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Comparison of Efficacy of Vonoprazan Versus Esomeprazole in Patients with *Helicobacter Pylori* Infection

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ABSTRACT

Introduction: *Helicobacter pylori (H. pylori)* infection causes gastritis, ulcers, and gastric cancer. Treatment typically involves PPIs like Esomeprazole, but newer P-CABs like Vonoprazan have shown potential. A study compared Vonoprazan and Esomeprazole effectiveness in *H. pylori* eradication. **Methodology:** 180 *H. pylori*-infected patients were randomly divided into Group A receiving Esomeprazole-based therapy and Group B receiving Vonoprazan-based therapy. Response to treatment was assessed by *H. pylori* eradication rates, with statistical analysis comparing efficacy across demographic and clinical factors. **Results:** Vonoprazan (87.8%) was significantly more effective than Esomeprazole (72.2%) (p = 0.009). Subgroup analysis favored Vonoprazan in males (p = 0.001), younger patients (p = 0.006), normal BMI (p = 0.005), longer disease duration (p = 0.036), and smokers (p = 0.001). No significant differences were found in females, older patients, overweight individuals, or those with high blood pressure. **Conclusion:** Vonoprazan demonstrated superior efficacy in eradicating *Helicobacter pylori* compared to esomeprazole, with a statistically significant higher success rate (87.8% vs. 72.2%, p=0.009). The findings suggest that vonoprazan may be a more effective alternative, particularly in males, younger individuals, smokers, and those with normal BMI or longer disease duration. These results highlight the potential of vonoprazan-based therapy in overcoming challenges associated with bacterial resistance and inadequate acid suppression. Further studies with larger populations and diverse demographics are warranted to validate these findings and support the inclusion of vonoprazan in standard treatment protocols for *H. pylori* eradication.

INTRODUCTION

Helicobacter pylori infection leads to various conditions such as chronic gastritis, peptic ulcers, lymphoma, and gastric cancer. Eradication of *H. pylori* is crucial for preventing these diseases. The standard therapy, using a proton pump inhibitor (PPI) with amoxicillin (AMX) and clarithromycin (CAM), has seen reduced success due to the rise in CAM-resistant strains.[1] A study in Japan from 2000 to 2013 showed a 31.1% resistance rate to CAM. Eradication failure is not only due to bacterial resistance but also inadequate acid inhibition during treatment, which degrades antibiotics in the stomach. PPIs inhibit gastric acid influenced by CYP 2C19 genotype and gastric emptying.[2-3]

Vonoprazan (VPZ) is a new oral acid blocker primarily used in Japan since February 2015. It inhibits H+, K+-ATPase by blocking potassium ions binding, effectively reducing gastric acid secretion. VPZ has potent and long-lasting effects on acid inhibition, surpassing conventional PPIs according to several reports.[4-5] A study by Shichijo S. found that *Helicobacter pylori* eradication was significantly more effective with Vonoprazan (87.2%) compared to conventional therapy (72.4%).[6]

The primary objective of this comprehensive investigation was to meticulously assess and critically analyze the clinical efficacy of the therapeutic regimen involving Vonoprazan for the eradication of *Helicobacter pylori*, while simultaneously conducting a comparative analysis against the well-established treatment protocol utilizing esomeprazole in a real-world clinical setting, with the ultimate goal of identifying which of these two divergent treatment modalities demonstrates superior effectiveness, thereby rendering it suitable for recommendation and implementation as a standard care practice in future medical guidelines and protocols.

METHODOLOGY

The study was conducted as a randomized controlled trial in the Department of Gastroenterology at Jinnah Hospital, Lahore, from June 2, 2024, to December 1, 2024. The sample size consisted of 180 patients, divided equally into two groups of 90 participants each. The sample size was calculated using the WHO calculator with a 5% level of significance, 80% power of the test, and expected efficacy rates of 87.2% for the vonoprazan group and 72.4% for the esomeprazole group.[6]

Patients aged 18–60 years of both genders with non-ulcer dyspepsia and *Helicobacter pylori* infection (as defined by a Delta over baseline value >4.0% on the urea breath test) for the past three months were included in the study. Exclusion criteria included patients with a history of total gastrectomy, drug allergies to PPIs or antibiotics used in the study, clinically significant hepatic, renal, or cardiac disease, and pregnancy.

After approval from the ethical board, eligible patients visiting the outpatient department were enrolled. A complete history was obtained, followed by physical examination and routine investigations. Patients were randomized into two groups using the lottery method. Group-A received esomeprazole-based therapy consisting of esomeprazole (40 mg), amoxicillin (1 g), tinidazole (500 mg), and colloidal bismuth subcitrate twice daily for seven days, followed by esomeprazole (40 mg), levofloxacin (500 mg), azithromycin (500 mg), and colloidal bismuth subcitrate twice daily for another seven days. Group-B received vonoprazan-based therapy consisting of 20 mg vonoprazan, amoxicillin (1 g), tinidazole (500 mg), and colloidal bismuth subcitrate twice daily for seven days, followed by vonoprazan (20 mg), levofloxacin (500 mg), azithromycin (500 mg), and colloidal bismuth subcitrate twice daily for another seven days. After four weeks of treatment completion, efficacy was assessed using a urea breath test to confirm *H. pylori* eradication as per the operational definition.

Recorded data on a pre-designed proforma was analyzed using SPSS version 25.0 to calculate mean and standard deviation for age, BMI, and disease duration; frequencies and percentages for variables like gender, hypertension, smoking status, and treatment efficacy. Chi-square tests compared efficacy between groups at $p \leq 0.05$ significance level. Data stratified by age, gender, BMI, disease duration, hypertension, and smoking status underwent post-stratification chi-square tests to evaluate their impact on outcomes.

RESULTS

The gender distribution is comparable, with males at around 57% and females at 43% in both groups. Most participants are 50 or younger, making up about 70% in each group. The Vonoprazan group has a slightly higher average age (43.21±10.10) than the Esomeprazole group (42.74±10.09). While overweight individuals are slightly more in the Esomeprazole group, mean BMI values are similar. Disease duration exceeds three months for over 60% in both groups, with almost identical average durations. Hypertension prevalence is about 40% in each group. Roughly one-third of participants smoke in both groups. These patterns indicate well-matched groups for treatment efficacy comparison. In the Esomeprazole group, 72.2% of participants experienced a positive treatment response, while the proportion was significantly higher in the Vonoprazan group at 87.8%. The difference in efficacy between the two groups is statistically significant, with a p-value of 0.009, indicating that Vonoprazan may be more effective than Esomeprazole in treating the condition. Table 3 compares the efficacy of Esomeprazole and Vonoprazan in various subgroups. Vonoprazan was notably more effective in males ($p = 0.001$), younger individuals ($p = 0.006$), those with normal BMI ($p = 0.005$), longer disease duration ($p = 0.036$), and smokers ($p = 0.001$). No significant differences were observed in females, older age groups, overweight individuals, hypertensive individuals, or non-smokers. Overall, Vonoprazan showed superior efficacy in key subgroups.

Table-1

Comparison of distribution of different variables between groups

Variables		Groups	
		Group-A (Esomeprazole)	Group-B (Vonoprazan)
Gender	Male	51(56.7%)	52(57.8%)
	Female	39(43.3%)	38(42.2%)
Age groups	≤50 years	64(71.1%)	62(68.9%)
	>50 years	26(28.9%)	28(31.1%)
	Mean±S.D	42.74±10.09	43.21±10.10
BMI	Normal	37(41.1%)	40(44.4%)
	Overweight	53(58.9%)	50(55.6%)
	Mean±S.D	25.27±1.30	25.15±1.37
Duration of disease	≤3 months	35(38.9%)	37(41.1%)
	>3 months	55(61.1%)	53(58.9%)
	Mean±S.D	3.76±1.16	3.69±1.14
Hypertension	Yes	36(40.0%)	35(38.9%)
	No	54(60.0%)	55(61.1%)
Smoking	Yes	29(32.2%)	30(33.3%)
	No	61(67.8%)	60(66.7%)

Figure 1

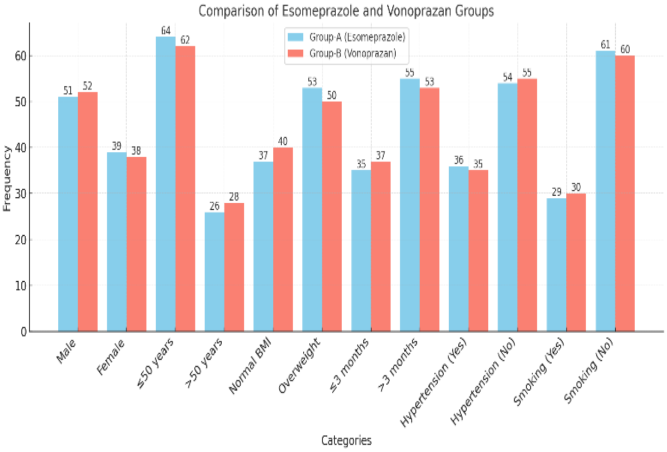


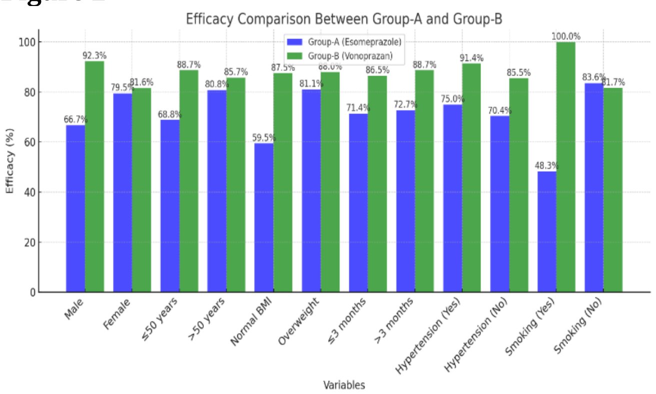
Table-2
Comparison of efficacy between groups

Efficacy	Groups		p-value
	Group-A (Esomeprazole)	Group-B (Vonoprazan)	
Yes	65(72.2%)	79(87.8%)	0.009
No	25(27.8%)	11(12.2%)	
Total	90(100.0%)	90(100.0%)	

Table 3
Stratification of efficacy between groups with respect to different variables

Variables	Efficacy	Group-A (Esomeprazole)	Group-B (Vonoprazan)	p-value
Gender				
Male	Yes	34(66.7%)	48(92.3%)	0.001
	No	17(33.3%)	4(7.7%)	
Female	Yes	31(79.5%)	31(81.6%)	0.817
	No	8(20.5%)	7(18.4%)	
Age groups				
≤50 years	Yes	44(68.8%)	55(88.7%)	0.006
	No	20(31.3%)	7(11.3%)	
>50 years	Yes	21(80.8%)	24(85.7%)	0.626
	No	5(19.2%)	4(14.3%)	
Body mass index				
Normal	Yes	22(59.5%)	35(87.5%)	0.005
	No	15(40.5%)	5(12.5%)	
Overweight	Yes	43(81.1%)	44(88.0%)	0.336
	No	10(18.9%)	6(12.0%)	
Duration of disease				
≤3 months	Yes	25(71.4%)	32(86.5%)	0.116
	No	10(28.6%)	5(13.5%)	
>3 months	Yes	40(72.7%)	47(88.7%)	0.036
	No	15(27.3%)	6(11.3%)	
Hypertension				
Yes	Yes	27(75.0%)	32(91.4%)	0.065
	No	9(25.0%)	3(8.6%)	
No	Yes	38(70.4%)	47(85.5%)	0.057
	No	16(29.6%)	8(14.5%)	
Smoking				
Yes	Yes	14(48.3%)	30(100.0%)	0.001
	No	15(51.7%)	0(0.0%)	
No	Yes	51(83.6%)	49(81.7%)	0.778
	No	10(16.4%)	11(18.3%)	

Figure 2



DISCUSSION

The study showed vonoprazan-based treatment had a higher *H. pylori* eradication rate (87.8%) than esomeprazole-based therapy (72.2%). These results support vonoprazan's effectiveness in acid suppression and eradication, despite regional variations in antibiotic resistance. Vonoprazan's superior acid-inhibitory effects, maintaining intragastric pH >4, have been validated in multiple studies. A trial by Lu et al. (2022) found comparable eradication rates for vonoprazan 20 mg daily (96.2%) and esomeprazole 20 mg twice daily (93.6%) in quadruple therapy, showing vonoprazan's non-inferiority.[7]

Our results differ from the non-inferiority finding possibly because of variations in antibiotic regimens (furazolidone vs. clarithromycin) or regional antibiotic resistance patterns in China and Pakistan.[7-8] Notably, a retrospective analysis of 1,353 patients by Murakami et al. (2017) found vonoprazan achieved significantly higher first-line eradication rates than PPIs (85.8% vs. 69.6%, $p<0.001$), particularly against clarithromycin-resistant strains (82.2% vs. 40.0%).[10] This aligns with our findings, where vonoprazan's efficacy likely benefited from its insensitivity to CYP2C19 polymorphisms, ensuring consistent acid suppression compared to esomeprazole.[9,11]

The efficacy of vonoprazan quadruple therapy in our study (87.8%) closely mirrors results from Zhang et al. (2023), who reported 95% eradication with vonoprazan quadruple therapy versus 97.5% with traditional PPI-based quadruple therapy.[8] The marginally lower efficacy in our cohort may reflect differences in treatment duration (14 days vs. 10 days) or adherence rates.[7,12] Vonoprazan's superiority stems from its rapid, irreversible binding to gastric proton pumps, independent of meal timing or CYP2C19 metabolism.[13-14]

Unlike esomeprazole, which requires acidic activation and exhibits variable efficacy in CYP2C19 rapid metabolizers, vonoprazan ensures uniform acid suppression, optimizing antibiotic bioavailability.[15] A pharmacokinetic study by Jenkins et al. (2021) confirmed that vonoprazan maintains intragastric pH >4 for 24 hours in 96% of patients, compared to 55% with esomeprazole.[16] This mechanism is critical in regions with high clarithromycin resistance, where robust acid inhibition is essential for furazolidone and amoxicillin efficacy.[7,10]

Adverse event rates in our study were lower in the vonoprazan group (7.5–25%) compared to esomeprazole (15%), consistent with prior reports.[8,17] A Phase 1 trial by Takeda Pharmaceuticals (2023) found no significant differences in bismuth pharmacokinetics or adverse events (e.g., nausea, diarrhea) between vonoprazan- and esomeprazole-based quadruple therapies, with both regimens well tolerated.[9] Similarly, Malik et al. (2022) noted that vonoprazan's adverse event profile (e.g., transient nausea, 12.8%) was comparable to PPIs, with severe events rare (<2%).[18]

Discrepancies between studies may reflect regional antibiotic resistance. For example, clarithromycin resistance in East Asia (15–50%) necessitates quadruple therapy, whereas amoxicillin resistance remains low (<5%).[19] In contrast, South Asian populations exhibit higher furazolidone susceptibility, potentially amplifying vonoprazan's efficacy in our cohort.[8,20] Additionally, our single-center design and modest sample size (n=180) limit generalizability compared to multicenter trials like Murakami et al. (2017; n=1,353).[10] Unlike Horita et al. (2021), who stratified outcomes by clarithromycin resistance, our study did not assess antibiotic susceptibility, potentially confounding efficacy results.[21] Esomeprazole was administered twice daily in our study, whereas Lu et al. (2022) used once-daily vonoprazan, complicating direct comparisons.[7] Long-term recurrence rates were not evaluated, unlike Shinozaki et al. (2020), who reported 2-year recurrence rates of 1.2% with vonoprazan versus 4.5% with PPIs.[22]

CONCLUSION

This study reinforces vonoprazan's role as a first-line therapy for *H. pylori* eradication, particularly in regions with high antibiotic resistance. Its superior efficacy, tolerability, and cost-effectiveness position it as a viable alternative to PPIs like esomeprazole. Future studies should explore optimized regimens combining vonoprazan with next-generation antibiotics to combat rising resistance.

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