapy as a first-line eradication regimen of *Helicobacter pylori.*

PATIENTS AND METHODS:

This is an open label observational comparative study. A total of 100 patients with *Helicobacter pylori* infection were selected; 50 patients were taking 10-day levofloxacin-based triple therapy and the other 50 patients were on 14-day clarithromycin based triple therapy. Eradication rate and adverse effects were evaluated.

RESULTS:

Helicobacter pylori eradication rates were: levofloxacin group 74%, and clarithromycin group 54%. There were a statistically significant differences in the efficacy between the two regimens (*p value* < 0.05). In addition, no relevant differences in adverse effects were demonstrated. There was no significant relationship between *Helicobacter pylori* eradication and gender, age, or smoking.

CONCLUSION:

This study showed that levofloxacin-based triple therapy is significantly more effective than clarithromycin-based therapy in the eradication of *Helicobacter pylori* infection but it does not reach the recommended eradication threshold.

KEYWORDS: Antibiotic resistance, Clarithromycin, Eradication rate, Helicobacter pylori, Levofloxacin.

[1](B pharm, FIBMS Clinical Pharmacy),Children Welfare Teaching Hospital, Iraq. Hematology-oncology department. 10052 Baghdad, Iraq;
[2](M.B.ch.B C.A.B.M. FICMS (GE & H)),Gastroenterology & Hepatology Teaching Hospital, Medical City -,Ministry of Health and Environment, Baghdad, Iraq.
[3](Prof. Pharmacology and Toxicology),University of AL-Kafeel-College of Pharmacy, Iraq.

Iraqi Postgraduate Medical Journal, 2025; Vol. 24(2): 212-217
DOI: 10.52573/ipmj.2025.145529 Received: March 28 , 2024, Accepted: October 20 , 2024

INTRODUCTION:

Infection with *Helicobacter pylori (H. pylori*) occurs worldwide, initial acquisition of *H. pylori* occurs primarily during childhood and can persist throughout individual life without antibiotic treatment[(1)]. An overall global *H. pylori* prevalence declined in the period between 2011 and 2022 and it has a lower prevalence in the developed countries than in the developing countries[(2)]. It is known to be a major responsibility for a significant number of gastric pathologies and extragastric diseases[(3)]. All individuals who test positive for an active *H. pylori* infection should be prescribed therapy for the infection[(4)]. In the early 1990s, triple therapy was the gold standard for treating H. pylori infections, with success rates ranging from >80% to >90% [(5)]. The Eastern Mediterranean and Western Pacific regions had ≥30% of H pylori resistant to clarithromycin, according to a 2018 systematic review and meta-analysis[(6)]. In the united states, a systematic review and meta-analysis between 2011 and 2021 revealed that the rate of resistance to clarithromycin 31.5% and that to levofloxacin was 37,6%[(7)]. In Europe H. pylori resistance of clarithromycin was 25%, levofloxacin 20% and dual resistance of both antibiotics were 13%[(8)]. In Turkey, the clarithromycin resistance rate ranged from 16.4%

to 48.2%[9] indicating that the global resistance rate of H. pylori has reached a worrisome levels worldwide. Levofloxacin-based triple therapy has been adopted as an alternative second and third-line therapy to eradicate H. pylori when clarithromycin resistance rates are higher than 15%. This regimen consists of 500 mg of levofloxacin once daily, PPI twice daily, and 1000 mg of amoxicillin twice daily[10,11].

The study aims to examine the effectiveness and tolerance of a10-day levofloxacin-containing triple therapy versus a similar regimen incorporating clarithromycin as a first-line treatment for Helicobacter pylori eradication.

PATIENTS AND METHODS:

Study design and patients

This is an open label observational prospective comparative study conducted on patients who visited the gastroenterology outpatient clinic of the Gastroenterology and Hepatology Teaching Hospital | Medical City complex from March 2020 to November 2020.

Inclusion criteria: Patients from both genders with age 18 and over, who are diagnosed with *H. pylori* infection by urea breath test that had not been treated previously. **Exclusion criteria:** Patients who have Liver or renal diseases or history of *H. pylori* eradication, using PPI less than 2 weeks or Antibiotics within 4 weeks before the test. Previously experienced an allergic response to or contraindication to antibiotics (nitroimidazole, amoxicillin, clarithromycin, and levofloxacin) and PPI.

Intervention

A 100 patients sample with *H. pylori* infection was selected after eligibility to inclusion and exclusion criteria. They were allocated into two groups (50 patients in each group), the first group is the clarithromycin group - clarithromycin 500 mg, b.i.d, lansoprazole 30mg bid tinidazole 500 mg, b.i.d for 14 days-, second group is the levofloxacin group - levofloxacin 500mg once daily, amoxicilin 1000 mg bid, esomeprazole 20 mg bid for 10 days. Patients were educated on how to take the medications appropriately and informed to record any adverse effects of the drugs, the patients were followed up by a phone call after regimen completion and, four weeks following the end of therapy, the response to the treatment was assessed. Patients were instructed not to take any antibiotics for four weeks or PPIs for two weeks prior to retesting for H. pylori using a stool antigen test or urea breath test, and if any was taken the test should be delayed. The study was approved by the Iraqi board for medical Specializations.

Statistical analysis:

Microsoft Excel software was used to enter and evaluate all patient data. Version 24 of the Statistical Package for Social Sciences (SPSS) was then used to import the data. Frequencies are presented as percentages and descriptive statistics are presented as mean ± standard deviation.

RESULTS:

For this study, one hundred patients were included. Regarding age and gender differences in the demographic characteristics of individuals receiving levofloxacin vs those receiving clarithromycin triple treatment were statistically not significant (Table1).

Table 1: Demographic features of the enrolled patients (n=100).

parameter	Clarithromycin group	Levofloxacin group	*p*-value
Age	37.9±13.4	36.62±12.59	0.53
Gender (%) Male Female	 20(40%) 30(60%)	 19(38%) 31(62%)	 0.838
Comorbid disease Hypertension Diabetes mellitus Hypothyroidism Crohn's disease	 5 (10%) 2 (4%) 0 (0.0%) 1 (2%)	 2 (4%) 2 (4%) 1 (2%) 0 (0.0%)	 0.37
Smoking	8 (16%)	13 (26%)	0.22
Alcohol	0 (0.0%)	1 (2%)	0.315

After completion of the treatment regimen in both groups, 93 patients were evaluated using the 14 carbon urea breath test, and seven patients were assessed by stool antigen test as the UBT kit was unavailable for a while. *H. pylori* eradication rates were fifty-four percent (54%) in the clarithromycin group and seventy-four percent (74%) in the levofloxacin group. The levofloxacin triple therapy group had a significantly greater rate of H. pylori eradication than the clarithromycin triple therapy group (P=0.037) (Table 2).

Table 2: Response to treatment of H. pylori infection.

Result of eradication	Clarithromycin group	Levofloxacin group	*p*-value
Negative test result	27 (54%)	37 (74%)	(0.037)
Positive test result	23 (46%)	13 (26%)	

Only 8 (16%) of the 12 cases (24%) in the levofloxacin group and 12 cases (24%) in the clarithromycin group had treatment-related side effects that were evident in relation to the regimen (Table 3). Of the total patient sample, 36% had positive cases, with 21% of those cases being female and 15% being male (Table 4).

Table 3: Adverse effect of the treatment of the studied groups.

parameter	Clarithromycin group	Levofloxacin group	Total %	*p*-value
Adverse effects	Yes: 12 (24 %) No : 38 (76 %)	Yes: 8 (16 %) No : 42 (84%)	Yes: 20 No: 80	0.317
Nausea	7	4	11	
Taste disturbance	5	1	6	
Abdominal pain	2	0	2	
Headache	0	3	3	
Diarrhea	2	1	3	

Table 4: Relation between multiple factors on *H. pylori* eradication outcomes in the whole patients sample.

Factor	Success rate	Failure rate	*p*-value
Age (mean±SD) 37.08 ± 12.97	37.06 ± 12.91	37.1 ± 13.25	0.638
Gender Male Female	 24 40	 15 21	0.682
Smoking	12	9	0.461

DISCUSSION:

The effectiveness of conventional H. pylori therapies has declined as a result of the rising prevalence of antibiotic-resistant forms of the infection. It is therefore essential to find substitute regimens that have equivalent or superior safety and efficacy. In Iraq, a study has been carried out to estimate the prevalence of mutations causing clarithromycin and fluoroquinolone resistance. It was found that 16.2% of the studied *H. pylori* strains were clarithromycin resistant and 4% has been reported to be levofloxacin resistant. The validity of these results requires confirmation through culture and sensitivity testing. If shown to be genuine, triple therapy with clarithromycin should no longer be considered for the eradication of H. pylori due to the significant failure rate [12]. The mean age of the individuals studied was (37.08±12.97) years which appear that majority of patients are young below 40 years old; this may be due to the fact that this study looks for patients who have never treated previously for *H. pylori* infection so, elderly individuals with an eradication history have been excluded. There were no significant differences (p value 0.638) between the two groups based on the mean age of infected patients, which was 37.9±13.4 years in the clarithromycin-based triple therapy group and 36.62±12.59 years in the levofloxacin-based triple therapy group. According to the majority of examined research, the prevalence of *H. pylori* increased with age, three studies carried out in Iraq supplied data relating to the frequency of infection with *H. pylori* according to various age groups, showed that the prevalence of *H. pylori* infection was increased markedly with age[13,15]. Curado *Et al* observed that the prevalence of *H. pylori* among adults was 69.26% (CI 95%: 61.54; 76.99) which were high in Latin American countries in comparison with other countries in the world[16]. The available data were not sufficient enough to Analyze the likelihood of *H. Pylori* infection with time for various age groups. Female gender seems to be more predominant than the male gender, with female to male ratio of 1.56:1

however, according to sex, there were no statistically significant differences. which is in agreement with other studies[17], while in Erbil-Iraq, there was a significant correlation ($p < 0.05$) between the gender and *H. pylori* infection rate (male 43.75% and female 59.72%), with the greater rate of *H. pylori* infection in female patients compared to male research participants[13].

According to the study, 54% of *H. pylori* cases were eradicated after using clarithromycin-based first-line therapy and 74% for levofloxacin-based first-line therapy. These variations suggest that levofloxacin-based triple therapy operates better to eradicate *H. pylori* infection than clarithromycin-based therapy, and it is statistically significant (p value= 0.037). These results of eradication are greater than that found in Syria, a study done by Khalid *Et al*. where clarithromycin based regimen cure rate was 32.5%, and was 27.5% in the levofloxacin based regimen[18]. The results in this study are agreeing to a prior Iranian study that examined the effectiveness of a 14-day triple treatment, clarithromycin-based versus levofloxacin-based therapy with a success rate of 51.7% and 75% respectively[19]. The low efficacy of these regimens can be explained by the regional pattern of bacterial resistance in the same country. In an earlier study conducted by Mohammed, S. A., *Et al*. on 192 patients in the region of Iraqi Kurdistan, the rates of *H. pylori* eradication were 81.25% in the regimen based on clarithromycin and 81.6% in the regimen based on levofloxacin[20]. Other studies conducted in a different region in Iran revealed fluoroquinolone containing regimens, used as H. pylori second-line therapeutics, had eradication rates of 86.7% and 78.3% in the group receiving bismuth-based quadruple therapy[21]. In the present study, smoking does not influence eradication outcomes (pvalue > 0.461), this result agreed with other Studies[20,22] while Itskoviz D *Et al*. found that smoking was significantly increase the likelihood eradication failure of *H. pylori* infection[23].

Overall, in the current trial, 24% of patients in the clarithromycin group and 18% in the levofloxacin group experienced medication adverse effects; nevertheless, there was not a statistically significant disparity in the safety of the two groups (P value=0.317), these findings are compatible with other studies[17,24,25]. Adverse effects were ranged from mild to moderate in severity. Their incidence in clarithromycin group versus levofloxacin group of taste disturbance was (10% vs 2%), diarrhoea (4% vs 2%), headache (0% vs 6%), abdominal pain (4% vs 0%), and nausea (14% vs 8%). Although the non-significant differences in adverse effects between clarithromycin and levofloxacin regimens observed in this study, the levofloxacin-containing regimen appears to be more tolerated than clarithromycin, primarily because there are less reports of nausea and taste disturbance.

The study illustrates that the eradication rate of the levofloxacin based regimen was better than that of the standard clarithromycin-based triple therapy, but the Maastricht and other consensus recommendations for *H. pylori* eradication support the use of regimens with 80% cure rates or more[5,26]; although it reaches statistical significance in this study, both regimens were nevertheless not within these recommendations. Unfortunately, the lack of antimicrobial susceptibility testing of *H. pylori* prevents the clinicians from choosing the appropriate antibiotics tailored according to the microbiological data. There is a great concern about increasing this resistance phenomenon as a result of unnecessary and irrational antibiotic use which could lead to a significant reduction in the efficacy of the levofloxacin-based regimens.

In conclusion, this study found that clarithromycin triple therapy was not effective to be used as a first-line regimen, and even though levofloxacin triple therapy cure rate was superior compared to standard therapy but it does not reach the eradication threshold of 80-90%, thus it is advisable to determine the prevalence of antibiotic resistance so, the choice of treatment could be guided by the regional and patient-specific antimicrobial resistance pattern.

ACKNOWLEDGMENTS:

The authors thank Iraqi Board for Medical Specialties and the Gastroenterology and Hepatology Teaching Hospital | Medical City complex for supporting the project.

REFERENCE:

1. Kaiyu Y, Yuqing L, Xuedong Z. Overview of researches for *Helicobacter pylori* in oral cavity and stomach. West China Journal of Stomatology. 2014;32. doi: 10.7518/hxkq.2014.03.025.
2. Li Y, Choi H, Leung K, Jiang F, Graham DY, Leung WK. Global prevalence of Helicobacter pylori infection between 1980 and 2022: a systematic review and meta-analysis. The Lancet Gastroenterology & Hepatology. 2023;8:553-64.
3. Tsay F-W, Hsu P-I. *H. pylori* infection and extra-gastroduodenal diseases. Journal of biomedical science. 2018;25:1-8. doi: 10.1186/s12929-018-0469-6.

4. De Francesco V, Bellesia A, Ridola L, Manta R, Zullo A. First-line therapies for *Helicobacter pylori* eradication: a critical reappraisal of updated guidelines. Annals of Gastroenterology. 2017;30:373. doi: 10.20524/aog.2017.0166.
5. Malfertheiner P, Megraud F, O'morain C, Gisbert J, Kuipers E, Axon A, *et al*. Management of *Helicobacter pylori* infection—the Maastricht V/Florence consensus report. Gut. 2017;66:6-30. doi: 10.1136/gutjnl-2016-312288.
6. Savoldi A, Carrara E, Graham DY, Conti M, Tacconelli E. Prevalence of antibiotic resistance in Helicobacter pylori: a systematic review and meta-analysis in World Health Organization regions. Gastroenterology. 2018;155:1372-82.
7. Ho JJ, Navarro M, Sawyer K, Elfanagely Y, Moss SF. Helicobacter pylori antibiotic resistance in the United States between 2011 and 2021: a systematic review and meta-analysis. The American Journal of Gastroenterology. 2022;117:1221-30.
8. Bujanda L, Nyssen OP, Vaira D, Saracino IM, Fiorini G, Lerang F, Georgopoulos S, Tepes B, Heluwaert F, Gasbarrini A, Rokkas T. Antibiotic resistance prevalence and trends in patients infected with Helicobacter pylori in the period 2013–2020: Results of the European Registry on H. pylori Management (Hp-EuReg). Antibiotics. 2021;10:1058.
9. Kocazeybek B, Tokman HB. Prevalence of primary antimicrobial resistance of *H. pylori* in Turkey: a systematic review. Helicobacter. 2016;21:251-60. doi: 10.1111/hel.12272.
10. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG clinical guideline: treatment of *Helicobacter pylori* infection. American Journal of Gastroenterology. 2017;112:212-39. doi:10.1038/s41395-018-0132-6.
11. Morcillo Muñoz J, Otero Regino W, Gómez Zuleta M. How can *Helicobacter pylori* eradication therapies be improved? Revista Colombiana de Gastroenterologia. 2018;33:437-47.
12. Hussein N, Tunjel I, Majed H, Yousif S, Aswad S, Assafi M. Duodenal ulcer promoting gene 1(dupA1) is associated with A2147G clarithromycin-resistance mutation but not interleukin-8 secretion from gastric mucosa in Iraqi patients. New microbes and new infections. 2015;6:5-10. doi: 10.1016/j.nmni.2015.02.005.
13. Majeed PD, KJ K. Seroprevalence of *Helicobacter Pylori* Infection among Patients with Gastroduodenal Disorders in Erbil City. Diyala Journal of Medicine. 2020;18:91-101. doi.org/10.26505/DJM.18014880818.
14. Al-Jubori SS, Al_Kademy IM, Ali MR, Ali ASM. Occurrence of *Helicobacter pylori* among Iraqi patients with suspected gastric ulcer: histopatological study for gastric mucosal biopsies. Advances in Environmental Biology. 2016;10:224-31.
15. Hussein NR, Robinson K, Atherton JC. A study of age-specific *Helicobacter pylori* seropositivity rates in Iraq. Helicobacter. 2008;13:306-7. doi: 10.1111/j.1523-5378.2008.00618.
16. Curado MP, de Oliveira MM, de Araújo Fagundes M. Prevalence of *Helicobacter pylori* infection in Latin America and the Caribbean populations: A systematic review and meta-analysis. Cancer epidemiology. 2019;60:141-8. doi: 10.1016/j.canep.2019.04.003.
17. Elantouny NG, Abo Bakr AA, EL-Sokkary RH, Elshahat YE. Levofloxacin versus Clarithromycin-based Therapy for Eradication of *Helicobacter Pylori* Infection: A Comparative Study. Zagazig University Medical Journal. 2019;25:500-7. doi: 10.21608/zumj.2019.8141.10510.
18. Cheha KM, Dib SOA, Alhalabi MM. Pilot study: comparing efficacy of 14-day triple therapy Clarithromycin versus levofloxacin on eradication of *Helicobacter pylori* infection in Syrian population single-center experience. Avicenna journal of medicine. 2018;8:14-17. doi: 10.4103/ajm.AJM_70_17.
19. Haji-Aghamohammadi AA, Bastani A, Miroliaee A, Oveisi S, Safarnezhad S. Comparison of levofloxacin versus clarithromycin efficacy in the eradication of *Helicobacter pylori* infection. Caspian journal of internal medicine. 2016;7:267.
20. Mohammed SA, Al-lela OQ, Hussein NR, Hajany RS, Alduhoky LS. Clarithromycin versus Levofloxacin-Based Regimens for *Helicobacter Pylori* Eradication in the Kurdistan Region of Iraq: A Randomized Clinical Trial. Gastroenterology Insights. 2019;10:5-9. doi.org/10.4081/gi.2019.8256.
21. Seyyedmajidi M, Abbasi L, Seyedmajidi S, Hosseini SA, Ahmadi A, Hajiebrahimi S, *et al*. Levofloxacin-containing triple therapy versus bismuth-based quadruple therapy as regimens for second line anti-*Helicobacter pylori*. Caspian journal of internal medicine. 2019;10:211. doi: 10.22088/cjim.10.2.211.
22. Aksoy EK, Sapmaz FP, Göktaş Z, Uzman M, Nazlıgül Y. Comparison of *helicobacter pylori* eradication rates of 2-week

levofloxacin-containing triple therapy, levofloxacin-containing bismuth quadruple therapy, and standard bismuth quadruple therapy as a first-line regimen. Medical Principles and Practice. 2017;26:523-9. doi: 10.1159/000484930.

23. Itskoviz D, Boltin D, Leibovitzh H, Perets TT, Comaneshter D, Cohen A, Niv Y, Levi Z. Smoking increases the likelihood of *Helicobacter pylori* treatment failure. Digestive and Liver Disease. 2017;49:764-8. doi:10.1016/j.dld.2017.03.010.

24. Cuadrado-Lavín A, Salcines-Caviedes JR, Carrascosa MF, Dierssen-Sotos T, Cobo M, Campos MR, *et al*. Levofloxacin versus clarithromycin in a 10 day triple therapy regimen for first-line *Helicobacter pylori* eradication: a single-blind randomized clinical trial. Journal of Antimicrobial Chemotherapy. 2012;67:2254-9. doi.org/10.1093/jac/dks209.

25. Peedikayil MC, AlSohaibani FI, Alkhenizan AH. Levofloxacin-based first-line therapy versus standard first-line therapy for *Helicobacter pylori* eradication: meta-analysis of randomized controlled trials. PLoS One. 2014;9:e85620. doi10.1371/journal.pone.0085620.

26. Fallone CA, Chiba N, van Zanten SV, Fischbach L, Gisbert JP, Hunt RH, et al. The Toronto consensus for the treatment of Helicobacter pylori infection in adults. Gastroenterology. 2016; 151:51-69 . e14. doi: 10.1053/j.gastro.2016.04.006.