COMPARING THE EFFICACY OF CONCOMITANT THERAPY WITH THE STANDARD TRIPLE REGIMEN AS FIRST LINE THERAPY OF HELICOBACTOR PYLORI ERADICATION

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Abstract

Objective: To compare the effectiveness of Concomitant therapy with standard triple regimen in H.pylori Eradication.

Methods: It was a randomised control trial at OPD of Department of Gastroenterology, Jinnah Hospital Lahore and involved 170 patients, who fullfilled the selection criteria of study were enrolled in the study from OPD of Department of Gastroenterology, Jinnah Hospital Lahore. 85 cases were given Concomitant therapy (Group-A) and 85 cases were given Standard triple regimen (Group-B). Informed consent was obtained. Demographic information (name, age, and sex) were taken. The mean age was 40.43 ± 17.01 years in the Concomitant therapy group and 42.99 ± 12.98 years in the Standard triple regimen group. In group A, 62% cases had ages less than 45 years, and 37.6% of cases had age 45 years or above. In group B, 68.2% cases had an age less than 45 years and 31.8% of cases had an age of 45 years and above. In group A, 50.6% cases were male and 49.4% cases were female. In group B, 72.9% cases were male and 27.1% cases were female. In group A, 58.8%, 22.4%, and 18.8% of cases had low, middle, and high socioeconomic status respectively. In group B, 57.6%, 29.4 and 13% of cases had low, middle, and high socioeconomic status respectively.

In the Concomiant therapy group, eradication was achieved in 93.8%. In conventional triple regimen, eradication was achieved in 61.4% cases (p-value<0.001).

Conclusions: Eradication achievement was significantly more common with Concomitant therapy as compared to the conventional triple regimen. Concomitant therapy was much effective than the Standard triple regimen in all age groups, both genders, and all socioeconomic groups.

Key Words: H. Pylori Induced Gastritis, Concomitant therapy, Standard triple regimen

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Helicobacter pylori infection affects more than 50% of the world's population. There is a definite correlation between this chronic infection and peptic ulcer disease as it causes atrophic and metaplastic changes in the stomach mucosa.[1] The usual route of infection is fecal-to-oral.[2] It can also cause a variety of other gastric disorders, including chronic active gastritis, stomach cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma. H pylori infection produces several bioactive factors that affect the gastric parietal cells (which produce HCL) and ECL cells (which secrete gastrin and somatostatin). D cells are repressed by H. pylori while G cells are stimulated. H Pylori infection is prevalent in underdeveloped countries. The clinical picture varies, although most patients develop superficial gastritis, a minority develop nodules and ulcers.[2] This infection is one of the most common causes of dyspepsia. On diagnosis, Standard triple therapy is recommended for 14 days, followed by acid-suppressive treatment (H2-receptor antagonists, or PPIs) for a total of 4-6 weeks. The test of choice to document eradication

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is a urea breath test (UBT) and stool antigen test. The patient must discontinue acid suppressive drugs for 2-4 weeks before having these tests.

Triple therapy consists of two antibiotics, such as amoxicillin-clarithromycin or amoxicillin-metronidazole plus a proton pump inhibitor (PPI) for 10-14 days. Antibiotic resistance is becoming more common, notably with clarithromycin. The success rate of triple therapy in real practice is 10% lower than the eradication rates seen in research trials. Following the failure of first-line therapy, several rescue therapies have been suggested, although they still have a failure rate ≥20%. Concomitant therapy, which includes a PPI, amoxicillin, metronidazole, and clarithromycin for 10 to 14 days, is one of the most successful first-line treatment options. Clinical trials have shown that, even in areas with somewhat high levels of clarithromycin resistance, this therapy successfully cures more than 90% of patients.[3-5] Concomitant therapy is frequently suggested around the world based on these findings.[6-9] We conducted a 14-day trial to assess the efficacy, applicability, and safety of a concomitant regimen of omeprazole 40mg, amoxicillin 1g, metronidazole 500mg, and clarithromycin 500 mg twice daily as an empirical first-line treatment for Helicobacter pylori infection.

The purpose of this study is to find the role of concomitant therapy in the treatment of H. pylori infection compared to traditional triple therapy in the Pakistani population. Due to variations in demographic profiles, differences in antibiotic resistance patterns, and variations in disease presentations, the study is of paramount importance in defining the best treatment. We may introduce it as a first-line treatment in place of a conventional regimen if sufficient results are obtained in favor of this therapy in the management of H. pylori gastritis.

METHODS

It was a Randomized Control Trial, which was done in OPD of Hijaz hospital Lahore and in Department of Gastroenterology, Jinnah Hospital Lahore. The duration of the study was 18 months (10-June-2020 to 09-December-2021). The sample size for this study was 170 patients with H pylori-associated gastritis (by using a 2% margin of error, 95% confidence level). The Sampling technique was Non-probability, purposive sampling. Patients aged 18-70 years of either gender presenting with a diagnosis of H. Pylori infection (as per operational definition) were included in the study. Patients with a history of gastric surgery, an allergy to study drugs, a history of taking any antibiotics within the previous two weeks, a history of H pylori eradication therapy within the previous five years, a history of using probiotic products within the past month, a history of taking bismuth, H2 receptor antagonist, PPIs, or antifungal medications within the previous two weeks, as well as those who did not sign an informed consent form were all excluded from the study.

Data collection procedure: After patient's informed consent and approval from ethical committee, 170 patients with H. Pylori gastritis were enrolled. Patients were randomly assigned to one of two groups, Group A or Group B, with 85 patients in each. Randomization was done using sealed envelopes that were numbered and labelled with the names of the groups. H. Pylori stool Antigen was done for diagnosis. Group A received Concomitant therapy (PPI, Amoxicillin, Metronidazole, and Clarithromycin for 10 to 14 days), while group B (Amoxicillin-clarithromycin or Amoxicillin-metronidazole plus a PPI for 10-14 days) received a standard triple regimen. Stool examination for H. Pylori antigen was also performed 4 weeks after completion of therapy for assessing eradication ('Negative' test labeled as treatment success). The relevant information was entered in an especially designed proforma.

Data Analysis: All collected data was analyzed by SPSS 25. For quantitative data like age, mean and standard deviation were calculated. For qualitative data like gender and eradication rate. The eradication rate of H. Pylori was compared between the two groups by using the chi-square test. Data was stratified for age, gender, and socioeconomic status to address the effect modifiers. A p-value less than 0.05 was considered significant.

RESULTS

The mean age was 40.43 ± 17.01 years in group A and 42.99 ± 12.98 years in group B. In group A, 62% cases had age < 45 years and 37.6% cases had age ≥45 years. In group B, 68.2% cases had age < 45 years and 31.8% cases had age ≥45 years. In group A, 50.6% of cases were male and 49.4% of cases were female. In group B, 72.9% of cases were male and 27.1% of cases were female. In group A, 58.8%, 22.4%, and 18.8% of cases had low, middle, and high socioeconomic status respectively. In group B, 57.6%, 29.4 and 13% of cases had low, middle, and high socioeconomic status respectively. In group A, eradication was achieved in 93.8%. In group B, eradication was achieved in 61.4% cases (p-value=0.00). Stratification of eradication rate was done with regards to age group, gender and socioeconomic status and p-values were depicted in respective tables (Table # 1, 2).

Table 1: *Distributions of variable with frequency and percentage*

Variable		Study Group		p-value
		Group A	Group B	
Age group	Less than 45 years	53(62.4%)	58(68.2%)	0.42
	Equal or more than 45 years	32(37.6%)	27(31.8%)	
Gender	Male	43(50.6)	62(72.94%)	0.003
	Female	42(49.4%)	23(27.06%)	
Socio-economic Status	Low	50(58.8%)	49(57.6%)	0.42
	Middle	19(22.4%)	25(29.4%)	
	High	16(18.8%)	11(13%)	
H pylori Eradication	Yes	78(91.8%)	53(62.4%)	0.00
	No	7(8.2%)	32(37.6%)	

Table 2: *Age group, Gender, Socioeconomic status wise stratification of Eradication rate*

Variable		Study Group	Eradication		p-value
			Yes	No	
Age group	Less than 45years	Group A	47	6	0.02
		Group B	41	17	
	Equal or more than 45years	Group A	31	01	0.00
		Group B	12	15	
Gender	Male	Group A	41	02	0.00
		Group B	39	23	
	Female	Group A	37	05	0.01
		Group B	14	09	
Socio-economic status	Low	Group A	46	04	0.2
		Group B	41	08	
	Middle	Group A	17	02	0.00
		Group B	06	19	
	High	Group A	15	01	0.01
		Group B	06	05	

DISCUSSION

Treatment regimens for H. pylori are becoming less successful as a result of rising antibiotic resistance, particularly to clarithromycin.[10-12] The success rate of triple therapy in clinical practice is approximately 10-25% lower than that shown in research trials, according to some studies.[13-15] Therapies that are effective, safe, and easy to follow are therefore crucial. After the failure of the first line treatment, several rescue therapies have evolved. In our study, the eradication rate in concomitant therapy group was 93.8 % and in conventional therapy group was 62.4% (p-value = 0.00). With high compliance and safety, concomitant therapy cure rates vary significantly between locations and populations. Concomitant therapy has several limitations, though: (a) The concomitant therapy comprises metronidazole and clarithromycin, two antibiotics with generally low tolerability (b) the treatment duration (10 or 14 days) is fairly long; (c) Three different antibiotics that must be given discretely; (d) complex schedule of antibiotics must be thoroughly explained to patients in order to ensure adherence. All studies that looked at concomitant therapy before were done in hospitals[16-18]. The majority of Helicobacter pylori treatments are provided at the primary care level, hence it is crucial to determine if concomitant therapy retains its efficacy on administering in a primary care setting. There are still several challenges that require more research. The limited data shows that the main factor influencing the efficacy of concomitant therapy is the dual resistance to clarithromycin and metronidazole. Furthermore, it was uncertain how long this therapy should last and how much should be the dosage of PPI. Only a few research have examined the variables affecting the efficacy of concomitant therapy, and effect of some of these variables, such as P450 isoenzyme 2C19 gene polymorphism, are still unknown.[19-21] It is necessary to assess

how much a concomitant therapy will cost. Analysis is made more difficult due to variations in patient recruitment, H. pylori detection techniques, dosages, duration, frequency, relationship to dietary intake and background antibiotic resistance. Similar to sequential and hybrid therapies, Concomitant therapy is equally effective, compliant, and safe.

CONCLUSION

Concomitant therapy has a high compliance and efficacy and is a secure treatment choice. Future research should focus on the cost-effectiveness and the efficacy of eradication in areas with high levels of antibiotic resistance.

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