

Eradication of Helicobacter Pylori Infection; The Efficacy of High Dose Vonoprazan and Amoxicillin Dual Therapy

Eradication of Helicobacter Pylori Infection

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ABSTRACT

Objective: This study aims to determine the role of the novel drug vonoprazan base dual therapy in high doses for HP eradication in the Pakistani population.

Study Design: Descriptive-cohort study

Place and Duration of Study: This study was conducted at the Ethical Board Khushal Medical Center Peshawar from September 2022 to February 2023.

Methods: This descriptive cohort study includes 102 HP positive treatment naïve patients. All the patients were given vonoprazan 40mg OD and amoxicillin 1gm BD for 10 days. All the patients were followed for 3 weeks and then re-evaluated. The data were recorded on predesigned proforma and all the data were analyzed using SPSS version 22.0.

Results: In 102 participants, the mean age was 50.2±3.2 years while distribution of males to females was 36.3 and 63.7% respectively. Vonoprazan-based treatment completely eradicated H.P in 84.3% of patients while 15.7% of patients were non-responders. Gender and age does not influence the treatment outcome of the patients (p values >0.05).

Conclusion: High dose vonoprazan plus amoxicillin might be superior to other treatment regimens in the eradication of HP infections particularly in our vicinity.

Key Words: Amoxicillin, dual therapy, Helicobacter pylori infection, vonoprazan

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INTRODUCTION

Helicobacter pylori (HP) is a gram-negative corkscrew shaped bacterium that leads to peptic ulcer disease, gastritis, mucosa-associated lymphoid tissue lymphoma, and gastric cancer. This bacterium affects 50% of the world population^(1, 2). It has been reported that 20-40% of adults in the developed countries and about 90% of adults in developing countries showed positive HP results⁽³⁾. Among the patients presenting with ulcers of gastrointestinal track, HP infection was reported in 85% of gastric ulcers and 95% of duodenal ulcers⁽⁴⁾. HP induced stomach cancer accounts for 75% of the cases worldwide⁽⁵⁾.

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WHO has listed HP as a priority pathogen along with 12 other antibiotic-resistant bacteria families⁽⁶⁾. Treatment is directed towards HP eradication. First-line treatment in regions where high clarithromycin resistance is found is bismuth-based quadruple therapy and non-bismuth concomitant quadruple therapy for 10-14 days. The bismuth quadruple therapy comprises of bismuth, proton pump inhibitor (PPI), and two antibiotics, conventionally metronidazole and tetracycline. Non-bismuth concomitant quadruple therapy consists of a PPI and three types of antibiotics, traditionally including clarithromycin, amoxicillin and metronidazole. The former showed elimination rates with intention to treat analysis (ITT) 74% and per protocol analysis (PP) 93% and the latter showed elimination rates with ITT 87% and PP 94%. Both studies showed greater than 90% eradication in real practice in Europe. The standard PPI-based triple therapy consisting of 14 days treatment with Amoxicillin, Lansoprazole, and Clarithromycin shows ITT eradication of 56% and PP eradication rates of 63%. In areas of low clarithromycin resistance, clarithromycin-containing triple therapy is effective for eradication. The standard triple therapy is still recommended as the first-line by Korean and Japanese guidelines. Other first-line therapies recommended by

international guidelines are Sequential therapy comprising of 5day treatment with PPI, and amoxicillin after that treatment with clarithromycin and tinidazole for 5 days showed 82% ITT and 95% PP eradication rates. The Hybrid therapy containing a 14 days treatment with PPI, Amoxicillin, and last 7 days treatment with clarithromycin, and metronidazole showed ITT 83% and PP 95% eradication rates. The Reverse hybrid therapy comprising of 14days of PPI, amoxicillin therapy with clarithromycin, and metronidazole for an initial 7 days showed 95% ITT and 96% PP eradication rates. A 14days treatment with High-dose PPI-amoxicillin dual therapy gives results of 87% ITT and 92% PP eradication rates. In 2015 in Japan, a new regimen consisting of Vonoprazan-based triple therapy replacing traditional PPI with Vonoprazan showed ITT 89% and PP 90% in its first randomized control trial. Another regimen of Vonoprazan-amoxicillin dual therapy for 7 days shows ITT 85% and 87% PP eradication rate⁽⁷⁾.

Vonoprazan is a potassium-competitive acid blocker inhibiting hydrogen-potassium ATPase, it is acid stable, has a longer half-life compared to PPIs, inhibits both active and resting hydrogen pumps, and Japan has approved it for HP eradication. Vonoprazan-containing triple therapy was better than PPI-containing triple therapy with 15% more eradication⁽⁸⁾. According to a recent meta-analysis, vonoprazan-based triple therapy (Vonoprazan/amoxicillin/clarithromycin) regimen reported >90% eradication in clarithromycin sensitive patients. The same regimen gives >80% eradication rates in clarithromycin resistant patients which is superior to traditional PPI containing triple therapy⁽⁹⁾. A comparison of Vonoprazan-based triple and Vonoprazan-based dual therapy by Suzuki et al shows that the dual therapy had acceptable eradication rates and there were less antibiotic use and fewer effects on gut micro biota⁽¹⁾ hence unnecessary antibiotic use⁽¹⁰⁾. Pakistan has a low socioeconomic status and has a high occurrence of metronidazole and Clarithromycin-resistant HP because of the over-the-counter use of antibiotics especially fluoroquinolones⁽¹¹⁾.

METHODS

The ethical board Khushal Medical Center Peshawar approved the study via letter approved this descriptive-cohort study no. KMC/EBO2/002. The sample size of study was 102 patients and was calculated using who sample size calculator with power of study 80, margin of error 7% and 95% confidence interval. The study duration was 6 months, from September 2022 to February 2023. Newly diagnosed and with no prior treatment, HP positive patients were enrolled in the study. HP stool antigen test were used for diagnosis of the patients⁽¹²⁾. All the patients were counsel verbally in their native language and after guaranteeing their willingness; a proper consent was signed. The

demographics consist of name, age, gender, and HP. Vonoprazan-based dual therapy consisting of Vonoprazan (40mgOD) and Amoxicillin (1g BD) daily for 10 days was prescribed⁽¹³⁾. All the 102 patients included in this study were re-evaluated for the treatment response by the HP stool antigen test after 3 weeks.

Data Analysis: Descriptive statistics were applied to determine mean + SD, frequency, and percentages of variables. Chi-square test was applied to find out any possible association between variables such as gender and age categories with treatment response. SPSS version 22.0 was used for data analysis, and Microsoft Excel was used for the construction of graphs.

RESULTS

Demographics of study participant: In 102 participants, the mean age was 50.2±3.2 year with minimum and maximum ages being 45 and 55 respectively. The study's distribution of males to females was 36.3 and 63.7%. Similarly, 49% of the patients were below 50 years while 51% were above 50 years. Vonoprazan-based treatment completely eradicated H.P in 84.3% of patients while 15.7% of patients were categorized as non-responders. All the details are shown in Table 1.

Table No. 1: Demographics of patients

| Variable | Type | Frequency | % |
|-------------------|----------------|-----------|------|
| Gender | Male | 37 | 36.3 |
| | Female | 65 | 63.7 |
| Age categories | <50 years | 50 | 49 |
| | >50 years | 52 | 51 |
| Treatment outcome | Responders | 86 | 84.3 |
| | Non responders | 16 | 15.7 |

Association of Gender and age with treatment outcome: In this study out of the 37 female patients, 32 had shown response to the treatment and were tested negative for H. pylori after the completion of treatment while 5 patients had tested positive for H. pylori after treatment with Vonoprazan-based dual therapy. Among the male population, 54 had shown eradication of H. pylori while 11 had not responded to the treatment. Chi-square test was applied to determine any association of gender with treatment response, which showed no significant association.

Among age categories, with age < 50years eradication was successful in 43 patients while it was not successful in 07 patients. Similarly, in patients above 50 years, 43 patients showed post-treatment eradication with Vonoprazan-based dual therapy while 9 showed no eradication post therapy. The chi-square test was applied to determine any association of age with HP treatment response, which was non-significant with a p-value > 0.5.

Table No. 2: Association of gender with treatment response

| Variables | Type | Treatment responders | Treatment non-responders | P-value |
|----------------|-----------|----------------------|--------------------------|---------|
| Gender | Female | 32 | 5 | 0.78 |
| | Male | 54 | 11 | |
| Age categories | <50 years | 43 | 7 | 0.71 |
| | >50 years | 43 | 9 | |

DISCUSSION

H.P-induced peptic ulcer is a common disease and is at risk of conversion to mucosa associated lymphoid tissue (MALT) lymphoma. Its eradication is necessary due to the rising number of patients and rising resistance to Clarithromycin. For this reason, new drugs have been introduced over the past few years. Among these, Vonoprazan-based dual therapy has gained popularity as there is less resistance to the therapy and this has resulted in good response in eradication.

The results in this study showed no significant association of gender with treatment response while a study done by Horie et al showed that women harbor a significantly high amount of CAM-resistant HP ⁽¹⁴⁾ showing gender had a role in treatment response especially to clarithromycin, amoxicillin and metronidazole. Similarly, another study conducted by Persons et al reported that female gender has more resistant cases than males, while younger age is more related to metronidazole resistance ⁽¹⁵⁾. There is no evidence of an association of gender to Vonoprazan-based HP eradication in recent studies.

Our study results reveals no impact of age in eradication rates of HP infection but a study done by Caiqiliu et al shows that vonoprazan-based therapy showed more eradication rate in young patients while in older patients the eradication rate with Vonoprazan was lower ⁽¹³⁾.

In our study 86 (84.3 %) of the patients had responded to treatment and HP was completely eradicated. The findings in our study resemble to that of a Japanese study conducted by Suzuki et al, where the eradication rate was 87.1%, and eradication rates for HP -resistant strain with dual therapy were significantly higher than VAC triple therapy (92.3% vs. 76.2%, p=0.048) ⁽¹⁾. Furthermore, our results also resemble to a Chinese study done by Ouyang et al, which showed eradication rate of 87.5% by ITT and 89.6% by per protocol analysis and there were fewer side effects with VA dual therapy compared to VAC triple therapy ⁽¹⁰⁾. A local study conducted by Zuberi et al showed that 93.5% of study population had shown eradication of HP with dual therapy compared to triple therapy which was 83.9% and there were fewer side effects with dual therapy compared to triple therapy ⁽¹⁶⁾.

CONCLUSION

High dose vonoprazan plus amoxicillin might be superior to other treatment regimens in the eradication of HP infections particularly in our vicinity.

Author's Contribution:

Concept & Design of Study: Muhammad Abid Shah

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

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