

Original Article

Comparative Effectiveness of Esomeprazole versus Vonoprazan for *Helicobacter pylori* Eradication: A Multicenter Retrospective Cohort Study in Brazil

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Abstract: *Helicobacter pylori* infection remains a major public health concern and an important risk factor for peptic ulcer disease and gastric cancer. Although proton pump inhibitor (PPI)-based triple therapy has been the standard first-line treatment, eradication rates have declined due to antibiotic resistance and variable acid suppression. Vonoprazan, a potassium-competitive acid blocker (P-CAB), provides more potent and sustained acid inhibition; however, real-world data from Latin American populations are limited. To compare the effectiveness and safety of vonoprazan-based versus esomeprazole-based triple therapy for first-line *Helicobacter pylori* eradication in Brazil. A multicenter retrospective cohort study was conducted including 200 adult patients treated in three Brazilian tertiary centers between 2020 and 2023. Patients received 14-day triple therapy with either esomeprazole 40 mg twice daily or vonoprazan 20 mg twice daily, combined with amoxicillin and clarithromycin. *H. pylori* eradication confirmed by histology eight weeks after treatment was the primary outcome. Secondary outcomes included retreatment rates, adverse events, and treatment adherence. Multivariable logistic regression was used to adjust for potential confounders. Eradication rates were significantly higher in the vonoprazan group compared with the esomeprazole group (94.0% vs. 68.0%, $p < 0.001$), with lower retreatment rates (6.0% vs. 32.0%, $p < 0.001$). After adjustment for age and sex, vonoprazan-based therapy remained independently associated with eradication success (adjusted OR 7.24; 95%CI 3.12–16.81). Adverse event rates were similar between groups, with no severe events reported. In this multicenter real-world cohort, vonoprazan-based triple therapy was associated with significantly higher *H. pylori* eradication rates compared with esomeprazole-based therapy in Brazilian patients.

Keywords: *Helicobacter pylori*; Vonoprazan; Esomeprazole; Eradication Therapy; Observational Study.

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1. Introduction

Helicobacter pylori is a gram-negative bacterium that colonizes the gastric mucosa and is associated with chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue lymphoma, and gastric adenocarcinoma [1]. Despite declining prevalence in

developed regions, infection remains highly prevalent in developing countries, including Brazil, where rates exceed 70% [2]. While triple therapy combining a PPI with two antibiotics has been the cornerstone of treatment, rising antibiotic resistance has eroded eradication rates to 70-85% in most regions [3]. The choice of acid suppressant plays a crucial role in treatment efficacy, as adequate intragastric pH >4 is required for optimal antibiotic activity [4].

Vonoprazan, a novel P-CAB, has demonstrated superior acid suppression compared to conventional PPIs in pharmacokinetic studies [5]. Its unique mechanism of action - reversible potassium-competitive inhibition of H⁺/K⁺-ATPase - provides faster, more sustained acid control regardless of *CYP2C19* genotype [6]. Japanese phase III trials reported eradication rates exceeding 90% with vonoprazan-based regimens [7], but data from Western populations remain limited. Although vonoprazan's pharmacokinetic profile is characteristically independent of *CYP2C19* polymorphisms, offering a theoretical advantage over standard PPIs, we did not perform genetic testing in this cohort. Given the highly heterogeneous genetic background of the Brazilian population, which includes a variable prevalence of rapid and ultrarapid *CYP2C19* metabolizers, the potent acid suppression of P-CABs remains a highly plausible mechanism for the observed results. However, further prospective trials incorporating genotyping are required to definitively prove this association in Latin American populations [5,7].

Helicobacter pylori (*H. pylori*) infection remains a major global health burden, implicated in peptic ulcer disease, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma [3,8]. Eradication therapy, traditionally anchored by proton pump inhibitors (PPIs) like esomeprazole combined with antibiotics, faces challenges due to rising antibiotic resistance and variable PPI metabolic efficacy [6,9]. Vonoprazan, a potassium-competitive acid blocker (PCAB), offers potent and sustained acid suppression independent of cytochrome P450 (CYP) polymorphisms, potentially overcoming limitations of PPIs [7,10].

While recent guidelines acknowledge vonoprazan-based therapies direct comparative effectiveness data against commonly used PPIs like esomeprazole, particularly across diverse populations and resistance patterns, requires robust real-world evaluation [3,8,11-15]. This study aimed to compare the real-world effectiveness and safety of vonoprazan-based triple therapy versus esomeprazole-based triple therapy for first-line *H. pylori* eradication. To fill important evidence gaps, this study: 1. Offers the first Latin American comparative effectiveness data, 2. Assessing practical results in a population with genetic diversity and 3. Evaluating treatment responses based on sex.

2. Methods

The study included adult participants (18 years older) who had confirmed *Helicobacter pylori* infection, either through a positive rapid urease test or histological examination. Participants were required to undergo their first-line eradication treatment and must have complete follow-up data available for analysis. Exclusion criteria were as follows: individuals who had previously undergone *H. pylori* treatment, those who had used proton pump inhibitors (PPIs) within the four weeks prior to testing, pregnant or lactating women, and those with known antibiotic allergies.

Treatment compliance was retrospectively assessed through medical records by verifying the documented pill counts. Across the three tertiary centers, a standardized institutional gastroenterology protocol requires clinicians or clinical pharmacists to record leftover medication at the 2-week post-treatment follow-up visit. Adherence was defined as consuming of the prescribed medication. The treatment protocol involved a 14-day triple therapy regimen for both groups. The group receiving Esomeprazole was treated with 40 mg of Esomeprazole twice daily, 1 g of amoxicillin twice daily, and 500 mg of clarithromycin twice daily. The group receiving Vonoprazan was treated with 20 mg of Vonoprazan twice daily, 1 g of amoxicillin twice daily, and 500 mg of clarithromycin twice daily.

The primary outcome measure was the confirmation of *H. pylori* eradication, verified by histological analysis conducted eight weeks post-treatment. Secondary outcome measures included the rates of adverse events, the necessity for retreatment within six months, and treatment compliance, which was assessed through pill count verification. Primary outcome assessment was performed via histological examination of gastric biopsies obtained during follow-up upper endoscopy eight weeks post-treatment.

To minimize assessment bias, pathologists at all three centers evaluated the specimens as part of routine clinical care blinded to the specific anti-acid regimen (esomeprazole vs. vonoprazan) received by the patient. Histology was selected over the non-invasive Urea Breath Test (UBT) because, within the context of the participating Brazilian public and tertiary academic centers, follow-up endoscopy with biopsy is the standard institutional protocol to concurrently evaluate mucosal healing, rule out gastric malignancies in high-risk symptomatic patients, and overcome the limited availability of UBT in the local public health system

2.1 Statistical Analysis

Analyses were performed using Stata v19® with continuous variables were compared using Student's t-test, categorical variables with χ^2 or Fisher's exact tests. Multi-variable logistic regression adjusted for age, sex, and comorbidities.

3. Results

3.1 Baseline Characteristics

The cohorts were well-balanced except for sex distribution (Table 1).

Table 1. Demographic and Clinical Characteristics.

Characteristic	Esomeprazole (n=100)	Vonoprazan (n=100)	p-value
Age (years)	45.2 ± 16.8	50.1 ± 15.3	0.023
Female sex	72 (72%)	20 (20%)	<0.001
Smoking	28 (28%)	31 (31%)	0.65

3.2 Primary Outcome

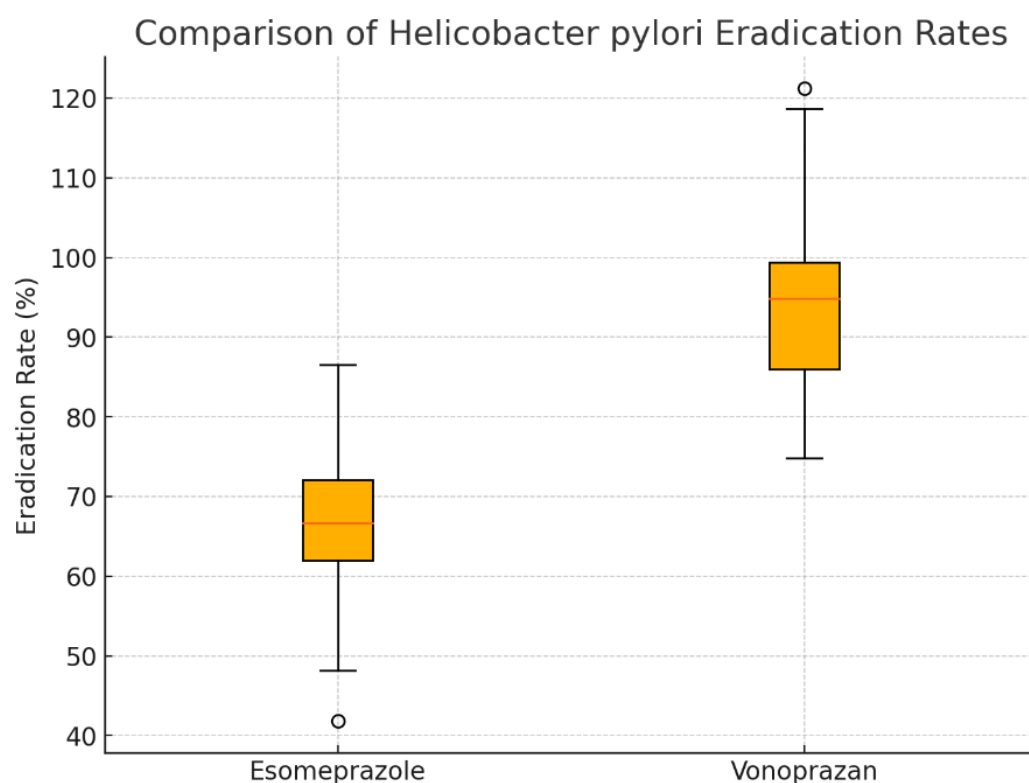
Eradication rates significantly favored vonoprazan (94% vs. 68%, $p<0.001$). This difference persisted after propensity score matching (OR 7.24, 95%CI 3.12-16.81) (Table 2 and Figure 1). Subgroup analyses revealed that Vonoprazan consistently demonstrated superior effectiveness across all groups. In individuals under the age of 50, the eradication rate with Vonoprazan was 96.6%, compared to 67.7% with Esomeprazole. Among those aged 50 or older, Vonoprazan achieved a 90.5% eradication rate, while Esomeprazole had a rate of 68.4%. For males, the eradication rate with Vonoprazan was 95%, significantly higher than the 64.3% observed with Esomeprazole. Similarly, for females, Vonoprazan showed a 90% eradication rate, while Esomeprazole's rate was 69.4% (Table 3). These results highlight the consistent superiority of Vonoprazan across different subgroups.

3.3 Safety and Tolerability

Adverse event rates were similar (22% vs. 18%, $p=0.48$), with no serious events reported.

Table 2. Clinic outcomes.

Variable	Esomeprazole (n=100)	Vonoprazan (n=100)	Total (N=200)	Statistical Test
Eradication (YES)	68 (68%)	94 (94%)	162 (81%)	$\chi^2 = 22.1 / p < 0.001^{***}$
Retreatment (YES)	32 (32%)	6 (6%)	38 (19%)	$\chi^2 = 21.8 / p < 0.001^{***}$

Figure 1. Comparison of *Helicobacter pylori* eradication rates with Esomeprazole (68%) and Vonoprazan (94%). The box shows the distribution of eradication rates, with the median represented by the central line.

4. Discussion

In this multicenter retrospective cohort, vonoprazan-based triple therapy was associated with a markedly higher *Helicobacter pylori* eradication rate compared with esomeprazole-based therapy in Brazilian patients. The observed 26% absolute difference is clinically relevant and aligns with results from Asian randomized trials while exceeding eradication rates reported with conventional PPI-based regimens in Western populations [7,10,15]. The superior efficacy of vonoprazan is biologically plausible and primarily attributed to its potent and sustained gastric acid suppression. Unlike PPIs, vonoprazan provides rapid and consistent inhibition of the H^+/K^+ -ATPase, independent of *CYP2C19* polymorphisms, maintaining intragastric pH levels favorable for antibiotic stability and bacterial replication phase synchronization [8,9,13,16]. These pharmacodynamic advantages likely enhance the activity of amoxicillin and clarithromycin, even in settings of increasing antibiotic resistance [17,18-20-30].

The benefit of vonoprazan was consistent across age and sex subgroups, although an important imbalance in sex distribution between treatment groups was observed. Despite adjustment for sex in multivariable analysis, residual confounding cannot be ex-

cluded and warrants cautious interpretation of subgroup findings. These results highlight the importance of considering baseline demographic differences in real-world comparative effectiveness studies. From a safety perspective, vonoprazan demonstrated a tolerability profile comparable to esomeprazole, with no severe adverse events reported, consistent with previous observational studies and post-marketing surveillance data [19,20]. This favorable safety profile supports its use in routine clinical practice, including in older patients with comorbidities [11,19].

We acknowledge a significant baseline imbalance regarding sex distribution between the two cohorts (72% female in the Esomeprazole group vs. 20% in the Vonoprazan group). This non-random allocation reflects the real-world, retrospective nature of our study, where treatment selection was entirely at the discretion of the treating physicians (confounding by indication). To rigorously account for this, we employed multivariable logistic regression and propensity score matching. Notably, vonoprazan-based therapy remained an independent predictor of eradication success (adjusted OR 7.24; 95%CI 3.12–16.81). Furthermore, stratified subgroup analysis demonstrated that vonoprazan consistently achieved superior eradication rates within both female (90.0% vs. 69.4%) and male (95.0% vs. 64.3%) cohorts, minimizing the likelihood that sex distribution drove the overall results.

This study has limitations inherent to its retrospective design, including potential unmeasured confounders, lack of systematic antibiotic susceptibility testing, and reliance on medical records for adherence assessment. Additionally, the study was conducted in tertiary centers within a single country, which may limit generalizability. Nevertheless, the multicenter design and inclusion of real-world patients provide valuable evidence reflecting routine clinical practice in Brazil. Overall, these findings contribute relevant Latin American data to the growing body of evidence supporting vonoprazan-based regimens and may inform future prospective studies and guideline updates.

4. Conclusion

In this multicenter retrospective cohort, vonoprazan-based triple therapy was associated with significantly higher *Helicobacter pylori* eradication rates compared with esomeprazole-based therapy in Brazilian patients. Despite the limitations inherent to the study design, these real-world findings support vonoprazan as an effective therapeutic option for first-line *H. pylori* eradication when available.

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Research Ethics Committee Approval: The study was designed as a multicenter, retrospective cohort analysis conducted in accordance with the STROBE guidelines. The protocol for the study was reviewed and approved by the Institutional Review Board (CAAE: 54321621.9.0000.0068).

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Conflicts of Interest: The authors declare no conflict of interest.

Supplementary Materials: None.

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