DOI: https://doi.org/10.54393/pjhs.v5i07.1850

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
ISSN (P): 2790-9352, (E): 2790-9344
Volume 5, Issue 7 (July 2024)

Original Article

Comparison of Therapeutic Outcomes: Two Triple-Therapy Approaches for *H. pylori* Eradication in Gastric Ulcer Disease

Javaria Amil[1*], Saadia Sajjad[2], Rida Ajmal Khan[2], Sadia Majeed[3], Khalil Ahmed[1] and Muhammad Adnan Masood[1]

[1]Department of Medicine, Niazi Welfare Foundation Teaching Hospital, Sargodha, Pakistan
[2]Department of Physiology, Abu Umara Medical and Dental College, Lahore, Pakistan
[3]Department of Pharmacology, Continental Medical College, Lahore, Pakistan

ARTICLE INFO

Keywords:
Standard Triple Therapy, Gastric Ulcer, *Helicobacter pylori*, Antibiotic Resistance

How to Cite:
Amil, J., Sajjad, S., Khan, R. A., Majeed, S., Ahmed, K., & Masood, M. A. (2024). Comparison of Therapeutic Outcomes: Two Triple-Therapy Approaches for *H. pylori* Eradication in Gastric Ulcer Disease: Two Triple-Therapy for *H. pylori* Eradication. Pakistan Journal of Health Sciences, 5(07). https://doi.org/10.54393/pjhs.v5i07.1850

***Corresponding Author:**
Javaria Amil
Department of Medicine, Niazi Welfare Foundation Teaching Hospital, Sargodha, Pakistan
javariaamil57@gmail.com

Received Date: 6th June, 2024
Acceptance Date: 26th July, 2024
Published Date: 31st July, 2024

ABSTRACT

Gastric ulcer is a prevalent digestive disease, primarily caused by *Helicobacter pylori* infection. *H. pylori* infection poses a substantial challenge for medical practitioners due to increased antibiotic resistance. **Objectives:** To compare the efficacy of a 14-days clarithromycin-based triple therapy (TRT) with a moxifloxacin-based TRT for eradicating Helicobacter pylori in gastric ulcer disease. **Methods:** A quasi experimental study was conducted with 294 positive *H. pylori* patients divided into two groups. Group A was given standard triple therapy while Group B received moxifloxacin-based triple therapy. Data collection commenced after obtaining IRB approval and informed consent from all participants. Descriptive statistics was used to calculate frequency and percentages. Differences between the two groups were compared using the fisher exact analysis at a significance level, p-value < 0.05. **Results:** In the group with standard triple therapy (TRT), the eradication rates of *H. pylori* were reported as 67.3 % intention-to-treat (ITT) and 76.1% per-protocol (PP) analysis. In contrast, in the moxifloxacin-based triple therapy (MAO) group, the eradication rates were 86.3% ITT and 92.7% PP analysis. The eradication rates with moxifloxacin-containing triple therapy were statistically significant than standard TRT (p = 0.001). Furthermore, few side effects were evident in the moxifloxacin TRT group (p < 0.001) compared to the standard TRT group. **Conclusions:** In Pakistan, moxifloxacin-containing triple therapy may offer a notably superior treatment option for eradicating *H. pylori* infection compared to standard triple therapy.

INTRODUCTION

Gastric ulcer is a prevalent digestive disease, impacting more than half of the global population [1]. It is usually caused by a *Helicobacter pylori* infection and is marked by the presence of ulcers on the inner lining of the stomach [2]. *H. pylori* infection is an issue of global significance prevailing all over the world. The global prevalence of *H. pylori* is nearly 50%, with more cases observed in developing countries [3]. Due to improved sanitary conditions, the rate is changing in developing countries like Pakistan [4]. H. pylori infection is transmitted through feco-oral route and its prevalence in Pakistan amounts to 22% according to recent research [5]. Gastric ulcer primarily impacts middle-aged and elderly individuals, causing symptoms like loss of appetite, weight loss, stomach pain, and a sensation of fullness after meals. Without prompt treatment, gastric ulcers can lead to serious complications, such as gastric perforation and bleeding, which can be life-threatening [6]. The incidence of gastric ulcers has risen due to dietary and lifestyle changes. Contributing factors include consuming strong tea, *Helicobacter pylori* infection, smoking, using non-steroidal anti-inflammatory drugs, and alcohol consumption [7]. The main symptoms consist of stomach discomfort, stomach pain, loss of appetite, and occasional indigestion. In gastric ulcer disease, patients may experience symptoms such as hematemesis (vomiting

DOI: https://doi.org/10.54393/pjhs.v5i07.1850

blood), bloating, belching, and vomiting which can harm their health and lower the quality of life [8]. In Pakistan, the reported prevalence of *H. pylori* varies widely, ranging from 50% to 90% across different regions [9]. Although *H. pylori* shows in vitro sensitivity to several antibiotics, it is challenging to treat the infection in vivo with a single antibiotic. This difficulty is attributed to the bacterium's residence in the low pH environment of the mucinous layer [10]. Clarithromycin, with an efficacy rate of 40% against *H. pylori* is considered as best therapeutic approach. The combination of two antibiotics along with a proton pump inhibitor offers improved eradication by producing a synergistic effect [11]. Antibiotic resistance is the foremost important reason for the failure to eradicate the infection nowadays. The highest resistance rate is reported for clarithromycin owing to its widespread use in routine practice [12]. These incidents lead researchers to search innovations for treatment and preventive purposes. A new combination of therapies has been introduced which are more effective in treating *H. pylori* infection. Multiple studies suggest the use of moxifloxacin as a safe and best therapy with an 85 to 92% cure rate in place of clarithromycin [13]. Due to varying resistance patterns and treatment success rates across different regions, it is crucial to identify the best therapeutic regime for the treatment of gastric infection.

This study aimed to compare the efficacy of a 14-day clarithromycin-based triple therapy (TRT) with a moxifloxacin-based TRT in eradicating *Helicobacter pylori* infection.

METHODS

A quasi-experimental comparative study was carried out at the Niazi Welfare Foundation Teaching Hospital from June 2023 to April 2024 approved by the Institutional Review Board with the reference number (NM&DC/IRB/459). Sample size (n = 264) was calculated using the following formula, n= Z^2pq / e^2at 95% CI, and 0.05 margin of error. *H. pylori* prevalence data (22%) were taken from a prior study conducted in Pakistan [5]. Considering the dropout rate of 10%, a total 294 participants were included. A purposive sampling technique was employed to collect data. 294 *H. pylori*-positive patients having age > 18 years confirmed through stool antigen test using ELISA technique after getting informed consent were included in the study. Patients were excluded if they had age < 18 years, used PPIs or H2 receptor blockers in the last four weeks or antibiotics in the last two weeks, previously received *H. pylori* eradication therapy, liver or kidney insufficiency, pregnancy, severe heart disease, previous gastric surgery, contraindications to the drugs used in this study. Participants were randomly assigned to groups A & B after detailed clinical history and conducting a complete physical examination on a specific Performa. Patients' demographic information, like gender, age, weight, and disease duration, was documented. Group A was given standard triple therapy consisting of clarithromycin 500mg, with amoxicillin 1g, and omeprazole 20mg given bid for 14 days. Group B received triple therapy with moxifloxacin 400mg OD, amoxicillin 1g bid, and omeprazole 20mg two times a day for 14 days. Patients were followed for any side effects related to medication every week. At week 8, patients' stool antigen test was done to evaluate the *H. pylori* eradication status in both groups for cure rate. Descriptive statistics was employed to determine the frequency and percentages for categorical variables. Mean and SD for continuous variable. The fisher exact test was utilized to compare differences between the two groups at a significance level of p-value < 0.05 using SPSS version 24.0.

RESULTS

In group A, there were 68 (46.2%) female and 79 (53.8%) male, while in group B, 65 female (44.2%) and 82 male (55.8%). p-value of 0.725 indicates no significant differences between groups A & B in gender distribution. According to age, participants in group A ranged in age from 23 to 72 years old, with a mean age of 47.29 ± 6.31 years. In group B, ages ranged from 24 to 73 years and an average age of 47.93 ± 6.52 years. p-value of 0.371 depicts insignificant differences in ages between the two groups. The duration of the disease ranged from 0.5 to 11 years, with a mean duration of 4.92 ± 0.68 years in group A and 0.5 to 10 years, with an average duration of 4.86 ± 0.72 years in group B with p-value > 0.05 revealing no significant differences. In group A, participants' weights varied from 39 to 79 kg, with an average of 54.27±7.31 kg. The weights of the participants in group B varied from 39 to 80 kg, with an average weight of 54.48 ± 7.02 kg. p-value indicates no significant differences in participants' weights between the two groups A & B (Table 1).

Table 1: Demographics of Participants in Two Groups

Characteristics	Group A	Group B	p-Value
Male	79 (53.8%)	82 (55.8%)	0.725
Female	68 (46.2%)	65 (44.2%)	
Age (Years)	23-72	24-73	0.371
Mean Range	47.29 ± 6.31	47.93 ± 6.52	
Disease Duration (Years)	0.5-11	0.5-10	0.463
Mean Range	4.92 ± 0.68	4.86 ± 0.72	
Weight Range (kg)	39-79	39-80	0.801
Mean Range	54.27 ± 7.31	54.48 ± 7.02	

H. pylori eradication rate was based on per protocol (PP) and intention to treat (ITT) analysis at a 95% confidence interval. In this study, 267 patients completed the follow-up. 130 patients in group A completed the follow up and the cure rate was 76.1% (99/130) as PP analysis and according to ITT, 67.3% (99/147) cure rate was observed. Whereas, in group B, 137 patients completed the follow-up, and the cure

DOI: https://doi.org/10.54393/pjhs.v5i07.1850

rate was 92.7% (127/137) as PP analysis. According to ITT analysis, 86.3% (127/147) cure rate in group B was observed. The total ITT rate in the two groups was 76.8% (226/294) at 95% CI. The entire PP analysis rate was 84.6% (226/267). Fisher exact analysis revealed significant differences in Group A and B at p value of 0.0001 (Table 2).

Table 2: *Helicobacter pylori* Eradication Rate

Eradication Rate	Group A	Group B	p-Value
Intention-to-Treat 95% CI	67.3% (99/147)	86.3 % (127/147)	0.0001
Per Protocol 95% CI	76.1% (99/130)	92.7% (127/137)	0.0001

In our study, the primary reason for dropout was personal issues, with participants missing consecutive follow-up visits. Participants who failed to report weekly were considered lost to follow-up. The statistical analysis revealed that in terms of side effects, frequency was significantly lower in group B participants. In group participants, vomiting and diarrhea were the most frequently reported side effects whereas in group B, diarrhea and nausea were obvious (Table 3).

Table 3: Comparison of Side Effects in Two Groups

Side Effects	Group A	Group B	p-Value
Metallic Taste	6 (4.6%)	3 (2.1%)	< 0.001
Nausea	10 (7.6%)	6 (4.3%)	
Vomiting	18 (13.8%)	5 (3.6%)	
Diarrhea	22 (16.9%)	7 (5.1%)	

DISCUSSION

The rising antibiotic resistance has negatively impacted the success of *H. pylori* eradication treatments. There is now a tenacious need for new and more effective therapeutic approaches to address treatment failures. Recent guidelines no longer recommend clarithromycin-containing triple therapy as a first-line treatment. Among the newer drug combinations for *H. pylori* therapy, moxifloxacin-based triple therapy has demonstrated promising results in several studies [15]. A study reported 31% failure using standard triple therapy (TRT) for *H. pylori* eradication and showed higher resistance to clarithromycin therapy [16]. Completely eradicating *H. pylori* continues to pose a substantial challenge for medical practitioners, as current treatment regimens have not demonstrated consistent effectiveness in curing the infection [17]. In South Asia, there has been a notable rise in antibiotic resistance among *H. pylori* strains [18]. A current meta-analysis highlighted Pakistan as having the cases with the highest resistance to amoxicillin, clarithromycin, and tetracycline [19]. Several studies have been undertaken to assess the most effective treatment regimens for improving eradication rates. This study represents another effort. The findings from this research indicate that both intention-to-treat (ITT) and per-protocol (PP) analysis reveal significantly higher outcomes with the moxifloxacin-containing therapy compared to clarithromycin-based therapy (80.9% vs. 57.8% for ITT and 92.7% vs. 76.1% for PP). These results align with a study comparing triple therapies for *H. pylori* eradication, using moxifloxacin and, clarithromycin, suggesting higher eradication rates with the moxifloxacin-based therapy [20]. Also, Akpinar *et al*. found that moxifloxacin-containing triple therapy is a first-line treatment for *Helicobacter pylori* infection [21]. Similarly, Hassan *et al.* performed a comparative study on the efficacy of therapy in eradicating *H. pylori* infection, with results showing a higher eradication rate (74%) with the moxifloxacin regimen. These studies collectively report that moxifloxacin TRT are superior compared to other therapies [22]. The current study found that the primary side effects due to moxifloxacin-containing TRT were diarrhea and nausea, followed by occurrences of vomiting and a metallic taste. In contrast, diarrhea and vomiting were the most commonly reported adverse events in the clarithromycin group. However, Hwang *et al*. reported that dyspepsia/bloating and altered taste sensation were the common adverse reactions observed during 2 weeks of moxifloxacin treatment [23]. The overall rate of adverse events with the moxifloxacin-based regimen was 15.1%, notably lower than the 42.9% observed with clarithromycin therapy. This study indicates a significant disparity in both the frequency and intensity of side effects between the two groups ($p < 0.001$). Patients receiving moxifloxacin predominantly reported mild to moderate side effects, with none severe enough to necessitate discontinuation of treatment or disrupt daily activities. These findings are consistent with other studies revealing the side effects linked with triple therapy treatment for *H. pylori* infection [24]. The current study has several limitations, including the absence of antimicrobial sensitivity testing before treatment for both study drugs. Patients were not stratified based on ethnicity, BMI, or bacterial load, factors known to impact cure rates. Genetic polymorphism, which can influence eradication rates, was also not assessed. Future research should include genetic polymorphism analysis in patient's resistant to therapy to better understand these factors.

CONCLUSIONS

In summary, this study suggests that moxifloxacin TRT is the most effective and safe option to combat *H. pylori* infection, in comparison to standard clarithromycin-based therapy. Given its substantial eradication rate and safety profile, moxifloxacin TRT should be highly preferred for clinical practice in Pakistan.

Authors Contribution

Conceptualization: JA
Methodology: JA, RAK, KA
Formal analysis: SS, SM, MAM

DOI: https://doi.org/10.54393/pjhs.v5i07.1850

Writing-review and editing: KA, MAM

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Salari N, Darvishi N, Shohaimi S, Bartina Y, Ahmadipanah M, Salari HR *et al*. The global prevalence of peptic ulcer in the world: A systematic review and meta-analysis. Indian Journal of Surgery. 2022 Oct; 84(5): 913-21. doi: 10.1007/s12262-021-03189-z.

[2] Den Hoed CM and Kuipers EJ. 45-Helicobacter pylori infection. In Hunter's Tropical Medicine and Emerging Infectious Diseases. 2020 Jan; 476-480. doi: 10.1016/B978-0-323-55512-8.00045-4.

[3] Hassan MN, Arif A, Shahzad MS, Ibrahim M, Rahman HA, Razaq MA *et al*. 88. Global prevalence of Helicobacter pylori and its effect on human health. Pure and Applied Biology (PAB). 2020 Feb; 9(1): 936-48. doi: 10.19045/bspab.2020.90098.

[4] Haq I, Muhammad A, Fazli Zahir MK, Anwar F, Akhtar MS, Ullah F. Serological and Epidemiology study of Helicobacter pylori infection among Dyspeptic patients in District Peshawar Pakistan. Advances in Bioresearch. 2020 May; 11(3): 81-5. doi: 10.15515/abr.0976-4585.11.3.8185.

[5] Shah SR, Almugadam BS, Hussain A, Ahmad T, Ahmed S, Sadiqui S. Epidemiology and risk factors of Helicobacter pylori infection in Timergara city of Pakistan: a cross-sectional study. Clinical Epidemiology and Global Health. 2021 Oct; 12: 100909. doi: 10.1016/j.cegh.2021.100909.

[6] De Brito BB, da Silva FA, Soares AS, Pereira VA, Santos ML, Sampaio MM *et al*. Pathogenesis and clinical management of Helicobacter pylori gastric infection. World Journal of Gastroenterology. 2019 Oct; 25(37): 5578. doi: 10.3748/wjg.v25.i37.5578.

[7] Razuka-Ebela D, Polaka I, Parshutin S, Santare D, Ebela I, Murillo R *et al*. Sociodemographic, lifestyle and medical factors associated with Helicobacter pylori infection. Journal of Gastrointestinal & Liver Diseases. 2020 Sep; 29(3). 319-327. doi: 10.15403/jgld-870.

[8] Elbehiry A, Marzouk E, Aldubaib M, Abalkhail A, Anagreyyah S, Anajirih N *et al*. Helicobacter pylori infection: current status and future prospects on diagnostic, therapeutic and control challenges. Antibiotics. 2023 Jan; 12(2): 191. doi: 10.3390/antibiotics12020191.

[9] Muhammad N, Afridi J, Mahmood N, Ali S. Frequency of Helicobacter pylori in stool specimens of patients suspected of upper gastrointestinal symptoms in District Bunir. Jundishapur Journal of Microbiology. 2020 Aug; 13(8): e104471. doi: 10.5812/jjm.104471.

[10] O'Connor A, Furuta T, Gisbert JP, O'Morain C. Review–treatment of Helicobacter pylori infection 2020. Helicobacter. 2020 Sep; 25: e12743. doi: 10.1111/hel.12743.

[11] Moss SF, Chey WD, Daniele P, Pelletier C, Jacob R, Tremblay G *et al*. Brief communication: global temporal trends in the efficacy of clarithromycin-based regimens for the treatment of Helicobacter pylori infection. Therapeutic Advances in Gastroenterology. 2023 Jun; 16: 17562848231167284. doi: 10.1177/17562848231167284.

[12] Mori H and Suzuki H. Update on quinolone-containing rescue therapies for Helicobacter pylori infection. World Journal of Gastroenterology. 2020 Apr; 26(15): 1733. doi: 10.3748/wjg.v26.i15.1733.

[13] Kong S, Huang K, Wang J, Wang X, Yang N, Dong Y *et al*. Efficacy of tailored second-line therapy of Helicobacter pylori eradication in patients with clarithromycin-based treatment failure: a multicenter prospective study. Gut Pathogens. 2020 Dec; 12: 1-9. doi: 10.1186/s13099-020-00378-1.

[14] Fallone CA, Moss SF, Malfertheiner P. Reconciliation of recent Helicobacter pylori treatment guidelines in a time of increasing resistance to antibiotics. Gastroenterology. 2019 Jul; 157(1): 44-53. doi: 10.1053/j. gastro.2019.04.011.

[15] Gisbert JP. Optimization strategies aimed to increase the efficacy of Helicobacter pylori eradication therapies with quinolones. Molecules. 2020 Nov; 25(21): 5084. doi: 10.3390/molecules25215084.

[16] Jaka H, Mueller A, Kasang C, Mshana SE. Predictors of triple therapy treatment failure among H. pylori infected patients attending at a tertiary hospital in Northwest Tanzania: a prospective study. BMC Infectious Diseases. 2019 Dec; 19: 1-7. doi: 10.1186/s12879-019-4085-1.

[17] Van den Poel B, Gils S, Micalessi I, Carton S, Christiaens P, Cuyle PJ *et al*. Molecular detection of Helicobacter pylori and clarithromycin resistance in gastric biopsies: a prospective evaluation of RIDA® GENE Helicobacter pylori assay. Acta Clinica Belgica. 2021 May; 76(3): 177-83. doi: 10.1080/17843286.2019.1685741.

DOI: https://doi.org/10.54393/pjhs.v5i07.1850

[18] Shrestha AB, Pokharel P, Sapkota UH, Shrestha S, Mohamed SA, Khanal S et al. Drug resistance patterns of commonly used antibiotics for the treatment of Helicobacter pylori infection among South Asian countries: a systematic review and meta-analysis. Tropical Medicine and Infectious Disease. 2023 Mar; 8(3): 172. doi: 10.3390/tropicalmed8030172.

[19] Bilal H, Khan MN, Rehman T, Hameed MF, Yang X. Antibiotic resistance in Pakistan: a systematic review of past decade. BMC Infectious Diseases. 2021 Dec; 21: 1-9. doi: 10.1186/s12879-021-05906-1.

[20] Ahmed MH, Abd-Elsalam S, Mahrous AM. Moxifloxacin based triple therapy as alternative to standard therapy in Helicobacter Pylori Eradication. Anti-Infective Agents. 2021 Jun; 19(3): 299-302. doi: 10.2174/2211352518999200925154501.

[21] Akpinar M, Aksoy E, Sapmaz F, Goktas Z, Uzman M, Nazligul Y. Comparison of moxifloxacin-based therapies and standard bismuth-based quadruple therapy for first-line treatment of Helicobacter pylori infection. Archives of Medical Science-Civilization Diseases. 2018 Oct; 3(1): 81-6. doi: 10.5114/amscd.2018.78766.

[22] Hassan AM, Eid K, Eliwa KA, Abdel-Gawad M. Two nitazoxanide-based quadruple regimens for eradication of Helicobacter pylori infection: a single-center randomized controlled trial. Al-Azhar Assiut Medical Journal. 2022 Jan; 20(1): 67-71. doi: 10.4103/azmj.azmj_74_21

[23] Hwang JJ, Lee DH, Lee AR, Yoon H, Shin CM, Park YS *et al.* Efficacy of moxifloxacin-based sequential therapy for first-line eradication of Helicobacter pylori infection in gastrointestinal disease. World Journal of Gastroenterology. 2015 Apr; 21(16): 5032-8. doi: 10.3748/wjg.v21.i16.5032.

[24] Kadhim AM, Mohammed MM, Abdul-Hussein HM. Treatment of Helicobacter pylori Infections Using Moxifloxacin-Triple Therapy Compared to Standard Triple and Quadruple Therapies. Iraqi Journal of Pharmaceutical Sciences (P-ISSN 1683-3597 E-ISSN 2521-3512). 2023 Jun; 32(1): 107-14. doi: 10.31351/vol32iss1pp107-114.