Comparative Study between Two Triple-therapy Regimens in Treating *Helicobacter pylori*: Related Peptic Ulcer Disease

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**ABSTRACT**

**Background:** *Helicobacter pylori* (*H. pylori*) infection has increased worldwide and it is found to be positive in more than 50% of the specimens taken during endoscopy. The goal of the study is to compare the efficacy of two triple-therapy regimens in eradication of *H. pylori* and to evaluate the cost factor involved.

**Aims:**
- To compare and study between two triple-therapy regimens in treating (*H. pylori*)-related peptic ulcer disease.
- To find the cost efficacy between two triple-therapy regimens.

**Materials and methods:** A randomized single-blinded study was conducted at a tertiary care hospital from 2016 to 2018. Upper gastrointestinal endoscopy was performed on all the patients after spraying them with a topical local anesthetic agent (10% lignocaine spray). Two biopsy specimens were taken from the antrum of the stomach. The rapid urease test (RUT) was considered positive, if a color change from yellow to pink was noted in the RUT kit within 10 minutes. The sample size was calculated and fixed at 60. The RUT-positive patients were divided into two groups by computer-generated random allotment. Group I patients were started on regimen I comprising omeprazole 20 mg twice daily, clarithromycin 500 mg twice daily, and amoxicillin 1,000 mg twice daily for 2 weeks. Group II patients were started on regimen II: OCM: omeprazole 20 mg twice daily, clarithromycin 500 mg twice daily, and metronidazole 400 mg twice daily for 2 weeks. The endoscopic RUT was performed in the beginning and after 6 weeks to check for eradication of *H. pylori*. The ethical committee approval was obtained (EC No. 2017/308) and data were collected using a proforma and were entered in the Excel sheet. The statistical analysis was done by SPSS (version 23). Descriptive statistics regarding age, sex, and inference with regimens were calculated and recorded.

**Results:** Among the patients administered regimen I, *H. pylori* was eradicated in 27 (90%). And among the patients administered regimen II, *H. pylori* was eradicated in 28 (93.3%). This difference was not statistically significant with p value of 0.323. However, it was observed that regimen II was cheaper than regimen I.

**Keywords:** Comparison, Endoscopy, *Helicobacter pylori*, Triple-therapy.

**SBV Journal of Basic, Clinical and Applied Health Science** (2019): 10.5005/jp-journals-10082-02222

**INTRODUCTION**

The identification of *Helicobacter pylori* and its causative connection to peptic ulcer diseases and gastric adenocarcinomas has thoroughly transformed our understanding of these diseases. An increase in metaplasia and atrophy of the stomach mucosa has been found to be linked to the presence of *H. pylori* infections. Both the oxidative and nitrosative pressure in grouping with inflammation plays a key role in the carcinoma of stomach.1 Although immune cells normally identify and attack invading bacteria such as those accumulating as *H. pylori* infection, here they are unable to reach the stomach lining. In addition, *H. pylori* has developed different ways of interfering with local immune responses, making them ineffective in eliminating these bacteria.2,3 *Helicobacter pylori* is a risk factor for the carcinoma of stomach and its eradication reduces the risk of carcinoma.4 The treatment option of *H. pylori* has remained a great challenge for the past 25 years. The first stomach parietal cell proton pump inhibitor (PPI) (omeprazole) was used widely in treating peptic ulcer disease. The S-isomer of omeprazole is esomeprazole, which was the first single optical isomer to be introduced.5-9 On the former, esomeprazole had better results compared to other PPIs.10 Esomeprazole has an advanced level of action against *H. pylori* when compared to other PPIs like omeprazole. Hence, these properties enhance the efficacy in the treatment of *H. pylori*-related peptic ulcer diseases.11-14

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Comparative Study between Two Triple-therapy Regimens in Treating Helicobacter pylori: Related Peptic Ulcer Disease

Materials and Methods
A randomized single-blinded study was conducted at a tertiary care hospital from 2016 to 2018. By universal sampling technique, 60 patients were included in the study as per inclusion and exclusion criteria. The rapid urease test (RUT) and endoscopy were the parameters of assessment. A total of 60 patients who were positive for H. pylori after endoscopy and RUT were divided into two treatment regimens by computer-generated random table number allotment.

Regimen I: OCA: omeprazole (20 mg BD), clarithromycin (500 mg BD), and amoxicillin (1000 mg BD) for 2 weeks.
Regimen II: OCM: omeprazole (20 mg BD), clarithromycin (500 mg BD), and metronidazole (400 mg BD) for 2 weeks.

A RUT during endoscopy was performed after 6 weeks of therapy in patients of both groups to check for eradication of H. pylori.

Inclusion Criteria
- Patients with history of dyspepsia, malena, and/or hematemesis
- Patients having evidence of H. pylori infection by RUT

Exclusion Criteria
- Age less than 16 and more than 80 years
- Pregnant women or lactating women
- Carcinoma or pyloric stenosis on endoscopy
- Cirrhosis

Upper gastrointestinal endoscopy was performed on all the patients after an overnight fasting. Two biopsy specimens were taken from the antrum of the stomach and RUT was done. A positive response was recorded if there was a colour change from yellow to pink in the RUT kit within 10 minutes.

Statistical Methods
The data were collected using a predetermined proforma and followed up for 6 weeks. The data collected were entered through the Excel sheet and the statistical analysis using the SPSS software (version 23) was carried out. Descriptive statistics such as frequency and percentage were calculated. Continuous variables were expressed in mean and standard deviation. Association between various study variables was done by the Chi-square test. A p value of 0.05 or less was taken to indicate a significant difference. Description of statistics: comparison of two triple therapy regimens using the independent sample test.

Ethical Consideration
After obtaining an informed and written consent, the study was conducted. Institutional ethical committee approval was obtained (IEC no. 2017/308) and the copy of the approval is attached in the annexure.

Results
Descriptive Statistics
Age Distribution
In the study population, mean age of the participants was 41.23 with age ranging from 18 to 68. We observed that the patients of third to fifth decade were more affected with H. pylori.

Association of Gender with Regimen
The proportion of males in the treatment regimen II was high compared to the females and vice versa. This difference was not statistically significant with the p value of 0.29.

Regimen Inference
Among the group I patients administered regimen I, H. pylori was eradicated in 27 (90%) and among the group II patients administered regimen II, H. pylori was eradicated in 28 (93.3%). This difference was not statistically significant with p value of 0.323.

Discussion
A total of 60 patients were included in the study, with ages ranging from 18 and 68. Majority were females with 57% and 43% were males. Among them, endoscopic findings suggestive of acid peptic disease were observed in 27 (45%) patients and GERD in 9 (15%).

Among the 60, 30 patients were administered regimen I, with eradication rate of 90%. Regimen II was administered for the other 30 patients, and an eradication rate of 93.3% was observed after 6 weeks. This difference was found to be not statistically significant with a p value of 0.323. This result correlates well with similar other studies.

In a study by Khanal et al., where Tinidazole was used instead of metronidazole for 2 weeks on 80 patients, it was observed that the eradication rates of regimen I and II were 93.8 and 91.4%, respectively.

In the OPTRICON study, Molina-Infante et al. found that addition of metronidazole (400 mg twice daily) to empirical triple therapy [esomeprazole (40 mg twice daily), amoxicillin (1 g twice daily), and clarithromycin (500 mg twice daily) for 2 weeks] had increased eradication rates by 10%. They also said that addition of metronidazole resulted in increased adverse effects.

Alsohaibani et al., in their prospective trial conducted in Saudi Arabia, compared the traditional triple therapy (2 weeks) with the sequential therapy (10 days) for treatment of H. pylori infection. In 65% of the patients, sequential and traditional triple therapies had equal efficacy in the treatment of H. pylori infection. Resistance to metronidazole and clarithromycin for strains of H. pylori is not uncommon.

According to meta-analytical study in a Cochrane review, using high-dose STT therapy showed less efficacy than SEQ therapy in eradication of H. pylori. And concluded that both regimens could not achieve favorable efficiency (≥90% abolition rate).

Yang et al., through their study, concluded that high-dose drug therapy has higher efficacy than standard regimens in the eradication of H. pylori.

Kim et al. studied new advances in eradication rates in H. pylori by first-line triple (one PPI along with two antibiotics) treatment, and the associated factor in eradication of H. pylori has been reduced over the past 10 years. They further concluded that the measures of antibiotic resistance in H. pylori infection have amplified, mainly with reverence to clarithromycin.

In a phase III, randomized, double-blinded study by Murakami et al., vonoprazan (potassium-competitive acid blocker), as a part of first-line and second-line triple treatment for H. pylori, was studied among 650 patients and reported that vonoprazan has high efficacy as part of first-line triple-therapy and also as part of second-line triple treatment for eradication of H. pylori-related peptic ulcer.
The role of addition of bismuth (14-day triple therapy with bismuth) in improving the eradication rates despite the problem of antimicrobial resistance was noted. The bismuth effect added an additional 30–40% to the success of treatment of resistant infections.

Meta-analysis of many other randomized controlled trials showed that *H. pylori* abolition treatment to avoid gastric cancer found out that *H. pylori* decreases the occurrence of carcinoma of stomach in asymptomatic Asian individuals.

Zhang et al. found that the addition of one probiotic to standard treatment was found to improve the *H. pylori* eradication rate.

“The Toronto Consensus” stated that the ideal cure of *H. pylori* infection requires cautious consideration of local antibiotic resistance and the abolition pattern. The quadruple therapy “PAMC” (one PPI and three antibiotics—amoxicillin, metronidazole, and clarithromycin) or “PBMT” (one PPI, one bismuth compound and two antibiotics—metronidazole and tetracycline) should play an additional important function in eradication of *H. pylori*.

**Limitations**

- Study with larger sample size will be of better accuracy.

**Conclusion**

Among the 30 patients who were administered regimen I: OCA (omeprazole 20 mg bid, clarithromycin 500 mg bid, amoxicillin 1000 mg bid for 2 weeks), *H. pylori* was eradicated in 27 (90%) patients. Among the 30 patients who were administered regimen II: OCM (omeprazole 20 mg bid, clarithromycin 500 mg bid, and metronidazole 400 mg bid for 2 weeks), *H. pylori* was eradicated in 28 (93.3%) patients. This difference was not statistically significant with p value of 0.323 and it was observed that the efficacy of both regimens remains significantly equal. Both the regimens can be suggested for abolition of *H. pylori*. However, it was observed that regimen II was less costly than regimen I. Regimen I is also suggested for those *H. pylori*-infected patients who are responsive to penicillin.

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