

Comparison of Sequential and Concomitant Therapy for Eradication of Helicobacter Pylori

Faisal Shabbir, Shazia Nisar, Nadeem Ashraf, Babar Khan, Farzana Hakim*, Hammad Khan

Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Foundation University Medical College, Islamabad Pakistan

ABSTRACT

Objective: To compare the effectiveness of sequential and concomitant therapy for the eradication of Helicobacter pylori.

Study Design: Quasi-experimental study.

Setting and Duration of Study: Department of Gastroenterology and Medicine, Pak Emirates Military Hospital, Rawalpindi Pakistan from Jun to Sep 2021.

Methodology: A total of 105 patients who were H-pylori positive on stool antigen tests and had to undergo eradication therapy were included in the study. Patients were randomized into Groups by lottery method. Group-A was given the Clarithromycin concomitant therapy (Omeprazole+ Amoxicillin+ Clarithromycin+ Metronidazole) for 10-14 days, while Group-B was given the Clarithromycin based sequential therapy (Omeprazole+ Amoxicillin for five days and then Omeprazole+ metronidazole+ Clarithromycin for next five days) for eradication of H pylori. A stool antigen test was done to determine the successful eradication in both Groups.

Results: Out of 105 H pylori antigen-positive patients included in the study, 69(65.7%) had successful eradication of stool antigen while 36(34.3%) had stool antigen positive even after adequate treatment. The mean age of the study participants was 39.53±7.647 years. Eradication of H pylori in the study population was statistically significantly found in patients with age less than 40 years (p -value=0.033) and those who were taking sequential therapy as compared to concomitant therapy (p -value<0.001).

Conclusion: H-pylori eradication was achieved in most of the patients taking treatment. However, in our study, patients younger than 40 and those taking sequential therapy had more chances of successfully eradicating this bacteria invading the gastric mucosa than patients taking concomitant therapy.

Keywords: Concomitant therapy, H-pylori, Sequential therapy.

How to Cite This Article: Shabbir F, Nisar S, Ashraf N, Khan B, Hakim F, Khan H. Comparison of Sequential and Concomitant Therapy for Eradication of Helicobacter Pylori. Pak Armed Forces Med J 2022; 72(5): 1787-1790.

DOI: <https://doi.org/10.51253/pafmj.v72i5.7963>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Epidemiological data reflects that medical and general practice outpatient departments cater to many patients suffering from gastrointestinal disorders.¹ These patterns remain the same across the globe, and upper GI tract disorders affect all age Groups in several ways.² These conditions of the GI tract may range from benign infectious conditions to malignant neoplastic potentially fatal diseases.³ Diagnosing these conditions in time and treating them efficiently may save the patients from severe consequences.⁴ Various antibiotics have been studied for their role in fighting against H-pylori infection.⁵ Guidelines from various parts of the world recommend a combination of antibiotics with proton pump inhibitors for definitive management of H-pylori-related GI conditions and prevent long-term consequences.⁶

Multiple types of combinations have been tried for the eradication of H-pylori. Yilmaz *et al.* studied the

efficacy of Clarithromycin-based regimens in patients suffering from H-pylori gastritis. They concluded that Clarithromycin-based regimens were efficacious in the eradication of H-pylori.⁷ Wu *et al.* conducted a randomized controlled trial comparing different regimens for eradication of H-pylori, concluding that a quadruplet regimen was better in managing these patients.⁸ Lee *et al.* performed a similar study revealing that concomitant therapy with Rabeprazole, Amoxicillin Clarithromycin and Metronidazole was much higher in efficacy than sequential therapy for successful eradication of H-pylori bacteria in patients suffering from gastritis.⁹

Limited individual and state resources compel clinicians to find the right and cost-effective choice so that disease gets eliminated in time and complete and does not pose a burden on both individual and health care system. Qureshi *et al.* published a study on our population and compared different combinations for eradicating H-pylori. They concluded that combining two antibiotics with proton pump inhibitors is effective for most patients in reducing symptoms and

Correspondence: Dr Faisal Shabbir, Department of General Medicine, Pak Emirates Military Hospital, Rawalpindi, Pakistan

Received: 30 Dec 2021; revision received: 15 Jun 2022; accepted: 20 Jun 2022

eradicating H-pylori.¹⁰ Limited data has been generated comparing Clarithromycin-based concomitant and sequential therapies in our population. Therefore, we planned this study to compare the effectiveness of sequential and concomitant therapy for eradicating Helicobacter pylori.

METHODOLOGY

This experimental study was conducted at the Department of Medicine and Gastroenterology, Pak Emirates Military Hospital, Rawalpindi Pakistan, from June to September 2021. The Ethical Review Board Committee of the hospital was approached to get ethical approval for this study, and approval was granted (Letter No A/28/EC/348/2021). WHO sample size calculator was used for the sample size calculation with population proportion of response of H-pylori to Clarithromycin-based regimens as 89.4% and margin of error as 10%.¹¹ Non probability consecutive sampling technique was used to gather the sample for this study.

Inclusion Criteria: Patients of either genders with gastritis or upper GI symptoms of acid peptic disease positive for H pylori stool between 18 and 65 years were included in the study.

Exclusion Criteria: Patients with malignancies (solid or haematological), active alcohol use in the past six months, B-12 or folate deficiency or replacement therapy, patients who underwent any recent surgical procedure or gave a history of NSAID use in routine (prescribed or un-prescribed) were excluded from the study. Patients with allergic reactions to the antibiotics or proton pump inhibitors used in the study were also excluded. Patients who were previously found resistant to Clarithromycin-based regimens were also not included.

The lottery method was used to ensure the random allocation of Groups (Group-A and B). Group-A was given the Clarithromycin concomitant therapy (Omeprazole+ Amoxicillin+ Clarithromycin+ Metronidazole) for 10-14 days.¹² In contrast, Group-B was given the Clarithromycin-based sequential therapy (Omeprazole+ Amoxicillin for five days and then Omeprazole+ Metronidazole+ Clarithromycin for the next five days) for eradication of H pylori.¹³

Stool for H pylori antigen was performed at the end of therapy for each patient and based on presence or absence of stool antigen patients were labelled as with successful eradication or not. In addition, the type of therapy used and other socio-demographic factors

were compared in the patients with the eradication of H pylori and those without successful eradication and persist-positive stool antigen even after the treatment.

All statistical analysis was performed using the Statistical Package for Social Sciences (SPSS-24.0.). Pearson chi-square test was applied to look for the association of age, gender, type of antibiotic therapy and smoking with successful eradication of H pylori. Differences between Groups were considered significant if *p*-values were less than or equal to 0.05.

RESULTS

One hundred and five patients were included in the final analysis. The mean age of the study participants was 39.53±7.647 years. Out of 105 patients, 47 (44.7%) were males, while 58(55.3%) were females. 69(65.7%) had successfully eradicated stool antigens, while 36(34.3%) had stool antigen positive even after adequate treatment. In addition, 68(64.7%) were non-smokers, while 37(35.3%) were tobacco smokers.

Table-I summarized the general characteristics of patients recruited in the analysis. 56(53.3%) took sequential therapy, while 49(46.7%) took concomitant therapy to eradicate H-pylori.

Table-I: Characteristics of patients included in the study (n=105)

Study Parameters	n(%)
Age (years)	
Mean±SD	39.53±7.647 years
Gender	
Male	47 (44.7)
Female	58 (55.3)
Eradication of H-pylori	
Yes	69 (65.7)
No	36 (34.3)
Type of Therapy Used	
Sequential therapy	56 (53.3)
Concomitant therapy	49 (46.7)
Smoking Status	
Non-smokers	68 (64.7)
Smokers	37 (35.3)

The results of the statistical analysis were summarized in Table-II. Eradication of H pylori in the study population was statistically significantly found in patients with age less than 40 years (*p*-value-0.033) and those who were taking sequential therapy as compared to concomitant therapy (*p*-value<0.001). The gender of patients (*p*-value-0.645) and tobacco smoking status (*p*-value-0.107) had no statistically significant relationship with the successful eradication of H-pylori in our patients.

Table-II: Factors associated with successful eradication of H pylori (n=105)

Factors studied	Successful eradication of H-pylori (n=69)	No eradication of H-pylori (n=36)	p-value
Age			
<40 years	36 (52.2)	11 (30.5)	0.033
>40 years	33 (47.8)	25 (69.5)	
Gender			
Male	32 (46.4)	15 (41.7)	0.645
Female	37 (53.6)	21 (58.3)	
Smoking			
No	41 (59.4)	27 (75.0)	0.107
Yes	28 (40.6)	09 (25.0)	
Type of Therapy Used			
Sequential	47 (68.1)	09 (25.0)	<0.001
Concomitant	22 (31.9)	27 (75.0)	

DISCUSSION

Gastritis is one of the most commonly encountered medical problems. General physicians, medical specialists and gastroenterologists share the burden of this GI ailment. Gastritis could be due to multiple etiologies. Bacterial infection is one of the common etiologies of this disorder.¹⁴ Multiple antibiotic and proton pump inhibitor bases regimens have been in clinical practice to eradicate H-pylori from patients suffering from gastritis.⁶ Different guidelines worldwide recommend different regimens based on type and duration. Limited local work has been available regarding differences in the effectiveness of sequential and concomitant therapy. This study was therefore designed and conducted to compare the effectiveness of sequential and concomitant therapy for eradicating *Helicobacter pylori*.

Wang *et al.*¹⁵ in their systematic review and meta-analysis published in 2016, compare different types of antibiotic therapies based on the duration of therapy. They concluded that concomitant therapy was superior to sequential therapy when given for ten days to patients with a confirmed H-pylori infection diagnosis. In addition, diarrhoea was the side effect more seen in patients with concomitant therapy than sequential therapy. We did not study the adverse effects in our study but found that sequential therapy was more associated with eradicating H-pylori than concomitant therapy.

A randomized trial was conducted by Das *et al.*¹⁶ in 2016, which evaluated and compared the same parameter in patients suffering from perforated duodenum ulcers. It was concluded that no significant difference was found in the Groups regarding effectiveness and adverse effects. Sequential therapy was found cost-effective as compared to concomitant therapy. We did

not include patients with perforated duodenal ulcers. However, in patients who just had H-pylori gastritis, those with ages less than 40 and taking sequential therapy had more chances of successfully eradicating this bacteria invading the gastric mucosa than patients taking concomitant therapy.

A study was conducted by Mestrovic *et al.* comparing two different therapeutic regimens for eradicating H-pylori.¹⁷ It was published in 2020 and revealed that hybrid therapy had lower side effects and both therapies were not different in terms of efficacy for eradicating H-pylori. They encouraged the use of fewer antibiotic-based regimens for various reasons. Our study supported their recommendations with results as well as in our study patients treated with sequential therapy had better outcomes than those treated with concomitant therapy.

A Korean study conducted by Jung *et al.*¹⁸ in 2016 evaluated the suitability of sequential vs concomitant therapy to combat GI infection by H-pylori bacteria. They concluded that no statistically significant difference exists between the eradication rates of both Groups; therefore, no single therapy could be rated as superior to others. Ours was a small study with a very basic design and found that sequential therapy was statistically significantly better than concomitant therapy in terms of H-pylori eradication. The type of population, multiple other patients, and medication-related factors may be responsible for the difference in our results from those generated by Jung *et al.*

LIMITATIONS OF STUDY

Patients of a single medical unit were targeted instead of taking sample representative of the whole population. This was one of the main limitations of this study. Moreover, sensitivity and specificity for stool for H-pylori antigen is less than biopsy; therefore, results may vary based on the diagnostic method used to detect H-pylori antigen. Studies with better design and addressing these limitations may generate generalizable results.

CONCLUSION

H-pylori eradication was achieved in most of the patients taking treatment. However, in our study, patients younger than 40 and those taking sequential therapy had more chances of successfully eradicating this bacteria invading the gastric mucosa than patients taking Concomitant therapy.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

FS & SN: Study design, conception, data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

NA & BK: Data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

FH & HK: Drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Dumic I, Nordin T, Jecmenica M, Stojkovic Lalosevic M, Milosavljevic T, Milovanovic T. Gastrointestinal Tract Disorders in Older Age. *Can J Gastroenterol Hepatol* 2019; 2019: 6757524. doi:10.1155/2019/6757524.
2. Sonne JU, Erckenbrecht JF. Chronic motility disorders of the upper gastrointestinal tract in the elderly. Pharmaceutical, endoscopic and operative therapy. *Internist (Berl)* 2014; 55(7): 852-858. doi: 10.1007/s00108-014-3504-z.
3. Nash S. Benign lesions of the gastrointestinal tract that may be misdiagnosed as malignant tumors. *Semin Diagn Pathol* 1990; 7(2): 102-114.
4. Lamont JT. Evidence-based management of gastrointestinal diseases. *Gastroenterol Rep (Oxf)* 2015; 3(1): 1-2. doi:10.1093/gastro/gou092.
5. Lahner E, Carabotti M, Annibale B. Treatment of Helicobacter pylori infection in atrophic gastritis. *World J Gastroenterol* 2018; 24(22): 2373-2380. doi:10.3748/wjg.v24.i22.2373.
6. Liu KS, Wong IO, Leung WK. Helicobacter pylori associated gastric intestinal metaplasia: Treatment and surveillance. *World J Gastroenterol* 2016; 22(3): 1311-1320. doi:10.3748/wjg.v22.i3.131.
7. Yilmaz B, Koseoglu H, Coskun Y, Devenci M, Kekilli M. Comparison between different first-line therapy protocols in eradicating Helicobacter pylori in a region with high clarithromycin resistance. *Prz Gastroenterol* 2018; 13(2): 150-156. doi:10.5114/pg.2018.72732.
8. Wu DC, Hsu PI, Tseng HH. Helicobacter pylori infection: a randomized, controlled study comparing 2 rescue therapies after failure of standard triple therapies. *Medicine (Baltimore)* 2011; 90(3):180-185. doi: 10.1097/ MD.0b013e31821c9d1c.
9. Lee HJ, Kim JI, Lee JS, Jun EJ, Oh JH, Cheung DY, et al. Concomitant therapy achieved the best eradication rate for Helicobacter pylori among various treatment strategies. *World J Gastroenterol* 2015; 21(1): 351-359. doi: 10.3748/wjg.v21.i1.351.
10. Qureshi H, Ahmed W, Arain GM, Mehdi I, Alarn SE. Comparison of Five Different Treatment Regimens for H. Pylon Eradication. *J Pak Med Assoc* 1999; 49 (11): 278-280
11. Fischbach W. Helicobacter Pylori Infection. *Dtsch Arztebl Int* 2018; 115(25): 429-436. doi:10.3238/arztebl. 2018.0429.
12. Safavi M, Sabourian R, Foroumadi A. Treatment of Helicobacter pylori infection: Current and future insights. *World J Clin Cases* 2016; 4(1): 5-19. doi:10.12998/wjcc.v4.i1.5.
13. Zullo A, Fiorini G, Scaccianoce G, Portincasa P, De Francesco V, Vassallo R, et al. Sequential therapy for first-line Helicobacter pylori eradication: 10- or 14-day regimen? *J Gastrointestin Liver Dis* 2019; 28(1): 11-14. doi: 10.15403/jgld.2014.1121.281.hpy.
14. Melese A, Genet C, Zeleke B, Andualem T. Helicobacter pylori infections in Ethiopia; prevalence and associated factors: a systematic review and meta-analysis. *BMC Gastroenterol* 2019; 19(1): 8. doi: 10.1186/s12876-018-0927-3.
15. Wang Y, Zhao R, Wang B, Zhao Q. Sequential versus concomitant therapy for treatment of Helico-bacter pylori infection: an updated systematic review and meta-analysis. *Eur J Clin Pharmacol* 2018; 74(1): 1-13. doi: 10.1007/ s00228-017-2347-7.
16. Das R, Sreenath GS, Kate V. Sequential versus concomitant therapy for eradication of Helicobacter Pylori in patients with perforated duodenal ulcer: A randomized trial. *Saudi J Gastroenterol* 2016; 22(4): 309-315. doi: 10.4103/1319-3767.187605.
17. Mestrovic A, Perkovic N, Bozic J, Pavicic Ivelja M, Vukovic J, Kardum G, et al. Randomised clinical trial comparing concomitant and hybrid therapy for eradication of Helicobacter pylori infection. *PLoS ONE* 2020; 15(12): e0244500. <https://doi.org/10.1371/journal.pone.0244500>
18. Jung SM, Cheung DY, Kim JI, Kim I, Seong H. Comparing the Efficacy of Concomitant Therapy with Sequential Therapy as the First-Line Therapy of Helicobacter pylori Eradication. *Gastroenterol Res Pract* 2016; 2016(1): 1293649.