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Original Article

Efficacy of 10-day Sequential Treatment for Helicobacter pylori Eradication

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ABSTRACT

Objective: To assess the effectiveness and tolerability of a ten-day sequential regimen for the eradication of *Helicobacter pylori*.
Study Design: Quasi-experimental study.
Place and Duration of Study: Department of Medicine, NESCOM Hospital, Islamabad Medical Complex, Pakistan from Aug 2021 to Aug 2022.
Methodology: The patients were divided into two groups. The sequential therapy group (Group-A) was administered dual therapy including a proton pump inhibitor (Lansoprazole 30mg) plus Amoxicillin 1 gram given twice daily for first five days, followed by a triple therapy including Lansoprazole 30mg, Levofloxacin 500 mg and Tinidazole 500mg, all twice daily for remaining five days. Whereas traditional therapy group (Group-B) was given Lansoprazole 30 mg, Clarithromycin 500 mg, and Amoxicillin 1000 mg twice daily for total 14 days.
Results: A total of 200 *Helicobacter pylori* positive cases were included. The mean age of all patients was 36.60±12.49 years whereas mean Body Mass Index was 28.19±4.02. A total of 140 patients had successful treatment in both groups out of which 87(87%) were in sequential treatment group and 53(53%) in the traditional treatment group (p-value <0.001). In terms of side effects, there were 18(8%) patients who suffered minor side effects out of which metallic taste was most common, 14(7%), followed by bloating and diarrhea. Both groups had comparable side effects (p =1.00).
Conclusion: Even with comparable side effects, the innovative 10-day sequential medication for the treatment of *H. pylori* is more successful than traditional triple regimen.

Keywords: Anti-bacterial agents, Gastritis *Helicobacter pylori*, Sequential therapy, Triple therapy.

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INTRODUCTION

Helicobacter pylori is the etiological agent behind diseases such as chronic gastritis, chronic atrophic gastritis, peptic ulcers, gastric lymphoma, and gastric cancer.[1] Contaminated food or water is the source of infection, and it is primarily seen in poor socio-economic classes. In Pakistan, the prevalence ranges from 50 to 90%.[2]

American College of Gastroenterology Clinical Guidelines recommend Bismuth Quadruple Therapy consisting of Proton Pump Inhibitors (PPI), Bismuth and any two antibiotics: Amoxicillin, Metronidazole, Tetracycline or Clarithromycin. Concomitant Quadruple Therapy consists of a PPI and three types of antibiotics including Amoxicillin, Metronidazole and Clarithromycin.[3]

The success rate with traditional regimes like triple therapy is disappointingly low at 35.6% and is probably due to an increased bacterial resistance of antibiotics, particularly against Clarithromycin.[4] As a result, in clinical practice, some patients need two or more treatment tries to get rid of their *H. pylori* infection.

In 2000, a novel therapeutic approach to cure H. PYLORI infection was conceived. A ten-day sequential therapy which achieved a very high eradication rate.[5,6] In Pakistan, there is paucity of research on this therapy which forms the rationale for our study.

METHODOLOGY

The quasi-experimental study conducted in Department of Medicine in outpatient department at NESCOM Hospital, Islamabad Medical Complex. It was conducted from 17 August 2021 till 31 August 2022. Prior approval was sought from Ethical Review Board (NESCOM-44(33)/2021-IMC). Sample size was calculated using WHO calculator using a previous eradication rate at end of treatment in Sequential Group as 90% and Traditional Group as 63.3%[4], and 80% power of test, which came to 200 (100 in each group). Non-probability consecutive sampling was done after seeking written informed consent from each respondent.

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Inclusion Criteria: Patients of either gender aged between age 20 to 60 years, presenting in OPD having symptoms of dyspepsia with *H. pylori* infection confirmed by urea breath test, stool for *H. pylori* antigen or endoscopic biopsy proven *H. pylori* were included.

Exclusion Criteria: Patients with previous treatment for *H. pylori*, allergic to any medication used in the study, pregnant females and previous gastric or duodenal surgeries, those with chronic hepatitis B or C, end-stage renal disease and patients with any proven malignancy were excluded.

The sequential therapy group (Group-A) was administered dual therapy including a proton pump inhibitor (Lansoprazole 30mg) plus Amoxicillin 1 gram given twice daily for first five days, followed by a triple therapy including Lansoprazole 30mg, Levofloxacin 500 mg and Tinidazole 500mg, all twice daily for the remaining five days. Whereas the traditional therapy (Group-B) was given Lansoprazole 30 mg, Clarithromycin 500 mg, and Amoxicillin 1000 mg twice for 14 days (Figure).

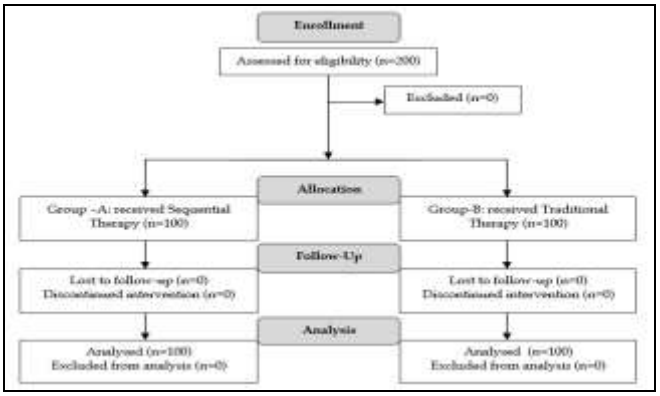

Figure: Patient Flow Diagram (n= 200)

Various demographic parameters as age, gender and Body Mass Index were entered in a pre-designated proforma. Eradication was defined as patients having negative Urea breath test conducted four weeks after completion of therapy. Side effects as diarrhoea, taste change and bloating were the secondary endpoints noted during the research. During therapy the patients were followed up on a weekly basis to assess their compliance and note any side effects.

All data were entered using Statistical Package for Social Sciences (SPSS) version 25. Continuous variables as age and BMI were represented in mean and standard deviation. Gender, result of urea breath test at end of therapy and side effects were presented as frequency and percentage. Independent t-test was applied to compare the age means between two groups after checking normality test using Shapiro-Wilk test. *p*-value was considered significant if ≤0.05. Chi-square test was applied to see effects discrete variables between groups and Fisher's exact test if any value is less than.[5]

RESULTS

A total of 200 *Helicobacter pylori* positive cases fulfilling the inclusion/exclusion criteria were enrolled to compare the 10 days sequential treatment with conventional antibiotic therapy. The age demographic data showed that patients within the age group of 20-40 years were more common; 118(59%). The mean age of all patients was 36.60±12.49 years whereas mean BMI was 28.19±4.02. Mean age in Groups A and B was 39.19±13.08 years and 35.94±10.86 years respectively and BMI was 28.63±3.69 and 27.75±4.30. There was no significant statistical difference in the data (Table-I).

Table-I: Age and Body Mass Index (BMI) Distribution among Participants (n=200)

Variables	Group-A n=100	Group-B n=100	*p*-value
BMI (Mean±SD)	28.63±3.69	27.75±4.30	0.121
Age (Mean±SD)	39.19±13.08	35.94±10.86	0.057

Table-II: Treatment Results Across Groups (n=200)

Treatment outcome	Group-A n=100 n(%)	Group-B n=100 n(%)	*p*-value
Successful	87(87%)	53(53%)	<0.001
Failure	13(13%)	47(47%)	

Table-III: Comparison of Side Effects Across Groups (n=200)

Side Effects	Group-A n=100 n(%)	Group-B n=100 n (%)	*p*-value
Absent	92(92%)	92(92%)	1.000
Present	8(8%)	8(8%)	

Gender distribution showed that 116(72.5%) were males while 44(27.5%) were females. There was no statistical difference between the two groups. A total of 140 patients had successful treatment in both groups out of which 87(87%) were in sequential treatment group and 53(53%) in the traditional treatment group. Hence, the curative rate in Group-A was 87% whereas it was 53% in Group-B. Further distribution is shown in Table-II. In terms of side effects, there were 18(8%) patients who suffered minor side effects out of which metallic taste was most

common, 14(7%), followed by bloating and diarrhea. Further distribution is shown in Table-III. No patient left the treatment plan because of side effects thus achieving 100% compliance.

DISCUSSION

Due to the high frequency of *H. pylori* infection among Pakistani citizens, an efficient treatment plan that completely eradicates the infection is required.[6] However, many *H. pylori* treatments are no longer successful in getting rid of *H. pylori* due to the rising incidence of antibiotic resistance. In our study the mean age of patients was 36.60±12.49 years whereas mean BMI was 28.19±4.02. This is in accordance with the studies done in Pakistan which showed a mean age of 40.0±24.4 years and in Qatar 38.85±11.78 years.[7] There was male preponderance in our study amounting to 67.5% of patients which is also consistent with published data.[8]

The cause attributed for the declining efficacy of triple treatment is clarithromycin resistance.[9] Sequential therapy is not the first-line treatment for eradication, because the best outcomes could not be achieved in earlier research.[10] The selection of second-line therapy following the failure of first line agents is still not standardized. Sequential treatment, on the other hand, also performed poorly in several studies. Sequential therapy's diminished effectiveness is a result of dual resistance to clarithromycin and metronidazole.[11] Thus, adjustments to management recommendations are based on antibiotic resistance pattern and the loco regional effectiveness of regimens.[12]

Our research showed that a total of 140 patients had successful treatment in both groups out of which 87(87%) were in sequential treatment group and 53(53%) in the traditional treatment group. So, curative rate in Group-A was 87% whereas it was 53% in Group-B and it was significant (p-value <0.001). In a prospective, randomized research conducted in Morocco, eradication rates for 10-day sequential therapy were 89.9% and for triple therapy were 71%, respectively.[13] Similarly, a study one in Pakistan institute of Medical Sciences Islamabad, showed eradication rate of 95% with sequential therapy as compared to 67.5% in traditional triple therapy.[7] In accordance with our results, randomized research including 7 Latin American locations came to the conclusion that the 10-days sequential regimen is better than traditional 14-days triple-drug therapy for treating *H. pylori* infection.[14] The efficacy of 10-days sequential regimen was comparable to triple treatment in regions with limited clarithromycin resistance, according to a randomized study conducted in Taiwan.[15] In Qatar, neither the 10-days sequential regime nor the traditional regime had the best eradication rate.[16] Despite taking the identical regime, these variations between nations may be caused by the existence or lack of antimicrobial resistance.[17]

In terms of side effects, here were 18(8%) patients who suffered minor side effects out of which metallic taste was most common, 14(7%), followed by bloating and diarrhea. Both groups had comparable adverse effects and achieved 100% compliance. A study by Farhaud et al. showed very mild side effects in Egyptian population.[3] Diarrhea was the main adverse impact in both groups receiving standard therapy and sequential therapy in a double-blind randomized controlled study in Eisig et al.[18] Choi and associates discovered that the main side effects of employing both groups were loose stools and epigastric pain.[19] Taste disturbance and diarrhea were the most common side effects in the multicenter, open-label, randomized study.[20] None of the trials previously cited found a discernible difference between the two treatments in the frequency of adverse events. Thus, both regimens were well tolerated and there was no drop out from treatment due to side effects.

LIMITATION OF STUDY

Limitations of this study included microbial sensitivity and resistance antibiotics were lacking in our investigation, which is a crucial component before beginning treatment and assessing its effectiveness. However, it increases the financial load. We could only include a small number of patients in our investigation. The brand names of the drugs utilized in the trial were not standardized. The effectiveness, price, and quality of various brands might vary.

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CONCLUSION

The novel 10-day sequential therapy for eradication of *H. pylori* is more effective than the standard triple regimen with comparable side effects.

Conflict of Interest: None.

Authors' Contribution

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

LN & AW: Data acquisition, data analysis, critical review, approval of the final version to be published.

MM & ARB: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

FI & ZR: Conception, data acquisition, drafting the manuscript, 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.

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