

# Comparison between Conventional Triple Therapy VS Sequential Therapy on Tolerance of Treatment and Eradication of Helicobacter Pylori Infection

Different Drugs  
Therapy for  
Helicobacter  
Pylori

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## ABSTRACT

**Objective:** To compare the efficacy of sequential therapy (levofloxacin) and triple therapy (clarithromycin) in treatment of helicobacter pylori eradication.

**Study Design:** Randomized Control Trial (RCT)

**Place and Duration of Study:** This study was conducted at the gastroenterology department of Nishtar hospital Multan from January, 2020 to December 2020 for a period of one year.

**Materials and Methods:** One hundred and forty diagnosed patients of H. pylori were selected for study. Patients were divided into two groups ST group and TT group by lottery method. Levofloxacin and clarithromycin were used. Patients' compliance and adverse effects were compared in both groups. SPSS software with version 23 was used for data analysis. Significant probability value  $\leq 0.05$  was considered.

**Results:** Antral gastritis, pangastritis, duodenitis, hiatus hernia and GERD of sequential group was observed as 61.4%, 25.7%, 10%, 21.4% and 45.7%, respectively. While, antral gastritis, pangastritis, duodenitis, hiatus hernia and GERD of standard group was observed as 50%, 27.1%, 15.7%, 20% and 50%, respectively. The differences were statistically insignificant.

**Conclusion:** Sequential therapy with levofloxacin is more effective in treatment of H pylori eradication as compared to conventional triple therapy with clarithromycin. Tolerability of sequential therapy is also better than conventional triple therapy. Great resistance has found against clarithromycin in Pakistani population.

**Key Words:** Helicobacter pylori, Sequential therapy, conventional triple therapy, Gastritis, GERD

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## INTRODUCTION

H. Pylori infection caused by Helicobacter pylori is main cause of disorders in upper gastrointestinal region<sup>1</sup>. Recent literature on this topic shows that many extragastric problems and disorders including cardiovascular, neurodegenerative, metabolic,

pancreatic, hepatobiliary and colorectal diseases are due to h. pylori infection<sup>2</sup>. In addition to rheumatic disease it also develops many skin diseases like urticaria and skin allergies<sup>3</sup>.

Its treatment and removal include multiple therapies among them most common and effective is triple therapy (TT). Triple therapy consist of amoxicillin (1g/12h), clarithromycin (500mg/12h) and proton pump inhibitor (PPI) (rabeprazole 20mg/12h, lansoprazole 30mg/12h, esomeperazole 40mg/24h, omeprazole 20mg/12h, pantoprazole 40mg/12h) for at least 14 days<sup>4,5</sup>.

Multiple studies have been conducted on duration of treatment; in a meta-analysis it was recommended that 14 days eradication therapy is 5% more effective and successful than 7 days treatment therapy<sup>6</sup>. Metronidazole is also effective that can be used in cases of allergic to penicillin. A recent survey on worldwide emergence on resistance development against antibiotic confirms that H. pylori eradication rate is reducing with increase in development against antibiotic<sup>7,8</sup>.

A recent Egyptian study conducted in Mansoura gastroenterology surgical center on 82 patients that were admitted with upper gastrointestinal symptoms. Biopsy samples were taken with endoscopy and sent to

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laboratory for culture developments and analysis for *H. pylori*<sup>9</sup>. It was found that 71% strains of *H. pylori* were resistant against clarithromycin which is primary treatment modality regime against *H. pylori*<sup>10</sup>.

## MATERIALS AND METHODS

Study was completed in of gastroenterology department of Nishtar hospital Multan from 1<sup>st</sup> January to 31<sup>st</sup> December 2020 in one-year duration. Study was started after permission from hospital ethical review board of hospital. Consent was taken from the patients after detailed information about the goals and purpose of study. Non probability consecutive sampling technique was used. Patients were diagnosed with campylobacter test and C13 urea breath test. Pregnant women, age less than 18 years, history of previous gastric surgery, lactating mothers and previous history of eradication therapy of *H. pylori* were excluded from the study.

Clinical examination, detailed medical and drug history was taken. Examination of esophagus, stomach, duodenum and upper GI was done with endoscopy. C13 breath test was performed on all patients. A sample of corpus of stomach and antrum was taken for biopsy. Patients were divided into two groups (ST group and TT group) by lottery method. Group ST patients were given 30mg lansoprazole (proton pump inhibitor) per 12 hours and 1-gram amoxicillin 12 hourly for initial five days and after that 30mg lansoprazole 12 hourly plus 500mg levofloxacin 24 hourly with 500 mg tinidazole 12 hourly for 5 days.

Patients in TT group were given proton pump inhibitor 30mg lansoprazole 12 hourly, 1g amoxicillin 12 hourly plus clarithromycin 500mg 12 hourly for 14 days. All patients were counseled for possible side effects and asked for good compliance. Adverse effects may include, abdominal pain, bitter taste, abdominal bloating, general weakness, epigastric pain, diarrhea, dizziness, constipation, headache, loss of appetite, skin eruptions, nausea, vomiting, mucosal ulcer and increased sleeping tendency. Compliance below 80% was considered as termination of therapy. C13 urea test and response of therapy was evaluated after 6 weeks termination of therapy.

SPSS software with version 23 was used for determination of mean and standard deviation for quantitative variables like age, weight and frequency percentages were calculated for qualitative data like gender, nausea, vomiting, epigastric pain, and diarrhea. Tests of significance (T test and chi-square test) were applied to see the association among variables. Significant probability value  $\leq 0.05$  was considered.

## RESULTS

One hundred and forty patients were included in this study, both genders. The patients were divided into two groups as sequential  $n=70$  and standard  $n=70$ . The mean age of sequential group was  $35.43 \pm 4.22$  years. There

was  $n=48$  (68.6%) males and  $n=22$  (31.4%) females. Smoking status, epigastric pain, nausea, vomiting, heart burn and hematemesis was noted as  $n=30$  (42.9%),  $n=51$  (72.9%),  $n=16$  (22.9%),  $n=21$  (30%),  $n=20$  (28.6%) and  $n=1$  (1.4%), respectively. Mean age of standard group was  $33.08 \pm 4.99$  years. There was  $n=49$  (70%) males and  $n=21$  (30%) females. Smoking status, epigastric pain, nausea, vomiting, heart burn and hematemesis was noted as  $n=22$  (31.4%),  $n=48$  (68.6%),  $n=21$  (30%),  $n=10$  (14.3%),  $n=19$  (27.1%) and  $n=0$  (0%), respectively. Statistically insignificant difference was observed except vomiting ( $p=0.025$ ). (Table. 1).

Antral gastritis, pangastritis, duodenitis, hiatus hernia and GERD of sequential group was observed as  $n=43$  (61.4%),  $n=18$  (25.7%),  $n=7$  (10%),  $n=15$  (21.4%) and  $n=32$  (45.7%), respectively. While, antral gastritis, pangastritis, duodenitis, hiatus hernia and GERD of standard group was observed as  $n=35$  (50%),  $n=19$  (27.1%),  $n=11$  (15.7%),  $n=14$  (20%) and  $n=35$  (50%), respectively. The differences were statistically insignificant. (Table. 2). Response to treatment of *Helicobacter pylori* by C13- urea breathe test and termination of therapy because of adverse effects of both groups were shown in table 3. The differences were statistically significant except termination of therapy because of adverse effects ( $p=0.649$ ). (Table. 3). Nausea, vomiting, abdominal pain and diarrhea of sequential group was observed as  $n=2$  (2.9%),  $n=14$  (20%),  $n=3$  (4.3%) and  $n=5$  (7.1%), respectively. While, nausea, vomiting, abdominal pain and diarrhea of standard group was observed as  $n=4$  (5.7%),  $n=10$  (14.3%),  $n=0$  (0%) and  $n=6$  (8.6%), respectively. The differences were statistically insignificant (Table. 4).

**Table No.1: Demographic characteristics and clinical presentation of both groups**

Variable	Sequential n=70	Standard n=70	P-value
Age (years)	$35.43 \pm 4.22$	$33.08 \pm 4.99$	0.985
Gender			
Male	$n=48$ (68.6%)	$n=49$ (70%)	0.855
Female	$n=22$ (31.4%)	$n=21$ (30%)	
Smoking status	$n=30$ (42.9%)	$n=22$ (31.4%)	0.467
Epigastric pain	$n=51$ (72.9%)	$n=48$ (68.6%)	0.577
Nausea	$n=16$ (22.9%)	$n=21$ (30%)	0.338
Vomiting	$n=21$ (30%)	$n=10$ (14.3%)	0.025
Heart burn	$n=20$ (28.6%)	$n=19$ (27.1%)	0.879
Hematemesis	$n=1$ (1.4%)	$n=0$ (0%)	0.316

**Table No.2: Endoscopic characteristics of both groups**

Variable	Sequential n=70	Standard n=70	P-value
Antral gastritis	$n=43$ (61.4%)	$n=35$ (50%)	0.173
Pangastritis	$n=18$ (25.7%)	$n=19$ (27.1%)	0.848
Duodenitis	$n=7$ (10%)	$n=11$ (15.7%)	0.313
Hiatus hernia	$n=15$ (21.4%)	$n=14$ (20%)	0.835
GERD	$n=32$ (45.7%)	$n=35$ (50%)	0.612

**Table No.3: Response to treatment of Helicobacter pylori by C13- urea breathe test of both groups**

Parameters	Sequential n=70	Standard n=70	P-value
Responders	n=66 (94.3%)	n=51 (72.9%)	0.001
Nonresponses	n=4 (5.7%)	n=19 (27.1%)	
Termination of therapy because of adverse effects			
Termination of therapy	n=2 (2.9%)	n=3 (4.3%)	0.649

**Table No.4: Adverse effects of the treatment of both groups**

Parameters	Sequential n=70	Standard n=70	P-value
Nausea	n=2 (2.9%)	n=4 (5.7%)	0.404
Vomiting	n=14 (20%)	n=10 (14.3%)	0.370
Abdominal pain	n=3 (4.3%)	n=0 (0%)	0.080
Diarrhea	n=5 (7.1%)	n=6 (8.6%)	0.753

## DISCUSSION

In Pakistani population limited data is available about incidence rate and eradication modalities of *H. pylori* which are may be because of unaffordability of medical treatment in remote areas or lack of awareness. Main contributing factors are low socioeconomic status, rural and tribal areas residence. In 2008 a study was conducted by EI Dine et al<sup>11</sup> on seroprevalence of *H. pylori* and reported 91.7% seroprevalence. It was also found that positivity of *H. Pylori* varies with variation in age advance or older.

High prevalence rate and complications associated with treatment of *H. pylori* are deep concerns of eradication therapy. In 2018 a study was completed by Waleed et al<sup>12</sup> and compare the sequential triple therapy and conventional triple therapy and reported 91% successful eradication with sequential triple therapy and 71.6% successful eradication with conventional triple therapy. Although patient's compliance is the main contributing factor in treatment of *H. pylori* eradication but literature supports sequential therapy more authentically.

Either conventional or sequential triple therapy used complications are main concern which is associated with both modalities. In our study epigastric pain is the main complaint which is also reported in a study by Karthick et al<sup>13</sup> in 100 cases, out of them 83 reported dyspepsia. *H. Pylori* Prevalence was 73.41% in this study.

Detailed literature search shows a serial association among gastritis and *H. Pylori*. In 2009 Diab et al<sup>14</sup> conducted a study and reported that 82.9% patients of gastritis diagnosed as *H. Pylori* positive. Our study also shows association with gastroesophageal reflux disease (GERD) and *H. pylori*. In a study completed by Corley et al<sup>15</sup> reported that *H. Pylori* infection also associated with GERD have direct association that's why patients of casual symptoms of GERD must be considered for

*H. Pylori* investigations and symptomatic treatment before starts of triple eradication therapy.

A study in 2014 by Rubenstein et al<sup>16</sup> reported that there is no association between GERD and *H. Pylori*. Findings of this study were in contrast with our results. Similarly, in a study by Grande et al<sup>17</sup> shows association between GERD, esophagitis and *H. pylori* but results were not significant.

Another study was conducted by Marzio et al<sup>18</sup> and concluded that symptoms of *H. pylori* are same in every case. No specific association was observed between symptoms of *H. pylori*. In a study conducted by Mayasa et al<sup>19</sup> compared regimes of our study (clarithromycin and levofloxacin) in eradication of *H. Pylori* infection and found success rate of Clarithromycin 71% and Levofloxacin 23.2%.

In a study conducted by Polat et al<sup>20</sup> compared sequential triple therapy and conventional triple therapy and reported 90% successful treatment with sequential therapy and 57% successful treatment with conventional triple therapy. In a Chinese study conducted by Qian et al<sup>21</sup> and reported a successful eradication with sequential therapy (Levofloxacin and proton pump inhibitors). A study was conducted by Zullo et al<sup>22</sup> found more successful eradication of *H. pylori* with sequential therapy as compared to conventional triple therapy. Sequential therapy was given with combination of proton pump inhibitors and levofloxacin in treatment of *H. Pylori* infection.

## CONCLUSION

Sequential therapy with levofloxacin is more effective in treatment of *H pylori* eradication as compare to conventional triple therapy with clarithromycin. Tolerability of sequential therapy is also better than conventional triple therapy. Great resistance have found against clarithromycin in Pakistani population.

### Author's Contribution:

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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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