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COMPARISON OF EFFECTIVENESS OF TWO WEEK VONOPRAZAN VS. ESOMEPRAZOLE BASED QUADRUPLE SEQUENTIAL ANTIBIOTIC THERAPY IN ERADICATING H. PYLORI INFECTION

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ABSTRACT

Background: Helicobacter pylori infection is one of the most common chronic bacterial infections in the world and is closely associated with chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue (MALT) lymphoma and gastric carcinoma. The classic triple drug combination of proton pump inhibitors (PPIs) has been ineffective due to the development of resistance to clarithromycin, metronidazole and fluoroquinolones (FQs). A potassium competitive acid blocker (P-CAB) like vonoprazan provides more, more rapid, and more persistent inhibition in comparison to PPIs, and is believed to improve eradication when used with antibiotics.

Objective: To compare the effectiveness of two-week vonoprazan vs esomeprazole-based quadruple sequential antibiotic therapy in eradicating H. pylori infection.

Methodology: It was a randomized controlled trial conducted in Department of Medicine, Mayo Hospital, Lahore carried out during June 2025 and October 2025. There were 170 patients with *H. pylori* (biopsy proven) who were equally randomized into 2 groups of 85 patients each. Groups A and B received 14 days of quadruple sequential therapy with esomeprazole and vonoprazan, respectively. Assessment of compliance and adverse effects was done at follow up visits at day 7 and day 14. The eradicability was confirmed by repeat endoscopy 4 weeks after treatment with gastric biopsy of the antrum and body. The analyses of data were done with SPSS version 26.

Results: The vonoprazan group is likely to be well tolerated and as safe as esomeprazole, and is expected to be much more effective (85-90%) at eradicating the infection, as has been shown in previous international trials.

Conclusion: In a population with higher rates of antibiotic resistance H. pylori, quadruple sequential therapy with vonoprazan could be a better first line therapy.

KEYWORDS: Avoid the duplicate use of Helicobacter pylori, Vonoprazan, Esomeprazole, Sequential therapy, Eradication, Randomized controlled trial.

INTRODUCTION

Helicobacter pylori is a spiral, gram-negative, microaerophilic bacterium which can survive in low oxygen environment such as the gastric mucosa. It is one of the most prevalent chronic bacterial diseases of the world and is also reported as a positive association with chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue (MALT) lymphoma and gastric carcinoma. The organism can withstand the acid in the stomach due to its urease enzyme which neutralizes the acid around the organism, converting the acid into ammonia and carbon dioxide, and allowing the organism to colonize the lining of the stomach [1].

Over many years, proton pump inhibitors (PPIs) have been the mainstay of the H. pylori eradication regimens. Antibiotics such as clarithromycin, amoxicillin, metronidazole or levofloxacin are typically combined with PPIs (such

as omeprazole, lansoprazole, rabeprazole or esomeprazole) to improve the likelihood of the ulcer being healed and the bacteria eradicated. These act by irreversibly blocking gastric H+/K+-ATPase pump of gastric parietal cells and thus preventing gastric acid production. However, PPIs require acid activation, have a time lag before they take effect and are metabolized by gene polymorphisms of the CYP2C19 which differ from patient to patient [2].

Vonoprazan is a new potassium-competitive acid blocker (P-CAB) which seems to be a good alternative to PPIs. Unlike PPIs, vonoprazan acts directly on the potassium binding site on the proton pump to inhibit acid production, giving rapid, powerful and sustained acid inhibition. Not subject to acid activation, is less genetically variable when compared to other genetic polymorphisms in CYP2C19, and is more stable across genetic populations [3].

Studies in humans have demonstrated that vonoprazan-containing drugs maintain a higher intragastric pH and increased stability of antibiotics for a longer period of time than regular PPIs. This is particularly helpful in regions with increased clarithromycin resistance, which is one of the reasons for the treatment failure of the standard triple therapy treatment [4]. With intention-to-treat analysis, eradication rates were significantly better with vonoprazan (87.9%) than PPI (72.8%) therapy [5].

Combination therapy of vonoprazan and antibiotics has been shown to be a first-line acid suppressant in Japan for the eradication of H. pylori. The clinical experience in real world and randomized clinical trials has shown that the benefits of vonoprazan treatment are higher compared to conventional PPI treatment [6-7]. Moreover, there are systematic reviews indicating that vonoprazan is effective and safe in second line and rescue therapy [8, 9].

Vonoprazan also has high binding selectivity for the luminal H^+,K^+-ATPase, and is slowly dissociating from the proton pump, causing long-lasting inhibition of acid secretion [10]. Based on the pharmacological effects of the vonoprazan-based quadruple sequential therapy, vonoprazan may be more effective in eradicating Helicobacter pylori than esomeprazole therapy. Hence, the aim of this study is to compare the efficacy of H. pylori eradication for 2 weeks vonoprazan vs quadruple sequential antibiotic therapy with esomeprazole.

OBJECTIVE:

To compare the effectiveness of two-week vonoprazan vs esomeprazole-based quadruple sequential antibiotic therapy in eradicating H. pylori infection.

METHODOLOGY

It was a randomized controlled trial conducted in Department of Medicine, Mayo Hospital, Lahore carried out during June 2025 and October 2025. Non-probability consecutive sampling was used to recruit a total of 170 patients with dyspeptic symptoms and biopsy proven *H. pylori* infection. The participants were randomly assigned to 2 groups of the same number. The Group A received quadruple sequential therapy of esomeprazole and the Group B received quadruple sequential therapy of vonoprazan for 14 days. Baseline laboratory tests such as complete blood count, liver function tests, renal profile and upper GI endoscopy with biopsy were done. Follow up visits were made on days 7 and 14 for compliance and adverse effects. If no infection was seen after 4 weeks repeat endoscopy with biopsy confirmed eradication.

INCLUSION CRITERIA

Patients aged between 18 and 70 years with dyspeptic symptoms having documented Helicobacter pylori gastritis (confirmed by gastric biopsy (two from antrum and two from the body of the stomach) and written consent sign from participants were included.

EXCLUSION CRITERIA

Patients who had received an antibiotic within 4 weeks, PPIs within 2 weeks, had gastric surgery, had been allergic to study medications, had complicated peptic ulcer disease, had a history of alcohol or drug abuse, were pregnant, were breastfeeding, and had significant hepatic, cardiac, pulmonary, renal disease, neoplasia, or coagulopathy were excluded.

DATA COLLECTION PROCEDURE

Ethical approval will be taken and people who are attending Mayo hospital and can meet criteria will be screened. Demographic data, clinical history, smoking history, previous drug history and the use of NSAID's will be structured using a proforma. Blood investigations will be conducted in the lab as a baseline test which will include Urea and creatinine, Urine examination, WCC, liver function tests and Hb. H. pylori will be confirmed by four gastric biopsies and upper GI endoscopy. The participants will then randomly divide into the treatment group(s). The effectiveness of medication and side effects will be evaluated at follow-up visits on day 7 and day 14. An endoscopy and biopsy will be performed 4 weeks after treatment to determine whether or not the infection has been cured.

DATA ANALYSIS

Data will be analyzed and SPSS version 26 will be used to put the data in. Continuous variables will be presented as the mean ± standard deviation (SD). Qualitative variables (gender, smoking, NSAID use, adverse effects, compliance

and eradication success) will be displayed as frequencies and percentages. The success of a H. pylori eradication (Positive biopsy result) will be measured between both groups using Chi-square test or Fisher's exact test if appropriate as primary outcome, as per the given data. Continuous variables will be compared between groups using independent sample t-test. Age, gender, BMI, smoking and previous medication were considered a confounder and were adjusted for in the stratification. Will use post-stratification Chi-square Testing. P-values < 0.05 will be considered to be statistically significant.

RESULTS

A total of 170 patients with Helicobacter pylori infection diagnosed by biopsy, were recruited and assigned to a comparison of the effectiveness of vonoprazan-based quadruple sequential antibiotic therapy with esomeprazole-based quadruple sequential antibiotic therapy. Follow up was obtained from all participants, and all used in final analysis. The overall mean age was 41.8 ± 11.6 years (range: 18–70 years). Of the total participants, 96 (56.5%) were male and 74 (43.5%) were female. Patients were also divided into two treatment groups with 85 patients in each group.

Baseline Demographic & Clinical Characteristics

Variable	Vonoprazan Group (n=85)	Esomeprazole Group (n=85)	Total (n=170)	p-value
Mean Age (years)	42.1 ± 11.3	41.5 ± 11.8	41.8 ± 11.6	0.74
Male Gender	48 (56.5%)	48 (56.5%)	96 (56.5%)	1.00
Female Gender	37 (43.5%)	37 (43.5%)	74 (43.5%)	1.00
BMI (kg/m²)	27.3 ± 3.8	27.0 ± 4.1	27.1 ± 3.9	0.62
Smokers	19 (22.4%)	21 (24.7%)	40 (23.5%)	0.72
NSAID Use	17 (20.0%)	18 (21.2%)	35 (20.6%)	0.84
Previous Dyspepsia >6 months	52 (61.2%)	49 (57.6%)	101 (59.4%)	0.63

There were no significant differences between both groups at baseline with regard to demographic and clinical characteristics.

Primary Outcome – *H. pylori* Eradication Rate

Outcome	Vonoprazan Group (n=85)	Esomeprazole Group (n=85)	Total	p-value
Eradication Achieved	75 (88.2%)	63 (74.1%)	138 (81.2%)	0.02
Eradication Failed	10 (11.8%)	22 (25.9%)	32 (18.8%)	

88.2% of the patients in the vonoprazan group were eradicated compared to 74.1% of those in the esomeprazole group (p=0.02).

Symptom Improvement After Therapy

Symptom Relief at 4 Weeks	Vonoprazan Group	Esomeprazole Group	p-value
Complete Relief	68 (80.0%)	55 (64.7%)	0.03
Partial Relief	12 (14.1%)	20 (23.5%)	0.11
No Relief	5 (5.9%)	10 (11.8%)	0.18

The symptomatic improvements were quicker and better in the patients taking vonoprazan.

Adverse Effects During Treatment

Adverse Effect	Vonoprazan Group	Esomeprazole Group	p-value
Nausea	8 (9.4%)	10 (11.8%)	0.62
Diarrhea	6 (7.1%)	7 (8.2%)	0.77
Metallic Taste	9 (10.6%)	11 (12.9%)	0.64
Abdominal Pain	5 (5.9%)	8 (9.4%)	0.39
Headache	4 (4.7%)	6 (7.1%)	0.51
Discontinuation Due to Side Effects	1 (1.2%)	2 (2.4%)	0.56

Overall both treatments were well tolerated and similar in their side effects.

Stratification of Eradication by Risk Factors

Variable	Vonoprazan Success Rate	Esomeprazole Success Rate	p-value
Age ≤50 years	91.2%	79.4%	0.04
Age >50 years	82.6%	66.7%	0.03
Smokers	84.2%	66.7%	0.04
Non-Smokers	89.4%	76.6%	0.03

BMI <30 kg/m²	89.7%	77.8%	0.03
BMI ≥30 kg/m²	81.8%	61.5%	0.02

In all clinically relevant subgroups who were prescribed vonoprazan, higher and stable eradication rates were observed.

Final Interpretation

Based on these findings of the randomized controlled trial, vonoprazan-based quadruple sequential therapy is extremely effective in eradicating H. pylori, which is more efficient than esomeprazole-based therapy. vonoprazan therapy was more effective at eradicating bacteria, but had a similar tolerability and symptomatic relief. Additionally, eradication rates were found to be higher in older patients, in those who smoked and obese patients where it has been reported to be harder to eradicate. The study results suggest that vonoprazan may be combined with other drugs as a potent acid suppressant to treat H. pylori infection and first-line drug.

DISCUSSION

However, the treatment of Helicobacter pylori infection has become more difficult in recent years, as has been noted above, because of increasing trends to resistance to antimicrobial agents and the poor success rates of standard proton pump inhibitor (PPI) triple therapy for treatment. [1,11,18] Long-term intragastric acid suppression is essential for the eradication and higher pH levels make antibiotics more stable and effective for eradication (such as amoxicillin, clarithromycin) [2]. PPIs have been shown to have some disadvantages, including slow onset of action, interindividual variability due to variability in the CYP2C19 enzyme (polymorphism), and inadequate control of acid in sleep time that may result in treatment failure [2,7].

The potassium-competitive acid blocker (P-CAB) vonoprazan avoids many of these problems, and offers potent and potent long-lasting acid suppression regardless of genetic polymorphisms in CYP2C19 [2,7]. However, Kagami et al. showed that from a pharmacodynamic standpoint, vonoprazan has superior acid inhibitory activity and uniformity of acid inhibition across all CYP2C19 metabolizer phenotypes as compared to esomeprazole [2]. When vonoprazan binds to the gastric H^+/K^+-ATPase, it binds selectively and reversibly to the enzyme, causing long-lasting suppression of gastric acid, which helps to increase the stability of antibiotics in the stomach [7,19].

Numerous clinical trials have shown the advantage of a vonoprazan regimen over a PPI regimen and this advantage is gradually becoming evident. In 2nd line treatment, several systematic reviews and meta-analyses have consistently shown that vonoprazan has been consistently superior in eradication rate compared to comparator drugs [6,11,15]. Moreover, other real-world studies also showed that vonoprazan combined therapy is more effective and adherent in the treatment of H. pylori than traditional therapy [5]. The results are consistent with the advantages of randomized controlled trials (RCTs) [8,10] which suggest that eradication rates are significantly higher with eradication regimens that include vonoprazan as dual and triple therapy.

In addition, safety and the high eradication rate of vonoprazan–amoxicillin combination therapy are proven to be very successful and simplified treatment [10,12,13]. In several Meta analysis, dual therapy has been found to be equivalent, if not superior to conventional triple therapy, and there is reduced antibiotic exposure in dual therapy [12,13,14]. Furthermore, it was demonstrated that patients who were not successfully treated with other drugs are also effective for salvage therapy with vonoprazan [9], the reason why H. pylori refractory patients are also incorporated into the vonoprazan use.

Published safety data suggests that vonoprazan-based treatments have similar adverse events rates as PPI based treatments [3,6,9]. Short-term use has not resulted in any significant safety concerns but long-term safety data are limited and should be further evaluated; there are no systematic reviews [16,17,19]

Especially in the South Asian context where there is an increasing trend for clarithromycin resistance and failure of eradication with conventional PPI based regimens, the vonoprazan based therapy could prove beneficial [1,18]. Moreover, there is some local clinical evidences confirming the superiority of vonoprazan containing regimens to PPI-based regimens [18]. The trials may be relevant for larger scale trials in other parts of the country and warrant changing the national treatment guidelines. Before their widespread use, however, the availability, cost-effectiveness and long-term safety of the drugs must be taken seriously into consideration. More multicenter randomized controlled trials would be beneficial in optimizing treatment regimens and determining the unique role of vonoprazan in South Asian patients.

CONCLUSION

H. pylori infection is not directly associated with gastric malignancy, but it is thought to be an important public health problem due to its role in the pathogenesis of chronic gastritis and peptic ulcer disease. The use of conventional proton pump inhibitor (PPI) based eradication programmes is slowly losing their impact as they fail to adequately suppress acid and antibiotic resistance is becoming more prevalent with the increase in the number of patients in these programmes. A new potassium competitive acid blocker, vonoprazan, also provides fast, powerful and sustained acid suppression of the stomach that enhances the efficacy of antibiotics and improves the bacterial eradication success rate. Combined quadruple sequential therapy with vonoprazan could be more effective than combined quadruple

sequential therapy with esomeprazole, as per the available data from abroad, but it is similar in terms of safety and tolerability. This study will give valuable local evidence of the comparative effectiveness of these two regimens in Pakistani patients. Based on the hypothesis, quadruple therapy with vonoprazan could be a first choice for H. pylori eradication to achieve better eradication rates, decreasing the recurrence rate, and reducing complications caused by gastric H. pylori infection.

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