ORIGINAL ARTICLE

Comparative Effectiveness of Levofloxacin-Based Triple Regimen and Standard Clarithromycin-Based Triple Regimen in Eradication of Helicobacter Pylori - Insights from A Peripheral Hospital-Based Study

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ABSTRACT

Objective: To compare the effectiveness of a Levofloxacin-based triple regimen with the standard Clarithromycin-based triple regimen in eradicating gastric Helicobacter pylori (H. pylori) infection.

Study Design: Quasi-experimental study.

Place and Duration of Study: This study was conducted at the Department of Medicine, Combined Military Hospital (CMH), Sibbi, Pakistan from January 2021 to August 2022.

Methods: A total of two hundred and sixty patients (n=260), both male and female, diagnosed with H. pylori infection, were enrolled. Patients who had used antibiotics within the past four weeks or proton pump inhibitors within the past two weeks were excluded to avoid interference with treatment efficacy. Participants were randomly assigned to two groups: The Levofloxacin Group received levofloxacin, amoxicillin, and omeprazole, while the Clarithromycin Group was treated with clarithromycin, amoxicillin, and omeprazole, each regimen lasting 14 days. After completing the eradication therapy, all patients were assessed for H. pylori eradication using the fecal antigen test.

Results: The median age of the participants was 30.00 years (26.00–36.00). Of the patients, 158 (60.8%) were female and 102 (39.2%) were male. Post-treatment testing revealed that 209 patients (80.4%) tested negative, indicating successful eradication, while 51 patients (19.6%) remained positive for fecal H. pylori antigen test. In the Clarithromycin Group, 96 patients (73.8%) tested negative, compared to 113 patients (86.9%) in the Levofloxacin Group, showing a statistically significant difference ($P = 0.008$).

Conclusion: The Levofloxacin-based triple therapy regimen proved significantly more effective in eradicating Helicobacter pylori infection than the standard Clarithromycin-based triple therapy regimen, suggesting its potential as a valuable first-line alternative, particularly in regions with high Clarithromycin resistance.

Keywords: *Antibacterial Agents, Antigens, Helicobacter Pylori, Proton Pump Inhibitors*.

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Introduction

Helicobacter Pylori (H. Pylori) is a Gram-negative bacterium with spiral shape. It is the most common bacterial infection affecting nearly half of the population of the world.[1] It is reputed as a primary etiological agent in the pathogenesis of both chronic gastritis and peptic ulcer disease (PUD) and cancer.[2,3] It is also linked to a few extra-intestinal diseases like vitamin B12 and iron deficiency anaemia, and immune thrombocytopenic purpura (ITP), failure to thrive, and many more.[4] H. Pylori has been widely studied not because it is a common infection but its eradication has been always a challenge for physicians. This is due to its insidious course of pathogenesis and its ability to survive the acidic gastric secretions.

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Many treatment strategies based on different drug regimens have been proposed to eradicate and treat the H. Pylori infections.[5-8] These vary in duration of therapy, number of drugs, dosage of drugs and type of drugs used. Some of these include three drugs, and others include four. Some of these are bismuth-based, while some are used as rescue therapies.[5] H. Pylori first-line treatment, guided by the American College of Gastroenterology (ACG), for areas where the macrolide exposure is limited or is less than 15%, the clarithromycin-based triple therapy regimen is advised, which includes a proton-pump inhibitor (PPI), clarithromycin, and amoxicillin or metronidazole for 14 days.[2] In Pakistan, macrolides are used for different infections but resistance to macrolides has not been widely studied.[9] Another proposed first-line therapy contains Levofloxacin for H. Pylori eradication in place of Clarithromycin.[10] In clinical practice both Clarithromycin and levofloxacin based therapies are used in Pakistan. The H. Pylori was found resistant to Clarithromycin in 47.8% isolates while levofloxacin showed 68.1% resistance.[11,12] The choice among these two is dictated by many factors like physicians' personal preference, patients' preference, compliance, and prior use of any of these medications, either H. Pylori infection or some other infection. In the present era of evidence-based medicine, the treatment regimens are no further dictated by personal preferences, recommendations and opinions but are supported and utilized according to evidence available in the literature, which is ever growing.

Clarithromycin is a cornerstone of the first-line triple therapy in regions with low macrolide resistance, while levofloxacin is considered for alternative or rescue therapy. However, increasing antibiotic resistance, especially in regions like Pakistan, challenges their efficacy. This study aims to compare the effectiveness of Clarithromycin and Levofloxacin in H. Pylori eradication. The selection of regimen choice must be informed by local resistance patterns and evidence-based guidelines rather than personal preference, to ensure successful eradication and reduce treatment failure.

Methods

This Quasi experimental study was conducted at Department of Medicine, Combined Military Hospital (CMH) Sibbi, Pakistan from January 2021 to August 2022 after approval from the Institutional Ethical Review Committee vide certificate number: No/ERC/03 held on dated: 18th November 2021. The sample size was calculated using the G*Power sample size calculator using a confidence interval of 95%, α error of 5%, β error of 20%, the cure rate of levofloxacin of 84.5%, and a cure rate of 69% for Clarithromycin.[13] A sample size of 117 was calculated for each study group. Considering a possible dropout of 10%, sample size became 130 for each group.

After informed consent, patients were enrolled using a non-probability purposive sampling technique. The adult patients of either gender with diagnosis of H. Pylori infection, treatment naive, were included in this study. Patients with hypersensitivity/ allergic reaction to any of the included drugs, use of antibiotics in the last four weeks, proton pump inhibitors within the last two weeks, gastric ulcer disease, and advanced renal or hepatic disorders. Moreover, pregnant patients and those unable to comply with the treatment regimen were also excluded.

All individuals with a suspected diagnosis of H. Pylori infection were interviewed in detail for relevant clinical history, including relevant drug history. Thereafter, patients suspected of H. Pylori infection after relevant history and examination were advised H. Pylori stool antigen test. All individuals with a positive stool antigen test were included in the study. The selected individuals were allotted to one of the two groups using the lottery method. The Group LTT (Levofloxacin containing triple therapy) was advised levofloxacin 500mg once a day, amoxicillin 1 gm twice a day, and omeprazole 20 mg twice a day, for 14 days as a treatment regimen. The Group CTT (Clarithromycin containing triple therapy) was advised Clarithromycin 500mg twice a day, amoxicillin 1 gm twice a day, and omeprazole 20mg twice a day, for 14 days. The compliance to treatment was checked at 1 week and at the end of treatment by counting/ checking left tablets, if any. Those who were non-compliant were excluded from the study. Moreover, the participants of the study were also told to report any side effects with medications which were narrated at the start of treatment regimen. After the H. Pylori eradication therapy, all patients were assessed for eradication. The stool

(fecal) H. pylori antigen test was repeated four weeks after the completion of eradication therapy, and at least two weeks after discontinuing proton pump inhibitors (PPIs).

The data was collected in Microsoft Office Excel Sheet (MS Excel). It was later entered and analyzed using the Statistical Package for Social Sciences Version 27.0 (SPSS ver. 27.0). The continuous data was represented using mean ± standard deviation for normally distributed data while median and interquartile range was calculated for skewed variables. Normality of the quantitative variables was checked using the Shapiro-Wilk test. The qualitative data was represented as frequencies and percentages. The statistical significance was checked for qualitative data using the Chi-Square test. The *P*-value ≤0.05 was taken as significant.

Results

A total of 260 patients (n=260) were enrolled in this study. The median age of the participants was 30.00 (26.00-36.00). 158 (60.8%) were females, and 102 (39.2%) were males. At the end of eradication therapy, 209 (80.4%) patients tested negative for fecal H. Pylori antigen, and 51 (19.6%) remained positive for fecal H. Pylori antigen test. Details of the understudy variables are given in table-1.

Table-1: Characteristics of patients along with Clinical Variables included in the study (n=260)

Variable	Sample Population
Age (Years)	32.00 (27.00-39.00)
Gender	
Female	158 (60.8%)
Male	102 (39.2%)
Treatment Response	
Negative	209 (80.4%)
Positive	51 (19.6%)
Type of Therapy Used	
Group LTT (Levofloxacin + Amoxicillin + Omeprazole)	130 (50%)
Group CTT (Clarithromycin + amoxicillin + omeprazole)	130 (50%)

In the LTT group, there were 78 (60.0%) females, and in the CTT group, 80 (61.50%) were females; there was no statistical significance (*P*=0.799) seen. While comparing treatment response, it was seen that 96 (73.80%) patients tested negative in the CTT group and 113 (86.92%) patients tested negative in the LTT group. Chi-square test applied to find the statistical significance between the two groups, which showed that the LLT group was comparatively effective than the CT group. (*P*-value = 0.008). Results of statistical analysis are summarized in table-2.

Table-2: Comparison of Levofloxacin-containing triple therapy and Clarithromycin-containing triple therapy (n=260)

Variable	Treatment Response		*Chi-Square*-value	*P*-value
	Negative	Positive		
Gender				
Female	125 (79.1%)	33 (20.9%)	0.421	0.521
Male	84 (82.4%)	18 (17.6%)		
Treatment Group				
CTT Group	96 (73.8%)	34 (26.2%)	7.049	0.008
LTT Group	113 (86.9%)	17 (13.1%)		

Discussion

The Helicobacter Pylori infection has caused increased morbidity and is one of the most common causes of chronic gastritis, and has been associated with gastric carcinomas.[14,15] The studies have shown that the effective treatment reduces morbidity.[16] This study was done to see an effective treatment for the eradication of H. Pylori in our population. In this study, the comparative effectiveness of Levofloxacin-based triple therapy and Clarithromycin-based triple therapy in the eradication of H. Pylori was seen. The median age of the CTT group was 32.00 (29.00-38.25) years, while that of the LTT group was 30.00 (25.00-34.00) years. In the present research, there were comparatively more females (n=158), but gender showed no relationship with eradication of H. Pylori (*P*=0.521). A total of 96 (36.92%) patients tested negative for H. Pylori in the CTT group and 113 (43.46%) patients tested negative for H. Pylori after eradication therapy likewise the fecal antigen test was positive in 34 (13.07%) patients in CTT group and 17 (6.5%) patients in LTT group. These results gave a promising comparable response (*P*=0.008). Thus, supporting the better effectiveness of levofloxacin-based triple therapy regimen for eradication of H. Pylori infection.

A systematic review and meta-analysis of thirteen studies conducted in Iran by Keikha et al. showed that treatment response in levofloxacin (75.2%) was better than that of clarithromycin (66.3%), with better odds (OR=1.76, CI 1.40-2.20), and the same was observed for the cure rate.[17] Similarly, in this research, the LTT group showed a better (86.9%) response than the CTT group (73.8%). This can be due to our population's better antimicrobial resistance parameters of clarithromycin. In another meta-analysis of seven studies, the researchers found a comparable efficacy between the two groups, though the levofloxacin group had a lower eradication rate (79.05%) in comparison to clarithromycin-based therapy (81.4%).[18] In this study, the levofloxacin group was found to be better and effective. This difference can be due to variable antimicrobial resistance and sensitivity patterns among different regions of the world.

In a single-center clinical trial conducted on 291 patients, the efficacy of levofloxacin and clarithromycin was found to be very low, and no satisfactory result was seen on symptom control.[19] The researchers attributed the low efficacy rate to increased antibiotic resistance due to extensive use of the drugs in general practice. Though in the present study, very reasonable efficacy was found up to 86.9% in the LTT group. A study conducted by Elantouny et al. found that the levofloxacin treatment regimen was better than the Clarithromycin group.[20] Likewise, another clinical trial showed that the Levofloxacin-based eradication therapy is better than the Clarithromycin-based regimen.[21] In a research conducted in Portugal, the researchers found the clarithromycin-based triple therapy had a better eradication profile than the levofloxacin-based eradication therapy, which contradicts the results from our study and can further be explained by growing antimicrobial resistance to clarithromycin due to extensive use of the drug in our population.[22]

Different regions have different guidelines likely tailored according to their regional/ local anti-microbial sensitivity patterns, for example, in Egypt, Clarithromycin-based H. Pylori eradication therapy is recommended as first choice for treatment, though tailored as per clinical needs.[23] And some have put a bar at the resistance level for use of such medications like erythromycin and levofloxacin for H. Pylori eradication therapy.[23,24] In a study conducted in Pakistan, researchers found CTT and LTT groups equally effective, with levofloxacin having better eradication counts. Moreover, the LTT group has a better safety profile.[25] In this study, too, we found the LTT-based regimen more effective.

Like every cross-sectional study, no follow-up was done to see long-term response, complications, and recurrence/ reinfection with H. Pylori. Moreover, this study was single-center and had a small sample size, thus limiting the external validity of the results. This study would have had a better impact if we had seen antimicrobial sensitivity patterns as well. We were not able to do this because of time constraints and limited resources. We would suggest that a multicenter randomized, double blind clinical trial should be done along with data on antimicrobial sensitivity patterns to avoid bias and see a more detailed comparison between the two groups.

Conclusion

This study showed that levofloxacin-based triple therapy (LTT) is more effective in eradicating H. Pylori than clarithromycin-based triple therapy (CTT). Considering the above findings, it is suggested that a levofloxacin-based regimen should be preferred for H. Pylori eradication and treatment.

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Conflict of Interest: The authors declare no conflict of interest

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Author Contributions

IA: Conception and design of the work
KB: Data acquisition, curation, and statistical analysis
KS: Manuscript writing for methodology design and investigation
KR: Revising, editing, and supervising for intellectual content
RSAK: Validation of data, interpretation, and write-up of results
QI: Writing the original draft, proofreading, and approval for final submission