Original Article

Comparing the Efficacy of Standard Triple Therapy with Proton Pump Inhibitor and Vonoprazan and Amoxicillin Dual Therapy for Helicobacter Pylori Eradication

Muhammad Mumtaz Ather[1], Muhammad Tahir[2], Talha Rasheeq[2], Shahid Mukhtar[3], Aamena Gardazi[3] and Muhammad Ibrahim[4]

ABSTRACT

Objective: To compare the effectiveness of dual therapy with amoxicillin plus vonoprazan and standard triple therapy with amoxicillin, clarithromycin and proton pump inhibitor in terms of *H Pylori* eradication.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the Department of gastroenterology in Bakhtawar Amin Medical & Dental College, Multan, from October 2021 to September 2022.

Materials and Methods: A total of 84 patients diagnosed as positive for Helicobacter Pylori infection through stool antigen test. Grouping of patients was done by lottery method in group A and B. In group A Vonoprazan and amoxicillin was given and in group B Amoxicillin with clarithromycin and proton pump inhibitor (PPI) were given. Main variables of study were Stool antigen (positive/negative), Bloating, diarrhea and nausea vomiting. SPSS version 24 was used for data analysis.

Results: The average age of Group A and Group B was 39.12±3.22 years and 38.51±2.84 years respectively. Male proportion is higher in both groups. In Group A, 71.4% patients had negative HP stool Ag and 59.5% patients had negative HP stool Ag, in Group B. (p>0.050). The prevalence of diarrhea, nausea vomiting and bloating in both the groups were 14.3% vs. 9.5%, 16.7% vs. 14.3% and 16.7% vs. 2.4 respectively (p>0.050).

Conclusion: Vonoprazan and amoxicillin dual therapy is better as compare to conventional triple therapy for h pylori eradication. In this era of rapidly developing antibiotic resistance, use of Vonoprazan based dual therapy for h pylori eradication is potentially new 1st line treatment.

Key Words: Helicobacter Pylori, Proton Pump Inhibitors, Amoxicillin, Clarithromycin, Vonoprazan

Citation of article: Ather MM, Tahir M, Rasheeq T, Mukhtar S, Gardazi A, Ibrahim M. Comparing the Efficacy of Standard Triple Therapy with Proton Pump Inhibitor and Vonoprazan and Amoxicillin Dual Therapy for Helicobacter Pylori Eradication. Med Forum 2022;33(12):101-104.

INTRODUCTION

Helicobacter pylori also named as H pylori is a microaerophilic gram negative bacteria that can cause gastric mucosa inflammation is the main cause of peptic ulcer disease in the world[1].

It lives in form of colonies in gastric mucosa and responsible for gastric diseases like lymphoma of lymphoid tissue, adeno-carcinoma of gastric region and chronic gastritis[2]. Prevalence rate of h pylori varies from 30 to 50 percent in developed countries and 85 to 95 percent in developing countries[3].

Eradication therapy is recommended in patients with evidence of h pylori active disease; number of antibiotics is in practice for the treatment of h pylori[4]. Some of these regimens like triple therapy with PPI and combination of two antibiotics like amoxicillin with metronidazole or clarithromycin have high eradication rate and considered as best eradication therapy[5]. After decreased in eradication efficacy of these treatment plans other therapies have been practiced[5].

Failure to maintain PH above 7.5 and development of resistance against antibiotics are during treatment period is main reasons of decreased in efficacy[6]. Maintenance of high pH is achieved by using double dose of PPI in all treatment regimens[7]. Since the day of PPI efficacy was approved over non PPI treatment use of antisecretory medication along with antibiotics is recommended. Among antisecretory drugs Vonoprazan potassium based acid blocker is common[8].

1. Department of Gastroenterology / Internal-Medicine[2] / Medicine[3], Bakhtawar Amin Medical & Dental College, Multan.
4. Department of Biochemistry, Bahauddin Zakariya University, Multan.

Correspondence: Dr. Muhammad Tahir, Associate Professor of Internal-Medicine, Bakhtawar Amin Medical & Dental College, Multan.
Contact No: 03336169287
Email: tahir77@gmail.com

Received: October, 2022
Accepted: November, 2022
Printed: December, 2022

Vonoprazan works on contending potassium on luminal side of cells in parietal region and inhibit the HK ATPase and thus prevent the acid excretion[9]. Vonoprazan is more potent that can inhibit acid secretion as compare to PPIs, other advantages include less anti secretory variation, rapid onset and greater tolerability and safety[10]. Main reason behind failure of eradication therapy is local resistance against antibiotics like resistance against clarithromycin was reported 43.9% in a study conducted by Alavifard et al[11].

Since the day of Vonoprazan was used as an alternative of proton pump inhibitor in eradication of h pylori no local study available on this topic before, so this study will be a new gate towards this latest dual therapy and will fulfill this local reference gap.

MATERIALS AND METHODS

Study completed in the department of gastroenterology in Bakhtawar Amin Medical & Dental College, Multan, from October 2021 to September 2022 in one year. After the ethical approval from the ethical review board of hospital data collection was done. Written consent was obtained from the patients after detailed information about the purpose of study and ensuring confidentiality of data. Sample size was calculated by using WHO sample size calculator with 95% confidence interval, 80% power of study, 83.9% eradication with clarithromycin amoxicillin and PPI and 93.5% with Vonoprazan and amoxicillin. Diagnosed patients of H. Pylori infection with C13 urea breath test and campylobacter test were included in the study. Patients with age less than 18 years, allergic to study drugs, breast feeding or pregnant women, alcohol or drug addict, patients with history of previous partial gastrectomy, history of H. Pylori eradication therapy, using psychiatric medicine and malignant neoplasm were excluded from the study.

Endoscopy for upper GI to examine the stomach, esophagus, and duodenum and C13 breath test were taken. A specimen for biopsy of the antrum and corpus of the stomach was taken. Grouping of patients was done by lottery method as group A and B. Patients in group A were given Vonoprazan 20 mg twice daily and one gram amoxicillin was given twice in a day for 14 days. In the B group 20 mg omeprazole (proton pump inhibitor) twice in a day plus one gram amoxicillin twice in a day and calithromycin 500mg twice in a day for fourteen days. Patients were asked for adverse effects and compliance. Adverse effects may include bitter taste, abdominal pain, abdominal bloating, epigastric pain, general weakness , constipation, diarrhea, dizziness, loss of appetite, headache, nausea, skin eruptions, mucosal ulcer, vomiting and sleeping tendency. Termination of therapy was considered when compliance was less than 80%. Response of the therapy was evaluated after 4 weeks of stop of therapy and stool Hp antigen test was used for confirmation. Data analysis was performed on SPSS version 24, variables were classified as numerical (age) and categorical (stool antigen, bloating, diarrhea, nausea vomiting) and represented in form of mean ± SD and frequency percentage. Chi square and t-test were applied to observe association among outcomes. Significant probability value was taken as ≤ 0.05.

RESULTS

Overall, 84 patients enrolled and study patients were equally divided into two groups; Group A and Group B. The average age of Group A and Group B was 39.12±3.22 years and 38.51±2.84 years, respectively. There were more males than females in both the groups (Table. I). In Group A, 30 (71.4%) patients had negative HP stool Ag and 25 (59.5%) patients had negative HP stool Ag, in Group B. (p>0.050) (Figure. 1). The prevalence of diarrhea, nausea and bloating in both the groups were almost equal, (p>0.050) (Table. 2).

Table No.1: Demographic variables among groups

Variable	Group		p-value
	Group A, N (%)	Group B, N (%)	
Age (years)	39.12±3.22	38.51±2.84	0.616
Sex			
Male	30 (71.4)	28 (66.7)	0.637
Female	12 (28.6)	14 (33.3)	

Table No.2: Helicobacter pylori eradication and adverse events of the study groups

Variable	Group		p-value
	Group A, N (%)	Group B, N (%)	
HP stool Ag			
Negative	30 (71.4)	25 (59.5)	0.362
Positive	12 (28.6)	17 (40.5)	
Diarrhea	6 (14.3)	4 (9.5)	0.500
Nausea/vomiting	7 (16.7)	6 (14.3)	0.763
Bloating	7 (16.7)	1 (2.4)	0.026

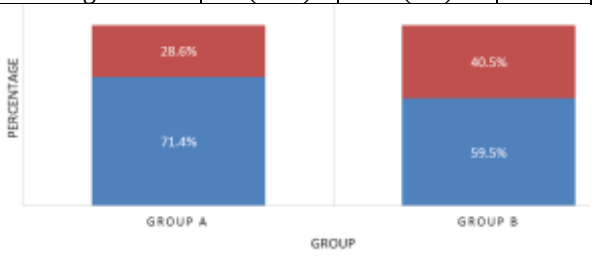

Figure No.1: Helicobacter Pylori Eradication

DISCUSSION

In our study in A group mean age of patients was 39.12±3.22 years and in B group mean age was 38.51±2.84 years, male ratio of patients is higher in both groups. A study was conducted by Suzuki et al[12] conducted a study to compare dual therapy with

Vonoprazan and triple therapy with clarithromycin mean age range of patients was 20 to 79 years in both groups. Eradication of h pylori after 7 days was observed 84.5% in triple therapy and 89.2% in dual therapy. Vonoprazan is not an antibiotic; its role in eradication is because of ability to maintain gastric pH.

In our study 59.5% patients with clarithromycin group have cure rate and in dual therapy 71.4% patients have cure rate. Graham et al[13] reported that cure rate with dual therapy (vonoprazan and amoxicillin) is 80% in patients with clarithromycin resistance. Addition of clarithromycin in dual therapy is associated with 12% cure rate remaining 88% patients used clarithromycin without any benefit. A study by Zuberi et al[14] on comparison of dual therapy with Vonoprazan and amoxicillin with triple therapy by adding clarithromycin and reported 93.5% cure rate with dual therapy and 83.9% by adding clarithromycin.

Adverse effects like bloating, diarrhea and nausea vomiting were also associated with eradication therapy in our study in Vonoprazan group minimal side effects observed. Qiu-Ju Lyu et al[15] conducted a study on this topic and shown minimum incidence of adverse effects in Vonoprazan group. Sakurai et al[16] also conducted similar study and reported higher tolerability with less adverse effects incidence in Vonoprazan group as compare to triple therapy with amoxicillin, PPI and clarithromycin.

In a report by Ozaki et al[17] in 2018 on comparison of Vonoprazan based triple therapy and proton pump based triple therapy and reported more than 90% eradication in Vonoprazan group and 80% in proton pump based triple therapy. Ouyang et al[18] also conducted a study on efficacy of Vonoprazan and reported that H pylori eradication rate with Vonoprazan is acceptable, it is safe to use and limits the unnecessary use of antibiotics. Vanoprazan can be used as an alternate to other regimens of H pylori eradication.

Furthermore, in United States and European countries efficacy of Vonoprazan based triple therapy was observed similar to triple therapy with proton pump inhibitors and its role in eradication of H pylori infection is also well accepted. These observations also support the use of Vonoprazan based eradication therapy in European and American region even in clarithromycin resistant population[19,20].

CONCLUSION

Vonoprazan and amoxicillin dual therapy is better as compare to conventional triple therapy for h pylori eradication. In this era of rapidly developing antibiotic resistance, use of Vonoprazan based dual therapy for h pylori eradication is potentially new 1st line treatment. Its use in terms of eradication rate and adverse effects is acceptable.

Limitations: Single center study with small sample size and poor compliance of patients are main limitations of our study.

Recommendations: More research with on larger number of patients or meta-analysis are recommended to evaluate the role of Vonoprazan with amoxicillin in h pylori eradication.

Author's Contribution:

Concept & Design of Study:	Muhammad Mumtaz Ather
Drafting:	Muhammad Tahir, Talha Rasheeq
Data Analysis:	Shahid Mukhtar, Aamena Gardazi, Muhammad Ibrahim
Revisiting Critically:	Muhammad Mumtaz Ather, Muhammad Tahir
Final Approval of version:	Muhammad Mumtaz Ather

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

REFERENCES

1. Abadi ATB, Ierardi E. Vonoprazan and Helicobacter Pylori Treatment: A Lesson from Japan or a Limited Geographic Phenomenon? Front Pharmacol 2019;10(316):23-45.
2. Hooi JKY, Lai WY, Ng WK, Suen MMY, Underwood FE, Tanyingoh D, et al. Global Prevalence of Helicobacter Pylori Infection: Systematic Review and Meta-Analysis. Gastroenterol 2017;153(2):420-429.
3. Munoz N, Sanchez-Delgado J, Baylina M, Lopez-Gongora S, Calvet X. Prevalence of Helicobacter Pylori Resistance after Failure of First-Line Therapy. A Systematic Review. Gastroenterol Hepatol 2018;41(10):654–662.
4. Wang YC, Chen YP, Ho CY, Liu TW, Chu CH, Wang HY, et al. The Impact of Gastric Juice Ph on the Intraluminal Therapy for Helicobacter Pylori Infection. J Clin Med 2020; 9(6) doi:10.3390/ jcm9061852.
5. Furuta T, Shirai N, Sugimoto M, Ohashi K, Ishizaki T. Pharmacogenomics of proton pump inhibitors. Pharmacogenomics 2004;5(2):181–202.
6. Kato M, Ota H, Okuda M, Kikuchi S, Satoh K, Shimoyama T, et al. Guidelines for the management of Helicobacter pylori infection in Japan: 2016 Revised Edition. Helicobacter 2019: e12597.
7. Kanizaj TF, Kunac N. Helicobacter pylori: future perspectives in therapy reflecting three decades of experience. World J Gastroenterol 2014;20(3): 699–705.
8. Nyssen OP, Bordin D, Tepes B, Pérez-Aisa Á, Vaira D, Caldas M, et al. European Registry on

Helicobacter pylori management (Hp-EuReg): patterns and trends in first-line empirical eradication prescription and outcomes of 5 years and 21 533 patients. Gut 2021;70(1):40-54.

9. Caldas M, Perez-Aisa A, Castro-Fernandez M, Bujanda L, Lucendo AJ, Rodrigo L, et al. European registry on Helicobacter pylori management: effectiveness of first and second-line treatment in Spain. Antibiotics 2020;10(1):13.
10. Jonaitis P, Kupcinskas J, Nyssen OP, Puig I, Gisbert JP, Jonaitis L. Evaluation of the effectiveness of helicobacter pylori eradication regimens in lithuania during the years 2013–2020: data from the European Registry on Helicobacter pylori Management (Hp-EuReg). Medicina 2021; 57(7):642.
11. Alavifard H, Mirzaei N, Yadegar A, Baghaei K, Smith SM, Sadeghi A, et al. Investigation of Clarithromycin Resistance-Associated Mutations and Virulence Genotypes of Helicobacter Pylori Isolated from Iranian Population: A Cross-Sectional Study. Curr Microbiol 2021;78(1): 244–254.
12. Suzuki S, Gotoda T, Kusano C, Ikehara H, Ichijima R, Ohyauchi M, et al. Seven-Day Vonoprazan and Low-Dose Amoxicillin Dual Therapy as First-Line Helicobacter Pylori Treatment: A Multicentre Randomised Trial in Japan. Gut 2020;69(6): 1019-1026.
13. Graham DY, Lu H, Shiotani A. Vonoprazan-Containing Helicobacter Pylori Triple Therapies Contribution to Global Antimicrobial Resistance. J Gastroenterol Hepatol 2021;36(5):1159-1163.
14. Zuberi BF, Ali FS, Rasheed T, Bader N, Hussain SM, Saleem A. Comparison of Vonoprazan and Amoxicillin Dual Therapy with Standard Triple Therapy with Proton Pump Inhibitor for Helicobacter Pylori eradication: A Randomized Control Trial. Pak J Med Sci 2022;38(4):965-969.
15. Lyu QJ, Pu QH, Zhong XF, Zhang J. Efficacy and Safety of Vonoprazan Based Versus Proton Pump Inhibitor-Based Triple Therapy for Helicobacter Pylori Eradication: A Meta-Analysis of Randomized Clinical Trials. Bio Med Res Int 2019;2019. https://doi.org/10.1155/2019/9781212
16. Sakurai Y, Nishimura A, Kennedy G, Hibberd M, Jenkins R, Okamoto H, et al. Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Single Rising Tak-438 (Vonoprazan) Doses in Healthy Male Japanese/ Non-Japanese Subjects. Clin Transl Gastroenterol 2015;6(6):e94.
17. Ozaki H, Harada S, Takeuchi T, Kawaguchi S, Takahashi Y, Kojima Y, et al. Vonoprazan, a novel potassium-competitive acid blocker, should be used for the Helicobacter pylori eradication therapy as first choice: a large sample study of vonoprazan in real world compared with our randomized control trial using second-generation proton pump inhibitors for Helicobacter pylori eradication therapy. Digestion 2018;97(3):212-8.
18. Ouyang Y, Wang M, Xu YL, Zhu Y, Lu NH, Hu Y. Amoxicillin-vonoprazan dual therapy for Helicobacter pylori eradication: A systematic review and meta-analysis. J Gastroenterol Hepatol 2022;37(9):1666-72.
19. Argueta EA, Alsamman MA, Moss SF, D'Agata EM. Impact of antimicrobial resistance rates on eradication of Helicobacter pylori in a US population. Gastroenterol 2021;160(6):2181-3.
20. Nyssen OP, Vaira D, Aísa ÁP, Rodrigo L, Castro-Fernandez M, Jonaitis L et al. Empirical second-line therapy in 5000 patients of the European registry on Helicobacter pylori management (Hp-EuReg). Clin Gastroenterol Hepatol 2022;20(10): 2243-57.