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ORIGINAL ARTICLE

10 Days Vonoprazan -Amoxicillin Dual Therapy Versus Concomitant (Drugs Regimen) for First Line Helicobacter Pylori Eradication

KAINAT LATIF[1], MURTAZA ALI[2], RIDA NASEER[3], BINISH ANWAR[4], SHAFQAT UR REHMAN ORAKZAI[5], HUMAIRA RAHIM[6]
[1]*Medical Officer Medicine City Medical Centre Thana Road Sanghar Sindh.*
[2]*Medical Officer Consultant Gastroenterologist & Hepatologist DHQ Teaching Hospital KDA kohat*
[3]*Demonstrator, Pharmacology Department Gujranwala Medical College.Gujranwala Pakistan*
[4]*Assistant Professor Pharmacologydepartment Al. Aleem Medical College, Lahore. Pakistan*
[5]*Consultant Gastroenterologist, Naseer Teaching Hospital, Gandhara University Peshawar*
[6]*Assistant Professor Medicine, Med Unit-3, Bolan Medical College Quetta*
Correspondence to: Murtaza Ali, Email: drmurtazaalii@gmail.com

ABSTRACT

Objective: This study was carried out to determine the outcomes of 10 days vonoprazan -amoxicillin dual therapy versus concomitant (drugs regimen) for first line helicobacter pylori eradication.

Material and Methods: This multicentre cross-sectional study was carried out at the DHQ hospital Kohat, from January 2023 to June 2023 after taking approval from the ethical committee of institute. Prior to study each participant provided written, informed permission. A total of 394 Individuals whose age was 18 to 70 years old and had H. pylori infection were included. The rate of various regimens based on the PP, modified intention-to-treat (mITT), and intention-to-treat (ITT) analyses. Overall of 3 participants (one hundred and fifty seven individuals in individual group) were anticipated for acceptance. Taking into account a 10% loss of follow-up. For analysis SSPSS Software was used (version 26.0).variables were presented in the form of percentage (%) and frequencies while continuous variable were shown in mean and standard deviation .comparisons were made using Student's t-test. variables were matched by the Chi-square test. Absolute non-inferiority of the two sets was evaluated using hypothesis testing and derivation of a 2-sided 95% CI. The value of p (0.05) was measured to be statistically significant.

Results: A total of 394 patients diagnosed with Helicobacter were included in this study. Out of them 314 were treated through VA-dual and B-quadruple for further ITT analysis. In the vonoprazan -amoxicillin dual treatment the eradication rate of H. pylori was eighty six (95 % CI: 80.6 to 91.4%, 135/ 157) and 88. (95% CI: 83.1 to 93.3%, 134/154), correspondingly. On other hand drugs regimen (B-quadruple) group eradication was 89.2% (95% CI: 84.3%–94.1%, 140/157) and 91.5 (95% CI: 87.1%–95.9%, 140/153) percent. In the same way PP analysis evolved ninety percent (95% CI: 86.0 to95.6%, 128/141) and 91 percent (95% CI: 86.6–96.0%, 126/138) in the vonoprazan -amoxicillin dual therapy and drugs regimen, correspondingly. The percentage adverse effects in concomitant treatment group was much higher (43.9%) while this was less (21.0%) in 10 day VA-dual therapy group.

Conclusion: Our study concludes that 10-day VA-dual therapy is effective for H. pylori eradication (90 %) with few adverse effects as compared to concomitant (drugs regimen) treatment. It is a promising cost-effective too.

Keywords: vonoprazan -amoxicillin dual therapy, concomitant, Pylori treatment

INTRODUCTION

Helicobacter pylori infects about 50% of people worldwide[1]. Although its incidence is declining globally, certain regions still show high infection and reinfection rates[2].It is the causative agent of diseases like gastritis, peptic ulcer, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer. To prevent these infections, eradication therapy is used worldwide[3-5]. Unfortunately, antibiotic resistance has increased in this bacterium, which has reduced the treatment's eradication impact. In areas with high infection rates, first-line therapy for H. pylori includes four-drug combination regimens including two to three types of antibiotic for 10 to 14 days[6]. There is a major challenge to H. pylori eradication therapy; primarily due to resistance to drugs like clarithromycin[7]. In areas with clarithromycin resistance (15%), primary treatment for H. pylori infections, bismuth-based quadruple (B-quadruple) regimens are still advised by worldwide guidelines and consensus conferences[8]. In order to overcome antimicrobial resistance, first-line B-quadruple treatments use two antibiotics along with bismuth and a proton pump inhibitor (PPI), which together has an eradication rate of over 90%. The use of multiple antibiotics may disrupt the diversity of the fecal micro biota and boost supplementary antibiotic resistance. This could restrict patients' options for rescue regimens when first-line eradication fails[9]. The most straightforward regimen now advised by recommendations is dual therapy, which consists of double-dose Omeprazole and high-dose amoxicillin (3 grams given 3–5 times daily) which shows great promise with a real-world cure percentage that can reach up to 90% in Asian patients who have never had treatment[10]. Low antibiotic resistance and increased intragastric pH caused by high-dose PPI, which enhances the efficacy of amoxicillin[11].

Vonoprazon has demonstrated enormous potential to increase the rate of H. pylori eradication. It is a new potassium-competitive acid blocker that offers a greater and longer-lasting acid inhibitory action than PPI. Research revealed that the 10-day vonoprazan-amoxicillin dual therapy had an inadequate eradication rate of 81.1% by PP analysis[12] Studies have shown comparable eradication rates between the 14-day vonoprazan-amoxicillin regimen and standard therapy[13]. And between the 10-day VA-dual regimen and the daily 10-day B-quadruple regimen and the ten days daily B-quadruplet regimen were demonstrated in subsequent trials[14]. High-quality data comparing the 10-day VA-dual therapy to the 14-day regimen is still lacking. The aim of this study was to determine 10-day vonoprazan-amoxicillin dual therapy versus concomitant drug regimen for first line helicobacter pylori eradication

MATERIAL AND METHODS

This multicentre cross-sectional study was conducted at DHQ Hospital Kohat from January 2023 to June 2023 after obtaining approval from the institutional ethics committee. Prior to the study, each participant provided written informed consent. A total of 394 individuals aged 18 to 70 years and had H. pylori infection were included. Inclusion criteria included: (i) age between 18 and 70 years, (ii) no prior history of Helicobacter pylori treatment; and (iii) confirmation of H. pylori through positive bacterial culture, histological examination, and urea breath test (UBT)

Exclusion criteria included: (i) use of bismuth, acid inhibitors., acid inhibitors, or antibiotics, including H2 receptor antagonists, PPI, or P-CAB four weeks prior to inclusion; (ii)

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lactation or pregnancy; (iii) allergy to any of the investigated medications; (iv) previous gastrostomy; (v) gastric malignancy; (vi) gastro duodenal ulcer with recent bleeding or signs of bleeding within 4 weeks; (vii) preexisting serious diseases or clinical conditions, such as heart disorders, liver or renal dysfunction, etc., that could interfere with the evaluation of study outcomes; and (viii) continuous administration of medication, such as oral midazolam, colchicine, ticagrelor/ranolazine, statins, atazanavir, or lopinavir.

Using a computer-generated random allocation sequence, participants were randomly assigned in a 1:1 ratio to undergo either 14 days of bismuth-based quadruple treatment or 10 days of vanoprazan-amoxicillin dual therapy. The vonoprazan-amoxicillin dual regimens entailed taking 1 gram of amoxicillin three times a day for ten days and 20 mg of vonoprazan twice a day. Vonoprazan was given 30 minutes prior to both meals, and amoxicillin was given 30 minutes after three meals. For a period of fourteen days, the bismuth-based quadruple regimen included 200 mg of colloidal bismuth two fold every day, 500 milligram of clarithromycin, 1 gm of amoxicillin and 10 mg of rabaprazole. The following dosages were given: 30 minutes before breakfast and dinner for rabeprazole and colloidal bismuth, and 30 minutes after for amoxicillin and clarithromycin.

The patients' initial demographics and features were noted. Each patient received comprehensive medical instructions after enrollment, both orally and in writing. They were also told about specific issues that required attention and potential negative outcomes. A follow-up took place after the conclusion of therapy. Negative consequences experienced by patients were documented using a standard questionnaire. At the conclusion of the course, patients were given the task to record and estimate the number of remaining tablets. Another researcher determined the amount that was missing. Eligible patients were required to take 80% of their prescribed medications; otherwise, they would miss two days of the 10-day therapy or three days of the 14-day quadruple therapy with each medicine. In per-protocol (PP) studies, poor compliance was defined as taking less than 80% of the recommended medications and was not included. Based on the Standard Terminology Criteria for Adverse Events[17], the investigator queried and graded the severity of the adverse events using a one to four categorizing scheme.

An assessment of H. pylori status confirmation was carried out using an after treatment ^{13}C-UBT four weeks or more following the last dosage. H. pylori status was assessed using a post-treatment ^{13}C-UBT conducted four weeks after the final dose using an after treatment ^{13}C-UBT four weeks or more following the last dosage. Each patient was reminded to schedule a follow-up examination and an inquiry about the medications they had taken while awaiting post treatment UBT during the fourth week following the final dosage. For H. pylori status, a result below 4% (delta over baseline) was deemed negative.

The study's principal goal was to determine the percentage eradication of various medications based on the PP, modified intention-to-treat (mITT), and intention-to-treat (ITT) analyses. All patients who were randomly assigned were included in the ITT analysis. In the ITT analysis, individuals who were lost during follow-up or who did not have post treatment UBT were considered treatment failures. The mITT analysis comprised all randomized participants who were administered at least one dose of medicine and had their UBT reexamined. Patients who completed post treatment UBT and consumed 80% of the recommended medication were included in the PP analysis. The frequency and intensity of unfavorable occurrences as well as compliance in both groups were the secondary outcomes.

A total of 314 participants (157 in each group) were included were anticipated for acceptance. This accounted for an anticipated 10% loss to follow-up. For analysis SPSS software (version 26.0) was used. Categorical variables were presented as percentages and frequencies while continuous variables were expressed as mean ± standard deviation. Data were compared using Student's t-test or 1-way analysis of variance and Categorical variables were compared using the Chi-square test. Absolute non-inferiority between the two groups was measured through hypothesis analysis (one -sided test) and based on a two-sided 95% confidence interval (CI). A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 394 patients diagnosed with Helicobacter pylori were included in this study. Of these, 314 patients received either VA-dual or B-quadruple therapy and were included in the ITT analysis. Among them, 2 patients in the vonoprazan-amoxicillin dual group and 3 in the B-quadruple group were lost to follow-up, Additionally, 2 patients in the VA-dual group and 1 in the B-quadruple group discontinued treatment due to adverse effects and lacked post-treatment UBT results. These 8 participants were excluded from analysis.

Due to poor compliance (less than 80% of recommended medication taken) 12 patients in Group A and 15 in Group B were excluded from analysis. Baseline characteristics are shown in Table 1. In Group A (VA-dual), 157 patients were enrolled: 72 males and 85 females and In Group B (B-quadruple), 157 patients included 62 males and 95 females. The mean age in Group A was 40.10 years, and 38.64 years in Group B.

In the vonoprazan-amoxicillin dual group, the H. pylori eradication rate was 86% (95% CI: 80.6–91.4%, 135/157) (95 percent CI: 80.6–91.4%, 135/ 157) and 88% (95% CI: 83.0–93.3%, 135/153), respectively. In the B-quadruple group, eradication rates were 89.2% (95% CI: 84.3–94.1%, 140/157) and 91.5% (95% CI: 87.1–95.9%, 140/153). In the same way Per-protocol (PP) analysis showed eradication rates of 90.8% (95% CI: 86.0–95.6%, 128/141) in Group A and 91.3% (95% CI: 86.6–96.0%, 126/138) in Group B. There were no significant differences between the two groups in H. pylori eradication rates as represented in table 2.

Table 1: Standard Features of Study Individual

Variables	VA-dual	B-quadruple	P-value
Gender			0.304
Male	72	62	
Female	85	95	
Age in yrs (mean, ±SD)	38.10± 612.37	38.64 ± 613.60	0.937
Level of Education			0.379
Junior high school or less	25.5%	30.6%	
High school or more	74.5%	69.4%	
Tobacco smoking			0.752
Use of alcohol	14.0%	15.9%	0.88

VA-dua , vonoprazon and amoxicillen dual therapy
B-quadruple, besmuth-based quadruple therapy
From 2 sided comparisons of difference between the VA dual group and B-quadruple groups the value of p was obtained

Table 2: Eradication rates of Helicobacter pylori in each group

Analysis	Vonoprazon and amoxicellin dual treatment n (%)	Bismuth- quadruple treatment n (%)	Difference from B-quadruple (adjusted 95% CI for dissimilarity
Intention to treat	157 (86.0) (80.6%–91.4%)	157(89.2) (84.3%–94.1%)	23.2% (210.5% to 4.1%
Modified intention to treat	141 (88.2) (83.1%–93.3%)	153(91.5) (87.1%–95.9%)	23.3% (210.1% to 3.5%
Per protocol	141(90.8) (86.0%–95.6%)	138(91.3) (86.6%–96.0%	20.5% (27.2% to 6.2%)

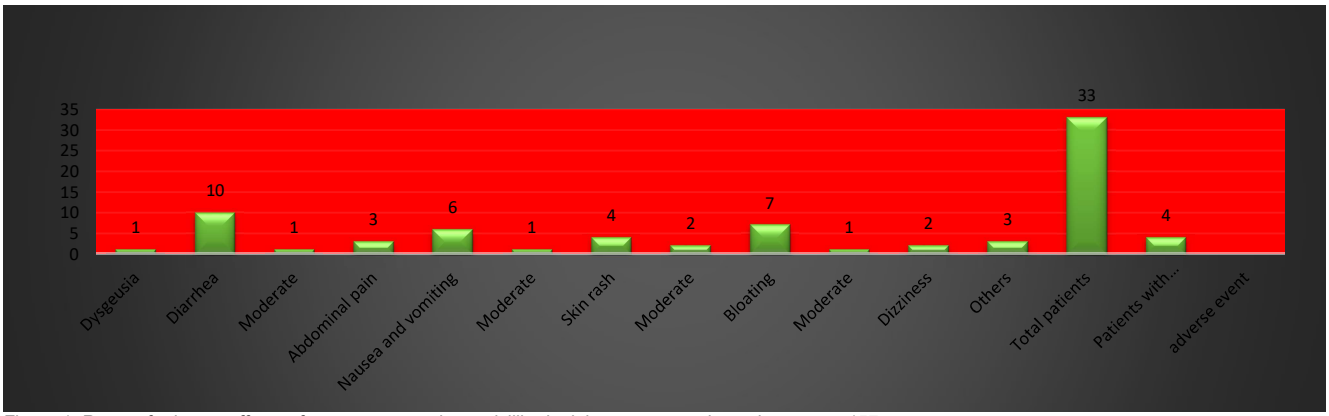

Figure 1: Rates of adverse effects of vonoprazan and amoxicillin dual therapy events in each group n=157

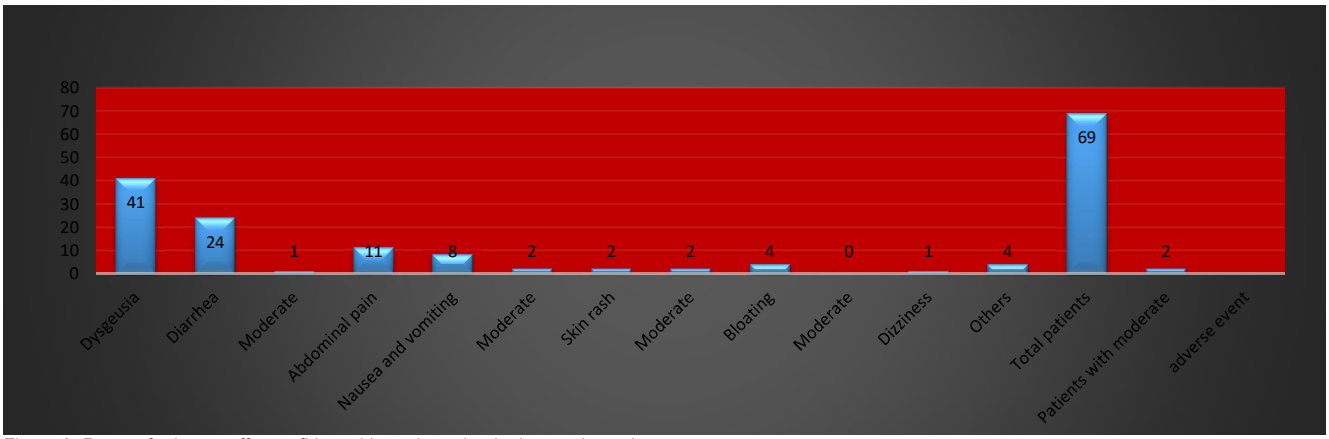

Figure 2: Rates of adverse effects ofbismuthbased quadruple therapy in each group

Adverse Effects: Fig 3 and fig 4 displays the adverse effects of overall patients .the percentage adverse effects in concomitant treatment group was much higher (43.9%) while this was less (21.0%) in 10 day VA-dual therapy group. Among these effects dysgeusia was the most common (26%) in B-quadruple group and 0.6% in VA-dual treatment while the remaining (abdominal pain, nausea and vomiting, skin rash, bloating, dizziness) effects were similar in both groups. 94. % of adverse effects were mild and 5.4% were moderate.

DISCUSSION

This study compared 10-day vonoprazan-amoxicillin dual therapy with 14-day concomitant drug treatment for Helicobacter pylori eradication. Results showed that VA-dual therapy achieved a remarkable eradication rate of 90.8%, outperforming the concomitant regimen. Additionally, VA-dual therapy resulted in fewer adverse effects than the B-quadruple group, particularly regarding diarrhea.

The 10-day vonoprazan-amoxicillin therapy has shown significant advantages over the concomitant regimen in treating H. pylori versus concomitant (drugs regimen). The 10-day VA-dual regimen is highly efficient for population-based H. pylori screening and treatment in Pakistan because in this due to fewer drugs and a shorter treatment duration, resulting in lower healthcare costs as in our study. The cost of the 10-day VA-dual regimen was 700 PKR per patient, compared to 1500 PKR for the B-quadruple regimen so the expenditure discount can be gained in each individual. Secondly, amoxicillin exhibits minimal resistance, fewer side effects, low allergenicity, and limited impact on gut microbiota[15].

Antibiotic sensitivity testing is not required prior to prescribing VA-dual therapy. If eradication fails, alternative treatment options remain available. As compared to high dose proton pump inhibiters taking vonoprazan twice daily can achieve similar gastric pH levels as high-dose PPIs. Its stronger and longer-lasting acid suppression enhances drug efficacy by increasing antibiotic concentration and improving pharmacodynamic activity in the gastric environment[16],[17]. There is a great debate going on the duration and antibiotic prescription among Pylori experts. Recent studies have shown that high-dose amoxicillin (3 g daily) in VA-dual therapy (3g taken daily based vonaprazan -amoxicillin dual therapy from outdated treble and augment regime[18]. A previous study reported a 95% eradication rate with 14-day dual therapy, supporting its clinical potential[18]. However, current evidence debates whether the duration can be reduced to 10 days[19]. In this study, we demonstrated an eradication rate of up to 90% for ten -day treatment and less side effects. These results strongly support the use of medication for shorter period of time as a viable option in Pakistan. Notably, treatment failure in the vonoprazan-amoxicillin group was strongly associated with poor compliance (e.g., 8-day treatment duration) (treatment duration of 8 days), but not in the 2nd group. This suggests that a ten -day course may be the appropriate duration for VA-dual, whereas a 14-day redundant course may be necessary for B-quadruple. It is plausible to hypothesize that rather than inadequate compliance, the failure of B-quadruple eradication may be due to other factors such clarithromycin resistance. Nevertheless, with VA-dual treatment, following the prescription was crucial to eradication success. Notably, this study did not perform antimicrobial susceptibility testing. But amoxicillin resistance is still uncommon, and the VA dual regimen can still be tolerated in the absence of screening for antimicrobial susceptibility[18]. Conversely, Clarithromycin-based concomitant therapy also achieved high eradication rates (>90%) of more than

90 in places with extraordinary levels of resistance to clarethromycin , which lessens the impact of the study's lacking antimicrobial susceptibility testing[20]. VA-dual therapy is contraindicated in patients allergic to penicillin or in areas with high amoxicillin resistance or areas with extraordinary amoxicillin resistance.

CONCLUSION

This study concludes that 10-day VA-dual therapy is effective for H. pylori eradication (90%) and is associated with fewer adverse effects compared to the concomitant regimen. It represents a promising and cost-effective first-line treatment option.

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