EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 9
Issue: 8
380-383
Year: 2022

EFFICACY AND SAFETY OF TRIPLE COMBINATION OF PANTOPRAZOLE, AMOXICILLIN, AND CLARITHROMYCIN IN PATIENTS WITH *HELICOBACTER PYLORI* INFECTION

Dr. Ajay Kumar[1], Dr. Dinesh Kansal*[2], Dr. Swatantra Gupta[3] and Dr. Atal Sood[4]

[1]MD (Pharmacology), Medical Officer (Specialist), Department of Pharmacology, Dr Radha Krishnan Govt. Medical College, Hamirpur, Himachal Pradesh.
[2]MD (Pharmacology), Professor & Head, Department of Pharmacology, Dr Rajendra Prasad Govt. Medical College, Kangra at Tanda, Himachal Pradesh.
[3]MD, DM (Gastroenterology), Assistant Professor, Department of Gastroenterology & Hepatology, Dr Rajendra Prasad Govt. Medical College, Kangra at Tanda, Himachal Pradesh.
[4]MD (Pharmacology), Associate Professor, Department of Pharmacology, Dr Rajendra Prasad Govt. Medical College, Kangra at Tanda, Himachal Pradesh.

***Corresponding Author: Dinesh Kansal**
MD (Pharmacology), Professor & Head, Department of Pharmacology, Dr Rajendra Prasad Govt. Medical College, Kangra at Tanda, Himachal Pradesh.

Article Received on 09/06/2022 **Article Revised on 29/06/2022** **Article Accepted on 19/07/2022**

ABSTRACT

Objective: To assess the effectiveness of pantoprazole 40mg twice daily per oral, cap. amoxicillin 1000mg twice daily per oral, tab. clarithromycin 500mg twice daily per oral in the eradication of *Helicobacter pylori*. **Methods:** This prospective, interventional study was conducted in the Department of Pharmacology and Department of Gastroenterology and Hepatology at Dr. R.P.G.M.C. Kangra at Tanda between April 2020 and March 2021. The study was conducted after due permissions from the Institutional Ethics Committee and registration with Clinical Trial Registry- India (CTRI). The study population was the consenting adult patients (18-75 years) of dyspepsia (ulcer or non-ulcer) who were found to be *H. pylori* positive on gastric biopsy belonging to different socio-economic strata. The patients were selected from those coming to gastroenterology OPD. **Results:** Eradication rate of *H. pylori* was 84% at day-14 weeks after treatment was given. Adverse events were recorded in one patient only. **Conclusion:** This study demonstrates that a 14-day pantoprazole, clarithromycin, and amoxicillin is an effective and well tolerated therapeutic approach for *H. pylori* eradication.

KEYWORDS: *Helicobacter pylori*, Duodenal ulcer, Triple regimen.

INTRODUCTION

Helicobacter pylori is a gram-negative, spiral, urease-producing organism. It is the most common cause of chronic gastritis worldwide. *H. pylori* damages gastric mucosa and leads to duodenal ulcer (DU) disease, gastric ulcer (GU) disease, gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue (MALT) lymphoma.[1–3] Essentially all *H. pylori* colonized persons have histologic gastritis, but only ~10–15% patients develop peptic ulceration, gastric adenocarcinoma, or gastric lymphoma.

The epidemiology of *H. pylori* infection is poorly understood. An analysis of 410879 participants from 73 countries from six continents showed overall prevalence of 44.3%. Prevalence was found to be 50.8% in developing countries, 34.7% in developed countries. There was a statistically non-significant decrease in the prevalence in 2009-2016 compared with the 2000-2009 period.[4] In Indian subcontinent, most of the cases are exposed to the infection in childhood and approximately 80% of the general population is infected when they reach adulthood. Epidemiological surveys indicate a "seroprevalence of 20%-50% in children <5 years of age, increasing to 80-90% by the age of 20 years, and remaining constant thereafter.

Several studies have been carried out to evaluate the efficacy of current combination pharmacotherapies for *H. pylori* infection.[5–7] The most common regimens are a combination of a proton-pump inhibitor (PPI) and two antibiotics (triple therapy, TT), or co-administration of these agents with bismuth salts (bismuth-based quadruple therapy, B-QT) for 14 days.[8] Clarithromycin with amoxicillin or metronidazole are the frontline antimicrobial therapy for *H. pylori* eradication. However, resistant strains pose treatment failure and decreased efficacy of these regimens worldwide.[9] Therefore, the

antibiotics should be selected based on the local *H. pylori* resistance.

The present study determined efficacy and safety of triple combination of pantoprazole, amoxicillin, and clarithromycin in patients with *Helicobacter pylori* infection.

METHODS

This prospective, interventional study was conducted in the Department of Pharmacology and Department of Gastroenterology & Hepatology at Dr. R.P.G.M.C. Kangra at Tanda between April 2020 and March 2021. The study was conducted after due permissions from the Institutional Ethics Committee and registration with Clinical Trial Registry- India (CTRI).

The study population was the consenting adult patients (18-75 years) of dyspepsia (ulcer or non-ulcer) who were found to be *H. pylori* positive on gastric biopsy belonging to different socio-economic strata. The patients were selected from those coming to gastroenterology OPD. The patients were excluded if not willing to give written informed consent, pregnant females, lactating females, active alcohol users, patients allergic or with known contraindications to any of study drugs, and/or patients who have already taken either of the above-mentioned *H. pylori* eradication regimens.

All patients of uninvestigated dyspepsia coming to Gastroenterology OPD and who require upper GI Endoscopy (UGIE), underwent UGIE and gastric biopsy. Gastric biopsy was sent for histopathological examination for *H. pylori* infection. The patients were given tab. pantoprazole 40mg twice daily per oral, cap. amoxicillin 1000mg twice daily per oral, tab. clarithromycin 500mg twice daily per oral for 14 days.

Baseline investigations were done in all patients before initiating the treatment and these investigations were repeated after completion of 14 days *H. pylori* eradication treatment (for safety).

Patients were contacted telephonically on the next day of initiating the therapy and were enquired for any discomfort or side effects. If any other investigations were required for 14 days treatment due to any adverse drug reaction or any other reason, which were advised by the physician and not mentioned above were also done. Adverse drug reactions (if any) were also noted on the follow-ups and if deemed necessary the medications were changed appropriately as per physician advice. Adverse drug reactions, blood biochemical parameters and ECG were considered.

The patients were called upon for follow up to undergo 'stool test for *H. pylori* antigen' to confirm the eradication, after a gap of one month following treatment (i.e. in non-ulcer dyspepsia patients treatment was given for 14 days and in ulcer dyspepsia patients treatment was given as 14 days of eradication therapy plus extra one month of pantoprazole 40 mg once daily) with either of above regimens.

Statistical Analysis

The data was entered in Microsoft® excel workbook 2019 and exported into Statistical Package for Social Sciences (SPSS) version 21.0 (IBM, USA) for statistical analysis. The categorical data was expressed as frequency and percentage. Quantitative variables were expressed as mean±standard deviation (SD) and compared between two time-intervals using paired t-test. P-value <0.05 was considered significant.

RESULTS

General characteristics

A total of 36 patients were included in this study. Mean age of the patients was 48.8±13.8 years. Forty-four percent of the patients aged >50 years. Male to female ratio was 1.25:1 (Table 1).

Table 1: General characteristics.

Age Group (years)	No. (%)
<30	4 (11%)
30-40	5 (14%)
40-50	11 (31%)
>50	16 (44%)
Gender	
Male	20 (56%)
Female	16 (44%)

Hemogram

Our study observed that there was no significant difference in hemoglobin TLC (mm3), polymorphonucleocytes, lymphocytes, monocytes, eosinophils, basophils, and ESR at day-14 when compared to baseline (P>0.05) (Table 2).

Table 2: Hemogram.

	Baseline	Day 14	P value
Hemoglobin	11.6±1.9	11.5±2.0	0.175
TLC (mm3)	7506.7±1246.7	8039.2±1257.9	0.075
Polymorphonucleocytes	59.4±4.9	60.5±5.3	0.191
Lymphocytes	32.1±5.0	31.2±5.5	0.294
Monocytes	5.9±1.6	5.8±1.9	0.827
Eosinophils	3.1±1.4	2.9±2.0	0.539
Basophils	0.04±0.01	0.04±0.01	1.000
ESR (mm in 1st hour)	16.5±5.0	17.4±6.3	0.16

Liver function

None of the liver function parameters was significantly different at day-14 compared to baseline (Table 3).

Table 3: Liver function.

	Baseline	Day 14	P value
Serum bilirubin (mg/dl)	0.89±0.20	0.86±0.16	0.209
Serum Bilirubin conjugated(mg/dl)	0.23±0.10	0.23±0.07	1.000
AST (U/L)	35.4±6.3	34.7±9.5	0.453
ALT (U/L)	35.1±7.9	37.1±18.8	0.52
Alkaline Phosphatase(IU/L)	103.4±19.7	104.5±20.7	0.71

Random blood sugar

Random blood sugar (RBS) levels at day-14 were not significantly different from the baseline (122.1±15.5 vs. 124.0±16.1 mg/dl; P=0.612).

Renal function

None of the renal function parameters was significantly different at day-14 compared to baseline (Table 4).

Table 4: Renal function.

	Baseline	Day 14	P value
Serum Urea(mg/dL)	28.8±6.0	29.2±5.8	0.376
Serum Creatinine (mg/dL)	0.85± 0.16	0.83 ± 0.13	0.486

Adverse events

Only one patient had adverse event in this study.

Efficacy

Stool test examination showed efficacy of 83% (Figure 1).

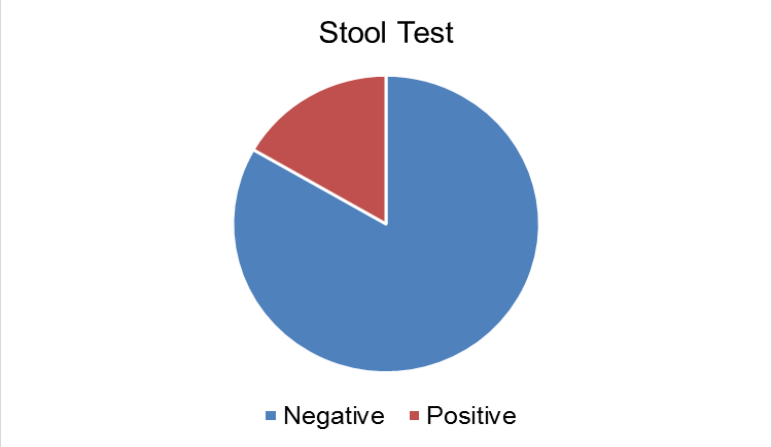

Figure 1: Stool test.

DISCUSSION

For many years, triple therapy combining a proton-pump inhibitor (PPI), amoxicillin and clarithromycin (PAC) for 7–10 days has been the undisputed choice for first-line therapy. In recent years, however, many studies worldwide have found unacceptably low cure rates for this 'classical' or 'legacy' triple therapy. These low cure rates have been linked to the rise in *H. pylori* primary resistance to clarithromycin.

In our study, efficacy of PAC treatment for 14-days was 83%. Ghazzawi et al assessed the effectiveness of a 7-day pantoprazole 40 mg twice a day (bid) plus clarithromycin 500 mg bid and amoxicillin one gram bid therapy in the eradication of *Helicobacter pylori* (*H. pylori*) in patients with *H. pylori* positive duodenal ulcers.[10] They found efficacy of 94% at 4 weeks after treatment was given. Dajani et al determined the efficacy and safety of one-week triple therapy regime consisting of pantoprazole, amoxicillin, and clarithromycin in the cure of *Helicobacter pylori* infection leading to duodenal ulcer disease and/or gastritis.[11] Overall eradication rate for *H. pylori* was 93%.

In our study, only one patient had adverse event in the form of raised liver enzymes. Labenz et al reported that 29 patients out of 60, reported 51 adverse events that were mostly mild to moderate.[12] Ghazzawi et al

reported that there was an improvement in gastrointestinal symptoms and adverse events were recorded in 5 patents only; however, in no case was withdrawal of treatment necessary.[10]

CONCLUSION

In conclusion, triple combination of pantoprazole, amoxicillin, and clarithromycin in patients with *Helicobacter pylori* infection is safe and effective in our population where there is low antibiotic resistance.

REFERENCES

1. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of *Helicobacter pylori* infection--the Maastricht IV/ Florence Consensus Report. *Gut*., 2012; 61(5): 646-664. doi:10.1136/gutjnl-2012-302084
2. Malfertheiner P, Chan FKL, McColl KEL. Peptic ulcer disease. *Lancet*., 2009; 374(9699): 1449-1461. doi:10.1016/S0140-6736(09)60938-7
3. Fock KM, Graham DY, Malfertheiner P. *Helicobacter pylori* research: historical insights and future directions. *Nat Rev Gastroenterol Hepatol*. 2013;10(8):495-500. doi:10.1038/nrgastro.2013.96
4. Zamani M, Ebrahimtabar F, Zamani V, et al. Systematic review with meta-analysis: the worldwide prevalence of *Helicobacter pylori* infection. *Aliment PharmacolTher*, 2018; 47(7): 868-876. doi:10.1111/apt.14561
5. Gisbert JP, González L, Calvet X, et al. Proton pump inhibitor, clarithromycin and either amoxycillin or nitroimidazole: a meta-analysis of eradication of *Helicobacter pylori*. *Aliment PharmacolTher*, 2000; 14(10): 1319-1328. doi:10.1046/j.1365-2036.2000.00844.x
6. Fischbach LA, van Zanten S, Dickason J. Meta-analysis: the efficacy, adverse events, and adherence related to first-line anti-*Helicobacter pylori* quadruple therapies. *Aliment PharmacolTher*, 2004; 20(10): 1071-1082. doi:10.1111/j.1365-2036.2004.02248.x.
7. Wang F, Feng J, Chen P, et al. Probiotics in *Helicobacter pylori* eradication therapy: Systematic review and network meta-analysis. *Clin Res Hepatol Gastroenterol*, 2017; 41(4): 466-475. doi:10.1016/j.clinre.2017.04.004.
8. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of *Helicobacter pylori* infection-the Maastricht V/Florence Consensus Report. *Gut*, 2017; 66(1): 6-30. doi:10.1136/gutjnl-2016-312288.
9. Mégraud F. H pylori antibiotic resistance: prevalence, importance, and advances in testing. *Gut*, 2004; 53(9): 1374-1384. doi:10.1136/gut.2003.022111.
10. Ghazzawi IM, Obeidat WA, Zuriekat FA. Triple therapy with pantoprazole, clarithromycin and amoxicillin for eradication in patients with *Helicobacter pylori* positive duodenal ulcers. *Saudi Med J*. 2004; 25(8): 1006-1009.
11. Dajani AI, Awad S, Ukabam S, et al. One-week triple regime therapy consisting of pantoprazole, amoxicillin and clarithromycin for cure of *Helicobacter pylori*-associated upper gastrointestinal diseases. *Digestion*, 1999; 60(3): 298-304. doi:10.1159/000007675
12. Labenz J, Tillenburg B, Weismüller J, Lütke A, Stolte M. Efficacy and tolerability of a one-week triple therapy consisting of pantoprazole, clarithromycin and amoxycillin for cure of *Helicobacter pylori* infection in patients with duodenal ulcer. *Alimentary Pharmacology & Therapeutics*. 1997; 11(1): 95-100. doi:10.1046/j.1365-2036.1997.130301000.x