Original Article

Comparative Efficacy Of Triple Therapy And Sequential Therapy In Helicobacter Pylori Eradication: A Randomized Controlled Trial

Munazza Ibrahim[1],Mujahid Aslam[2] , Shams Uz Zaman[3], Shakeel ur Rahman[4], Moeen ud Din Khan Khalil[5], Mujeeb Ur Rahman[6]

1. Resident Gastroenterology LRH Peshawar
2. Assistant professor Gastroenterology LRH Peshawar
3. Fellow Gastroenterology LRH Peshawar
4. Fellow Gastroenterology LRH Peshawar
5. Resident Gastroenterology LRH Peshawar
6. Resident Gastroenterology LRH Peshawar

Corresponding Author :Mjuahid Aslam[2]
EMAIL: mujahidaslamm@gmail.com
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Abstract

Background: Helicobacter pylori is identified to be a cause of several diseases associated with the GI tract including gastritis, ulcer and gastric cancer. In Pakistan, you find that 81 percent of adult population has been infected by this type of disease. The emergence of resistance to antibiotics has reduced the efficacy of the conventional triple therapy; it has become necessary to evaluate other new chewing regimens like sequential therapy which appear superior in this regard in terms of eradication.

Objectives: To compare the outcome of conventional triple therapy with that of sequential therapy in the eradication of Helicobacter pylori in infected local population.

Study Design: A randomized controlled trial

Place and Duration of Study: The study was conducted at the Department of Gastroenterolgy, ward and OPD, Lady Reading Hospital (LRH), Peshawar, Pakistan. The duration of the study was six months, from 16th September 2021 to 24th March 2022.

Methods: This study was a randomized controlled trial was conducted at Gastroenterolgy ward and OPD, Department of Gastroenterolgy, LRH Peshawar. In each group there were two arms, one of which included 326 patients in total. The therapies offered to the patients were evaluated using consecutively collected samples and compared statistically. The duration adopted in the study of the eradication rates among the patients was six months counting from the treatment period.

Results: The age of the patients was mean of 38.5 ± 11.59 and male to female ration was estimated as 0.55 each. Sequential therapy yielded a significantly higher eradication rate than triple therapy: p = 0.04.

Conclusions: Closely, there was also better evidence of tolerability when compared to triple therapy regardless of grade of favourable eradication and fewer side effects which was significant at p< 0.05. It is time that the solution of the sequential therapy strategy as the first choice of treatment should be produced, in order to improve the condition of the patient, and to prevent the interruption of the cyclic antibiotic resistance.

Keywords: Triple regimen, stepwise regimen, Heliobacter pylori, cure.

Introduction

Helicobacter pylori (H. pylori) is an anaerobic spiral-shaped bacterium which can live in human gastric mucosa because of the presence of multiple flagella. H. pylori is found in 50.1% of the population globally, with higher case reports from the developing countries [1]. This scourge is estimated to have affected 81% of the adult population in Pakistan [2]. This bacterium is a well-established hazard for a variety of GI diseases and illness such as peptic ulcer,

chronic gastritis, dyspepsia and several types of cancers including gastric adenocarcinoma and MALT lymphoma [3]. Since Hp can indeed cause severe infection and prompt serious complications, it can be reduced greatly and the morbidity nearly eliminated if the infection is detected early [4]. The first-line H. pylori eradication therapy is known as triple therapy where include a PPI, amoxicillin, and clarithromycin. However, antibiotics usage has been provoking increased resistance and its effectiveness can reduce to 18.4% which basically is below the 70 per cent threshold as recommended in Maastricht IV Consensus guidelines [5]. These can be far as low as 11.6% for amoxicillin, 18.9% for clarithromycin, and as high as 37.1% for metronidazole and are particularly evidenced in asian countries such as Pakistan further aggravating favourable treatment outcomes [6]. The demand for other regimens has brought the emergence of the sequential therapy that was introduced by Zullo et al., whereby phase one is PPI and amoxicillin, phase two is a PPI, clarithromycin and metronidazole. Some studies have proposed that sequential therapy's eradication rates exceed 90% [7]. The two clinical trials showed that compared with triple therapy; the sequential therapy has better eradication rates, 93.4% opposed to 76.9% [8]. Also, a meta-analysis of an RCT in Korea, that assessed the effectivity of the sequential therapy as 85.9% to its 75% to the TT [9]. Still, the data presented in this study are scarce for the local South Asian population in Pakistan, specifically proportion of H. pylori and potential differences in antibiotic resistance. To cater to this need, the present work was planned with the aim to assess the efficacy of sequential therapy against standard triple therapy in H. pylori positive intervening patients in a tertiary care teaching hospital. The detailed findings could be useful for clinicians in selecting the correct treatment for this frequent pathogen.

Methods

This parallel, randomized, controlled trial was conducted for six months in the ward and Out Patient Department (OPD), Department of gastroenterolgy, Lady Reading Hospital (LRH) Peshawar. Participants are patients of either sex, aged between sixteen and seventy-five years diagnosed with the H. pylori bacterial infection. Consecutive non-probability sampling was used to allocate 163 patients to each treatment group: Group A received triple therapy that included PPI, amoxicillin and clarithromycin for two weeks while Group B received sequential therapy of PPI, amoxicillin for 5 days and then PPI, clarithromycin and metronidazole for the remaining 5 days.

Data Collection

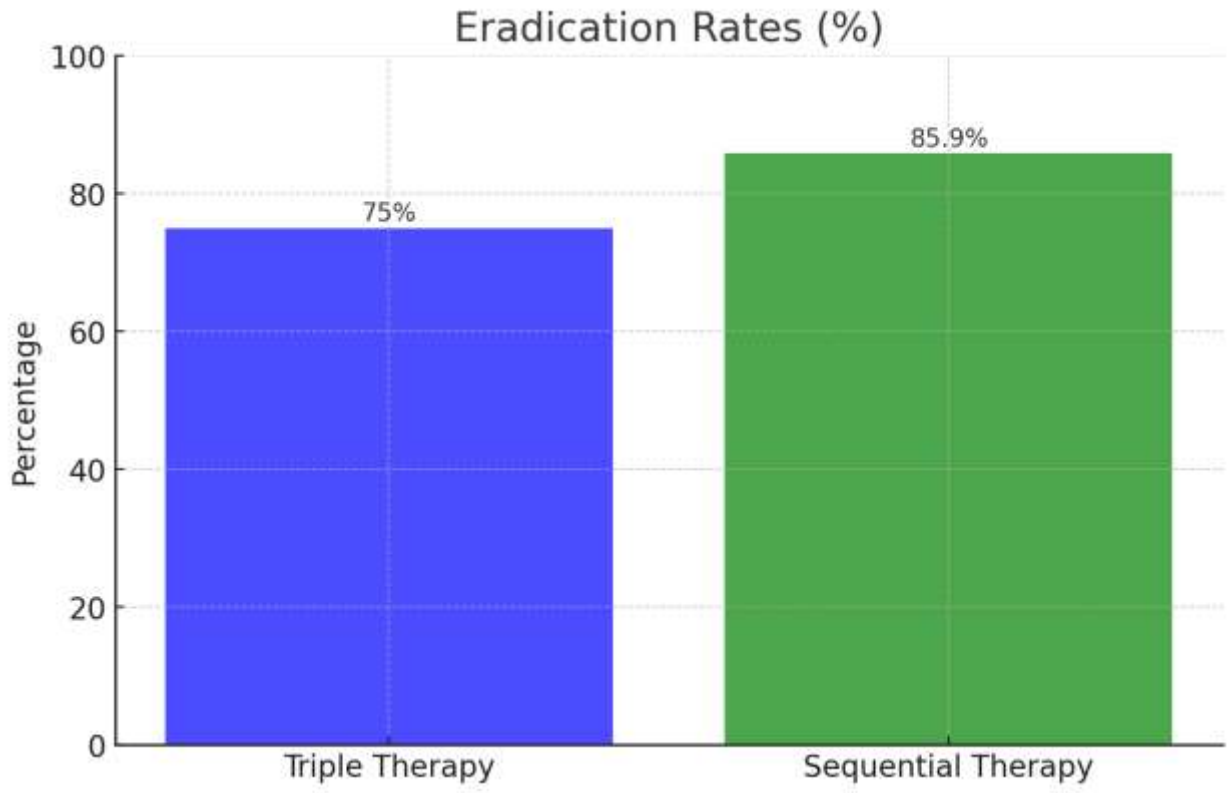
The following particulars were noted: age, gender, clinical symptoms at first time of contact, and adherence to laid down management strategies. Treatment was stopped when either the urea breath test or the stool antigen test performed at four weeks post treatment was negative. Non-compliant patients, those diagnosed with prior erosion treatment failure were excluded from the study.

Statistical Analysis

Data were computed and analyzed using Statistical Package for Social Service (SPSS) version 24. All continuous data and compared groups were presented as mean ± standard deviation, qualitative and categorical data were presented by frequency and percentages, respectively. To compare the eradication rates the chi-square test was used and the level of significance used was $p < 0.05$.

Results

Of the 266 patients who were randomised, 163 were assigned to the immediate treatment group. The mean age was 38.5 ± 11.59 years (range 16-75), and the male-to-female ratio was 0.55:1. Compared to the triple therapy arms the sequential therapy has had a high chance of H. pylori eradication with the patients recording 85.9% success rates as opposed to the 75% rates on the triple therapy treatments ($p = 0.04$). Neo-adjuvant endocrine therapy side effects were tolerable and comparable across the 3 trials and included nausea 15%, diarrhoea 10% and abdominal pain 12%. The consequent compliance uptake was 93% among the sequential group while that of the triple therapy group was 89%.


Eradication Rates (%)
Percentage
100
80
60
40
20
0
75%
85.9%
Triple Therapy
Sequential Therapy

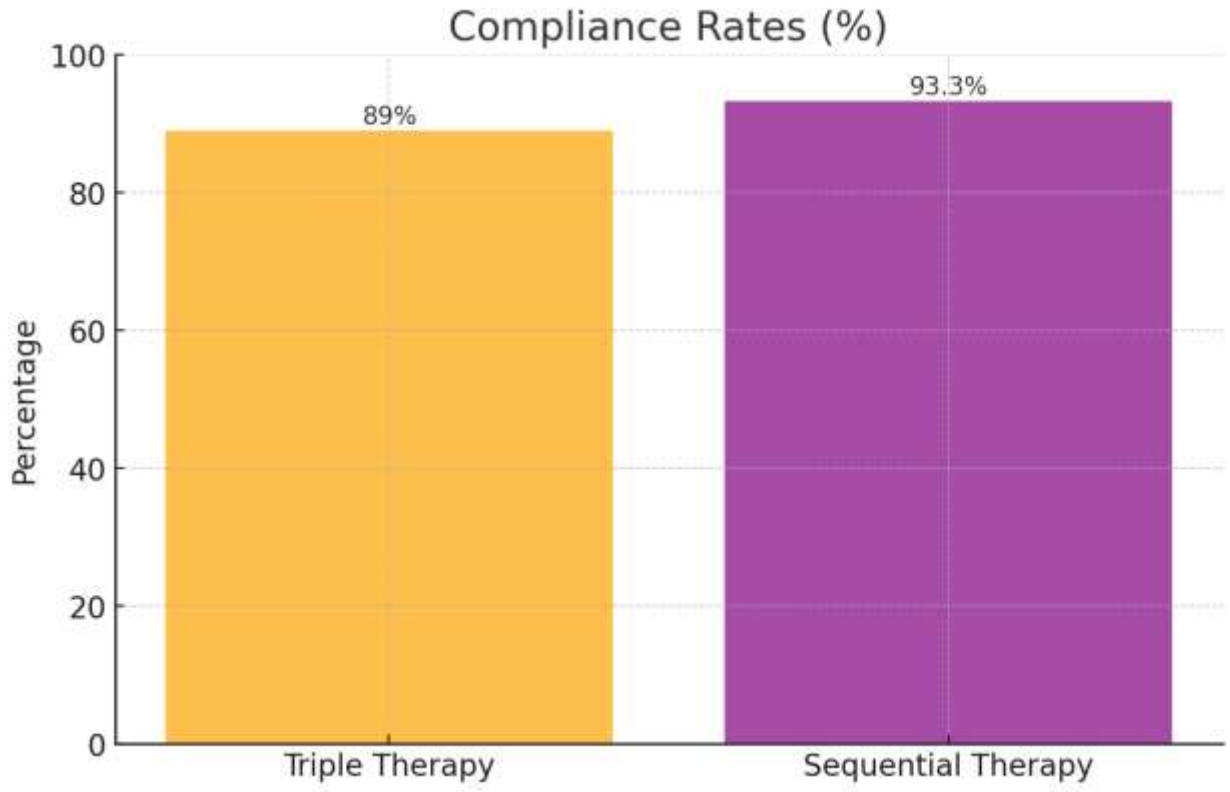

Compliance Rates (%)
Percentage
100
80
60
40
20
0
89%
93.3%
Triple Therapy
Sequential Therapy

Table 1: Baseline Characteristics

Variable	Triple Therapy (n=163)	Sequential Therapy (n=163)
Age (years)	38.7 ± 11.5	38.3 ± 11.7
Male	72 (44.2%)	74 (45.4%)
Female	91 (55.8%)	89 (54.6%)
Mean Age ± SD	38.7 ± 11.5	38.3 ± 11.7
Range (years)	16-75	16-75

Table 2: Adverse Effects Distribution

Adverse Effect	Triple Therapy (n=163)	Sequential Therapy (n=163)
Nausea	18 (11%)	17 (10.4%)
Diarrhea	14 (8.6%)	16 (9.8%)
Abdominal Discomfort	20 (12.3%)	19 (11.7%)

Table 3: Treatment Outcomes

Outcome	Triple Therapy (n=163)	Sequential Therapy (n=163)
Eradication	122 (75%)	140 (85.9%)
Non-Eradication	41 (25%)	23 (14.1%)

Table 4: Compliance Data

Compliance	Triple Therapy (n=163)	Sequential Therapy (n=163)
Adherent	145 (89%)	152 (93.3%)
Non-Adherent	18 (11%)	11 (6.7%)

Discussion

The purpose of this research was to evaluate whether standard triple therapy could be equally effective as sequential therapy in the local population with H. pylori infection. The results showed that sequential therapy was superior with an eradication rate of 85.9% compared to triple therapy of 75%. These results are within and add to the more prominent literature of how combined sequential therapy should be considered a superior first-line treatment plan. These efficacy patterns of sequential therapy evidenced in this study are similar to those observed in various other studies conducted, in different countries. For example, a meta-analysis of Cochrane Systematic Review of RCTs published between 2005 and 2014 revealed that eradication rates with sequential regimens were significantly higher in comparison with triple therapy: 93.4% vs 76.9%, p- 0.0001 [10]. Our results, albeit somewhat lower, are consonant with those presented here and speak to the problem of antibiotic resistance in the local population. P. lower has developed high level of resistance to the drugs: clarithromycin and metronidazole which are some of the drugs used in triple therapy. One study from Turkey described a 21.5 percent resistance to clarithromycin and 38.2 percent to metronidazole, yielding regimen eradication percentages lower than 80 percent, using triple therapy [11]. Other observations on resistance profiles in South Asian countries are available; metronidazole resistance we found as high as 37% followed by clarithromycin 18.9% in Pakistan indicating that a new regimen is required [12]. Sequential therapy, which amoxicillin in the first phase, interrupts bacterial cell walls so that the second phase of clarithromycin and metronidazole is more effective [13]. The effectiveness of this approach has proven in a study done in Taiwan that showed higher eradication rates as compared with the triple therapy (90.1% compared to 77.5%) [14]. Our study also substantiates these trends, although at a somewhat lower eradication rates, probably reasons by differences in population parameters and resistance to antibiotics. Korea perform a study comparing sequential and triple therapies and they have been obtaining the same level of eradication rates we got, that is 85.9% of the first group of patient who took sequential therapy while 75% of

the patient in group who took triple therapy hence support the efficiency of sequential therapy [15]. Further, another Italian, randomised controlled trial noted lesser side effects and better patient compliance with sequential therapy, very much in conformity with the compliance rates of this study 93.3% for sequential therapy and 89% for the triple therapy. Nonetheless, sequential therapy too poses its own difficulties, though it is more effective. However, this method of use takes at least five steps and may compromise patient compliance especially patients with low health literacy. But problems of compliance caused by this limitation could be addressed by patient education, or simple regimens of dose administration. Therefore, on the basis of the evidence, we can assert that sequential therapy should be a first-line regimen for H. pylori eradication in the local population [16]. The fate should be devoted to analyzing the standard sequential regimens and their adaption according to the local resistance phenomenon; there should be an analysis of the newer antibiotics in an attempt to improve the overall eradication rates significantly.

Conclusion

Sequential therapy was more effective in the elimination of Helicobacter pylori than the standard triple therapy; 85.9% compared to 75%. Its higher endoscopicMagic and less toxicity make it reasonable to use as the first-line therapy of H. pylori, especially in the era of antibiotic resistance.

Limitations

Limitations of this study included limited sample size and single-centre recruitment, therefore, the results cannot be generalised to other patients or settings. Furthermore, a standard assessment of the antibiotic resistance patterns was not done; moreover, the degree of adherence to sequential therapy, although improved, remained dependent solely on patient education and clinical supervision, which might be scarcely available and thus not easily transferable to other practicing clinical settings.

Future Findings

Further studies should look at expanding the data into multi-centre platform to confirm these results in other populations. Exploring the effectiveness of improved conception of antibiotics or new and local patterns of antibiotic resistance might also improve the local rates of eradication and combat the threat of antibiotic resistance that is upsurge internationally.

Abbreviations based on your study:

- H. pylori: **Helicobacter pylori**
- PPI: **Proton Pump Inhibitor**
- LRH: **Lady Reading Hospital**
- MALT: **Mucosa-Associated Lymphoid Tissue**
- SD: **Standard Deviation**
- SPSS: **Statistical Package for the Social Sciences**
- OPD: **Outpatient Department**

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Authors Contribution:

Concept & Design of Study: Munazza Ibrahim[1],Mujahid Aslam[2]

Drafting: Shams Uz Zaman[3], Shakeel ur Rahman[4], Moeen ud Din Khan Khalil[5], Mujeeb Ur Rahman[6]

Data Analysis: Shams Uz Zaman[3], Shakeel ur Rahman[4], Moeen ud Din Khan Khalil[5], Mujeeb Ur Rahman[6]

Critical Review: Shams Uz Zaman[3], Shakeel ur Rahman[4], Moeen ud Din Khan Khalil[5], Mujeeb Ur Rahman[6]

Final Approval of version: Munazza Ibrahim[1],Mujahid Aslam[2]

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