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Efficacy of Potassium Competitive Acid Blockers (P-CABs) versus Proton Pump Inhibitors (PPIs) in the First and Second Line Eradication Regimens for Helicobacter pylori in Egyptian Patients

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Abstract

Background: The eradication of *Helicobacter pylori* (*H. pylori*) infection continues to be a challenge due to the evolution of drug-resistant bacteria. It was hypothesized that a more potent acid suppressant agent, by using Potassium Competitive Acid Blockers (P-CABs) such as Vonoprazan, may help to improve eradication rates.

Aim of the work: The aim of this study is to compare the effectiveness of Vonoprazan-based therapy versus Proton Pump Inhibitor (PPI)-based therapy for the eradication of *H. pylori* infection in treatment-naïve and treatment-experienced Egyptian patients.

Methods: This prospective, non-randomized, comparative study was conducted on*H. pylori* positive symptomatic patients admitted to the Tropical Medicine Department at Ain Shams University Hospitals from the 1st of January 2022 to the 1st of June 2023. A total of 232 patients were assigned to Group I (treatment-naïve), which included arm 1 (intervention arm) with 58 patients receiving Clarithromycin 500 mg BID + Amoxicillin 1 gm BID + Vonoprazan 20 mg BID, and arm 2 (comparator arm) with 58 patients receiving Clarithromycin 500 mg BID + Amoxicillin 1 gm BID + Esomeprazole 20 mg BID. Group II (treatment-experienced) included arm 3 (intervention arm), where 58 patients received Levofloxacin 500 mg OD + Vonoprazan 20 mg BID + Nitazoxanide 500 mg BID + Doxycycline 100 mg OD, and arm 4 (comparator arm), where 58 patients received Levofloxacin 500 mg OD + Esomeprazole 20 mg BID + Nitazoxanide 500 mg BID + Doxycycline 100 mg OD. All patients received treatment regimens for 14 days. *H. pylori* eradication was checked 4 weeks after treatment.

Results: The successful eradication rate was higher in Arm 1 “58.6%” in relation to Arm 2 “50%” and higher in Arm 3 “50%” in relation to Arm 4 “43.1%”, but without reaching statistical significance with a p-value of 0.455. The response to treatment by Intention To Treat (ITT) analysis was higher in Arm 1 “58.6%” in relation to Arm 2 “50%”, but without reaching statistical significance with a p-value of 0.351. By calculating the Per Protocol analysis (PP), the eradication rate was 64% in Arm 1 vs. 56.9% in Arm 2. No statistical significance could be obtained either, with a p-value of 0.447. For Arm 3, the intention to treat percentage was 50% in comparison to the higher per protocol analysis of 72.5%, with

no statistical significance. For Arm 4, the intention to treat percentage was 43.1% in comparison to the higher per protocol analysis of 59.5%, with no statistical significance, with p-values of 0.457 and 0.216, respectively.

Conclusion: Results of eradication in P-CABs based groups are comparable to that of the PPI-based group. Treatment-experienced groups showed lower eradication rates, which indicates increased *H. pylori* resistance. *H. pylori* eradication regimens including P-CABs are tolerable with a low incidence of adverse events.

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Introduction

Helicobacter pylori (*H. pylori*) is the most common chronic bacterial infection in humans. Conservative estimates suggest that 50 percent of the world's population is affected [1]. Infection is more frequent and acquired at an earlier age in resource-limited countries compared with industrialized nations. Once acquired, the infection persists and may or may not produce gastro-duodenal disease. *H. pylori* infection is usually acquired during childhood [2]. Risk factors for acquiring the infection include low socioeconomic status [3], an increasing number of siblings, and having an infected parent, especially an infected mother [4].

In resource-limited nations, where the majority of children are infected before the age of 10, the prevalence in adults peaks at more than 80 percent before age 50 [5].

In North European and North American populations, about one-third of adults are infected, whereas in South and East Europe, South America, and Asia, the prevalence of *H. pylori* is often higher than 50% [3].

A study on Egyptian school children reported that the prevalence of *H. pylori* infection among children had reached about 72.38%. This study also concluded that school children living in Upper Egypt have a higher infection rate than those in Giza and Cairo (96.7% - 61.9% respectively). This indicates the effect of geographical location and socioeconomic status on the prevalence of infection [6].

A more recent study from Egypt on 1,120 patients by Abdelmonem et al. (2020) reported that the overall prevalence of *H. pylori* infection in the Nile Delta was 52%. It was observed that the prevalence of *H. pylori* in children was 41%. [7]

If left untreated, *H. pylori* infection can lead to serious complications, such as peptic ulcer disease and non-cardia gastric cancer. [8]

The eradication of *H. pylori* infection continues to be a challenge due to the evolution of drug-resistant bacteria, lack of a gold standard diagnostic method, and ineffectiveness of current vaccines. [9]

Eradication rates with classical PPI-based triple therapy have dropped below 80% in Europe and the United States[10][2], mainly attributed to rising rates of clarithromycin resistance [11]. *H. pylori* susceptibility to antibiotics is influenced by intragastric pH, which can modify their stability and activity, and affect the replication status of *H. pylori.* [12] Acid suppressant therapy has long been established as a backbone for *H. pylori* treatment regimens to enhance antibiotic effectiveness. [13] Some antibiotics require active *H. pylori* replication for optimal antimicrobial activity. [14] Therefore, sustained control of intragastric pH may improve *H. pylori* eradication rates. [15]

It was hypothesized that a more potent acid suppressant agent such as vonoprazan may help improve eradication rates of current regimens [16]. Vonoprazan is a potassium-competitive acid blocker currently approved for the treatment of*H. pylori* infection and other acid-related diseases in several countries. It increases intragastric pH rapidly and potently and maintains it to a greater degree than PPIs; this has been associated with higher *H. pylori* eradication rates. [17]

Vonoprazan could therefore enhance *H. pylori* therapy by optimizing gastric acid suppression and antimicrobial activity. In meta-analyses of Asian trials, the triple combination of vonoprazan, amoxicillin, and clarithromycin was associated with significantly higher eradication rates than PPI-based triple therapy [18], including patients with clarithromycin-resistant strains (P <.001). [19]

Aim of the Work

The aim of this study is to compare the effectiveness of vonoprazan-based therapy vs. PPI-based therapy for the eradication of *H. pylori* infection in treatment-naïve and treatment-experienced Egyptian patients.

Patients and Methods

This prospective, non-randomized, controlled study was conducted on symptomatic patients admitted to the Tropical Medicine Department at Ain Shams University Hospitals and those presenting at the outpatient clinic. The study was conducted in the period from January 1, 2022, to June 1, 2023.

Study Population

Patients with the following criteria were considered for inclusion in or exclusion from the study:

- Inclusion Criteria:

- Age above 18 years of both genders.

- Asymptomatic patients who have been diagnosed as *H. pylori* positive by using the *H. pylori* stool antigen test.
- Patients who did not receive *H. pylori* eradication regimens before were included in group I of the study (First-line eradication regimen).
- Patients who received only one eradication regimen before were included in group II of the study (Second-line eradication regimen). Patients signing an informed consent.

- Exclusion Criteria:

- Patients refusing to sign an informed consent.
- Patients who were on PPIs, P-CABs, and/or antibiotics starting one month before inclusion in the study.
- Patients who have chronic debilitating and advanced systemic diseases.
- Patients treated with low-dose aspirin and/or non-steroidal anti-inflammatory drugs for a long time.
- Any lactating or pregnant female.

Sample Size: Based on the sample size calculation equation, a total of 232 participants were assigned to two groups. Group I: Treatment-naïve patients (116) and group II: treatment-experienced patients (116). Each group was divided into two arms, with 58 participants assigned to each arm.

Ethical Considerations: The principal investigator obtained the approval of the Ain Shams University Faculty of Medicine Research Ethics Committee FWA 000017585 before starting the work in the study. The approval number is FMASU MS 36/2022. All participants in the study signed an informed consent before participation in the study, and the procedures were done according to the Declaration of Helsinki for ethical principles for medical research involving human subjects.

Study Procedures: Patients who fulfilled the study inclusion criteria were non-randomly assigned to one of the following arms:

Group I: Treatment-naïve group

- **Arm 1: Vonoprazan Triple therapy** (intervention arm): The patients received Clarithromycin 500 mg BID, Amoxicillin 1 gm BID, and Vonoprazan 20 mg BID.
- **Arm 2: PPI Triple therapy** (comparator arm): The patients received the classic triple therapy: Clarithromycin 500 mg BID, Amoxicillin 1 gm BID, and Esomeprazole 20 mg BID.

Group II: Treatment-experienced group

- **Arm 3: Vonoprazan quadruple therapy** (intervention arm): The patients received a non-bismuth quadruple therapy: Levofloxacin 500 mg OD, Vonoprazan 20 mg BID, Nitazoxanide 500 mg BID, and Doxycycline 100 mg OD.
- **Arm 4: PPI quadruple therapy** (comparator arm): The patients received non-bismuth quadruple therapy: Levofloxacin 500 mg OD, Esomeprazole 20 mg BID, Nitazoxanide 500 mg BID, and Doxycycline 100 mg OD.

Patients took their treatment with water 30 minutes before meals under supervision. It was not possible to carry out the provided treatment.

After inclusion in the study, all patients were subjected to the following:

- Full history taking including “Age, sex, smoking habits, any clinical comorbidities, the presenting symptoms, and any laboratory tests, especially ‘CBC and INR’”; in addition to “the detailed eradication regimen and duration of the treatment for the treatment-experienced patients, who will be allocated to Group II patients.”
- Complete clinical examination.
- Laboratory tests including: Initial *H. pylori* stool antigen test (Dia Sure, Azure Biotech Inc.), before inclusion in the study and 4 weeks after finishing the eradication regimens. The intake of antibiotics and acid suppressive therapies was prohibited 2 weeks before doing the test.

Principle of the Procedure

- The *H. pylori* SA assay by Dia Sure, Azure Biotech Inc.[20] is a delayed one-step sandwich assay for the detection of *H. pylori* stool antigen. The assay uses a monoclonal antibody for the detection of *H. pylori* stool antigen. The assay uses 200 µL of a sample consisting of a mixture of sample diluent and stool-extracted *H. pylori* stool antigen. It is incubated with paramagnetic particles coated with a capture antibody for *H. pylori* stool antigen. Following incubation, an isoluminol-conjugated antibody for *H. pylori* stool antigen is added to the reaction and incubated. After the second incubation, the unbound material is removed with a wash cycle. The starter reagents are then added, and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as relative light units (RLU) and is proportional to the concentration of *H. pylori* stool antigen present in the calibrators, controls, or samples.
- Dispensing medications to each arm as follows (Medications were taken for 14 days in the 4 arms of the study as previously mentioned).
- Telephone contact by the principal investigator with each participant in the study after one week of starting the regimen to check compliance.
- Patient adherence to the prescribed treatment and adverse drug reactions were evaluated by self-reporting that was documented by the principal investigator.
- Good compliance was defined as drug consumption >75% of the total dosage.
- Two follow-up visits: The first follow-up visit was done after completing 2 weeks of treatment to register adverse events, whether minor such as “nausea, gastric upset, vomiting, or diarrhea,” or even more serious side effects such as “severe intolerable gastric upset or vomiting that leads to hospitalization.” The second follow-up visit was done after 4 weeks of completing the treatment regimen to register the eradication results.
- Success rates of *H. pylori* eradication treatment were compared in both treatment-naïve and treatment-experienced patients.
- The rate of symptom relief was studied and compared between equivalent groups.
- Successful *H. pylori* eradication was defined as a negative *H. pylori* Stool Antigen test 4 weeks after treatment discontinuation.

Statistical Package: Data entry and the statistical analysis of the collected data will be performed using a reliable,

genuine software statistical program.

Data management and statistical analysis: Data were collected, revised, coded, and entered into the Statistical Package for the Social Sciences (IBM SPSS) version 23. The quantitative data were presented as means and standard deviations when normally distributed and as medians with interquartile ranges (IQR) when the data distribution was not normal. Also, qualitative variables were presented as total numbers and percentages.

Comparison between groups with qualitative data was done using the ***Chi-square test***.

The comparison between two independent groups with quantitative normally distributed data was done using the ***Independent t-test***.

When the quantitative data were not normally distributed, the ***Mann-Whitney test*** was applied.

The confidence interval was set to 95%, and the margin of error accepted was set to 5%. Thus, the p-value was considered significant as follows:

- P-value > 0.05: Non-significant (NS)
- P-value < 0.05: Significant (S)

Results

This prospective, non-randomized, controlled, interventional study was conducted on 232 patients selected from the Tropical Medicine Department at Ain Shams University Hospitals and its outpatient clinic in the period from the 1st of January 2022 to the 1st of June 2023. There were 115 males (49.6%) and 117 females (50.4%) with ages ranging from 18 to 89 years and with a mean±SD of 41.50±16.89.

- Table 1 shows that there was no statistically significant difference between the four studied groups regarding demographic data and medical history among the studied patients at baseline.
- Table 2 shows that there was no statistically significant difference between the four studied groups regarding major S/E such as “severe intolerable gastric upset or vomiting that leads to hospitalization,” minor side effects such as “nausea, gastric upset, vomiting, or diarrhea,” and S/O relief with p-values = 0.390, 0.375, 0.515, respectively. Regarding treatment regimen adherence, the percentages were found to be significantly higher in arms 1 & 2 (94.8% for both of them) followed by arm 4 (84.5%) and lastly arm 3 (77.6%) with a p-value = 0.008. The successful eradication rate was higher in Arm 1 “58.6%” in relation to Arm 2 “50%” and higher in Arm 3 “50%” in relation to Arm 4 “43.1%,” but without reaching statistical significance with a p-value = 0.455.
- Tables 3 and 4 show that there was no statistically significant difference between the two studied groups regarding major side effects such as “severe intolerable gastric upset or vomiting that leads to hospitalization,” minor side effects such as “nausea, gastric upset, vomiting, or diarrhea,” and S/O relief with p-values = 0.315, 0.154, 0.142, respectively. The response to treatment by Intention To Treat (ITT) analysis was higher in Arm 1 “58.6%” in relation to Arm 2 “50%,”

but without reaching statistical significance with a p-value = 0.351. By calculating the Per Protocol (PP) analysis, the eradication rate was 64% in arm 1 vs. 56.9% in arm 2. No statistical significance could be obtained either with a p-value = 0.447.

- Tables 5 and 6 show that there was no statistically significant difference between arms 3 and 4 regarding major side effects such as “severe intolerable gastric upset or vomiting that leads to hospitalization,” minor side effects such as “nausea, gastric upset, vomiting, or diarrhea,” and S/O relief with p-values = NA, 1.000, and 1.000, respectively. Regarding treatment regimen adherence, the percentage was found to be higher in arm 4 (84.5%) than in arm 3 (77.6%) with a p-value = 0.897. The response to treatment was higher in Arm 3 “50%” in relation to Arm 4 “43.1%,” but without reaching statistical significance with a p-value = 0.427. For Arm 3, the intention to treat *H. pylori* eradication percentage was 50% in comparison to the higher per protocol analysis 72.5% with no statistical significance. For Arm 4, the intention to treat *H. pylori* eradication percentage was 43.1% in comparison to the higher per protocol analysis 59.5% with no statistical significance.
- Table 7 shows that the treatment adherence in both groups was similar with “86.2%” in the vonoprazan-based treatment group, while being “89.2%” in the PPI-based treatment group. There was only one patient in the vonoprazan-based treatment group who developed a major side effect in the form of “severe intolerable gastric upset and vomiting that led to hospitalization.” There were three patients in the vonoprazan-based treatment group who developed minor side effects such as “nausea, gastric upset, vomiting, or diarrhea.” On the other hand, five patients in the PPI-based treatment group developed treatment-related minor side effects. The response to treatment was higher in patients in the vonoprazan-based treatment group “54.3%” in relation to patients in the PPI-based treatment group “46.6%,” but without reaching statistical significance with a p-value = 0.393.

Discussion

Vonoprazan, a newly tried P-CAB in *H. pylori* eradication regimens, can be taken regardless of meal ingestion, and the rate of absorption is not affected by meals. The absorption speed of P-CAB is rapid, and the time taken to reach maximum concentration in plasma is less than 2 hours after oral administration. After absorption, the half-life time in plasma is approximately 2 hours for conventional PPIs, but it is up to 9 hours for P-CAB. Therefore, P-CAB stays in the blood longer and can block acid secretion continuously [21]. Therefore, the current study was conducted aiming to assess the efficacy of P-CABs vs. PPIs, with identical antibiotics regimens, in the eradication of *H. pylori* infection in the Egyptian population. To our knowledge, the current study is the first one to address this point of research in Egyptian patients.

Regarding the treatment outcome among treatment-naïve patients in the current study, in Arm 1 out of 58 patients, 34 patients (58.6%) achieved *H. pylori* eradication as per intention to treat analysis (ITT), while according to the per protocol analysis (PP), the percentage was 64.2%. Whereas those in Arm 2 out of 58 patients, 29 patients (50%) achieved *H. pylori* eradication according to ITT analysis, while according to PP analysis, the percentage was 56.9%.

In comparison, a similar study on a cohort of Japanese[22] showed a higher *H. pylori* eradication rate in the treatment-naïve P-CABs group of patients (89.6%), whereas those in the treatment-naïve PPIs group achieved a 71.9% *H. pylori*

eradication rate according to ITT analysis.

P-CABs had a higher success rate tendency among treatment-naïve *H. pylori* patients in comparison to the PPI-based group in the Japanese study, with no statistically significant difference between both groups. This result is in accordance with the results of the present study, as the eradication rate in the current study showed a higher tendency of eradication in treatment-naïve patients without a statistically significant difference.

Contrary to the results of the current study, ***Yamada et al.*** (2016) concluded that P-CABs had a statistically significant higher success rate among treatment-naïve *H. pylori* patients in comparison to the PPI-based group (85.7% vs. 73% by ITT analysis - P-value > 0.001) [23].

Regarding the treatment outcome among treatment-experienced patients in the current study, those in Arm 3 out of 58 patients (50%) achieved *H. pylori* eradication according to ITT analysis, while according to PP analysis, the percentage was 72.5%. Whereas those in Arm 4 out of 58 patients (43.1%) achieved *H. pylori* eradication according to ITT analysis, while according to PP analysis, the percentage was 59.5%.

In comparison to the results of the current study, *Matsumoto et al. (2016)* [22] reported in their results that, in two groups of treatment-experienced patients, the introduction of P-CABs in the second-line eradication regimen in one group resulted in 76.1% *H. pylori* eradication, whereas the results of the reuse of PPIs in the second-line eradication regimen in the other group achieved *H. pylori* eradication in 40.2% of the cases.

Yamada et al.'s study (2016) [23] that assessed the efficacy of PPIs vs. P-CABs in treatment-experienced *H. pylori* patients reported that P-CABs achieved *H. pylori* eradication in 89.4% of patients according to ITT analysis, while according to PP analysis, the percentage was 96.7%. Whereas PPIs achieved *H. pylori* eradication in 89.9% of the patients according to ITT analysis, while according to PP analysis, the percentage was 92.8%.

In accordance with the results of the current study, Chey et al. (2022) [24] reported data from the first phase 3 clinical trial from the United States and Europe to compare the efficacy and adverse events of vonoprazan triple and dual therapy with PPI-based triple therapy for the eradication of *H. pylori*. A total of 1064 treatment-naïve adult patients with *H. pylori* infection were randomized 1:1:1 to open-label vonoprazan dual therapy (20 mg vonoprazan twice daily; 1 g amoxicillin three times daily), or double-blind triple therapy twice a day (vonoprazan 20 mg or lansoprazole 30 mg; amoxicillin 1 g; clarithromycin 500 mg) for 14 days. Primary outcome eradication rates (nonresistant strains): vonoprazan triple therapy 84.7%, dual therapy 78.5%, vs. lansoprazole triple therapy 78.8% respectively. Eradication rates in clarithromycin-resistant infections: vonoprazan triple therapy 65.8%, dual therapy 69.6%, vs. lansoprazole triple therapy 31.9%.

Taking into consideration the results of the current study added to the results of the Japanese studies, we can find that there is a trend towards higher eradication rates in the P-CABs treatment groups than that of the PPI-based groups in the three studies, in spite of the absence of statistical significance between the compared drugs among the three studies.

On the contrary to Yamada et al.'s study (2016) [23], the current study reports a higher percentage of dropouts, being the most significant within the treatment-experienced group "Arm 3 and 4," unlike the treatment-naïve group "Arm 1 and 2,"

where both studies show comparable dropout rates. Furthermore, regarding the treatment adherence among the four arms selected to participate in the current study, it was found that patients in Arm 1 and 2 have a percentage of “94.8%”, whereas those in Arm 3 and 4 showed 77.6% and 84.5% adherence, respectively.

Thus, it appears that adherence was higher in the triple therapy group than in the quadruple therapy group.

Regarding the treatment-related side effects experienced by the participants in the current study, it was found that out of the 116 “vonoprazan-based treatment” recipients, both Arm 1 and 3, there was 1 patient “0.9%” who experienced a major event in the form of “severe intolerable gastric upset and vomiting that led to hospitalization,” while 3 patients “2.6%” experienced minor side effects such as “nausea, gastric upset, vomiting, or diarrhea.”

Out of the 116 “PPI-based treatment” recipients, both Arm 2 and 4, there were 5 patients “4.3%” who experienced minor side effects such as “nausea, gastric upset, vomiting, or diarrhea.”

In comparison, Chey et al. (2022)[24] reported that among 694 patients who received vonoprazan-based regimens, Treatment Emergent Adverse Events (TEAEs) were reported in 34.1% (118 of 346) and 29.9% (104 of 348) of vonoprazan triple and dual therapy groups, respectively, and by 34.5% (119 of 345) in the lansoprazole triple therapy group. Serious TEAEs occurred in 1.7% (6 of 346), 1.4% (5 of 348), and 0.9% (3 of 345), and TEAEs related to discontinuations occurred in 2.3% (8 of 346), 0.9% (3 of 348), and 1.2% (4 of 345) of patients in the vonoprazan triple, vonoprazan dual, and lansoprazole triple therapy groups, respectively. Overall, 3 deaths occurred: 2 due to COVID-19 (1 patient each on lansoprazole triple therapy and vonoprazan triple therapy), and 1 fatal, sudden cardiac arrest (patient on vonoprazan triple therapy).

High dropout rates and low treatment adherence in the experienced groups in the current study could be attributed to polypharmacy that may cause noncompliance in comparison with the naïve groups.

Higher success in eradication rates in Japanese studies than in the current study could be attributed to racial differences. Besides, the current study was conducted in 2023, unlike the Japanese studies conducted in 2016. More aggressive resistant *H. pylori* strains had definitely developed by then, and according to Alboraie et al. (2019)[25], a percentage of 50% or less among the *H. pylori* Egyptian population is believed to harbor “clarithromycin-resistant *H. pylori* strains,” evidenced by culture techniques. Another explanation for the difference between eradication rates in the current study and the Japanese studies is the difference between medications used in the present study and other studies.

Conclusions

Results of eradication in P-CABs based group are comparable to that of the PPI-based group. Treatment-experienced groups showed lower eradication rates, which indicates increased *H. pylori* resistance. It appears that adherence was higher in the triple therapy group than in the quadruple therapy group, which was reflected in the eradication rates. *H. pylori* eradication regimens including P-CABs are tolerable with a low incidence of adverse events.

Tables

Table 1. Basal demographic data and medical history of the four studied groups

		Arm 1	Arm 2	Arm 3	Arm 4	Test value	P-value
		No. = 58	No. = 58	No. = 58	No. = 58		
Age	**Mean±SD**	40.36 ± 18.49	37.79 ± 16.25	43.12 ± 16.53	44.74 ± 16.28	1.904•	0.130
	Range	19 - 89	18 - 70	20 - 80	18 - 85		
Sex	**Male**	25 (43.1%)	35 (60.3%)	32 (55.2%)	23 (39.7%)	6.673*	0.083
	Female	33 (56.9%)	23 (39.7%)	26 (44.8%)	35 (60.3%)		
Diabetes mellitus	**Negative**	53 (91.4%)	54 (93.1%)	49 (84.5%)	53 (91.4%)	2.848*	0.416
	Positive	5 (8.6%)	4 (6.9%)	9 (15.5%)	5 (8.6%)		
Hypertension	**Negative**	53 (91.4%)	48 (82.8%)	47 (81.0%)	45 (77.6%)	4.284*	0.232
	Positive	5 (8.6%)	10 (17.2%)	11 (19.0%)	13 (22.4%)		
Bronchial asthma	**Negative**	57 (98.3%)	55 (94.8%)	57 (98.3%)	54 (93.1%)	3.121*	0.373
	Positive	1 (1.7%)	3 (5.2%)	1 (1.7%)	4 (6.9%)		
Chronic liver disease	**Negative**	54 (93.1%)	58 (100.0%)	53 (91.4%)	52 (89.7%)	5.916*	0.116
	Positive	4 (6.9%)	0 (0.0%)	5 (8.6%)	6 (10.3%)		
Chronic Kidney disease	**Negative**	56 (96.6%)	57 (98.3%)	58 (100.0%)	57 (98.3%)	2.035*	0.565
	Positive	2 (3.4%)	1 (1.7%)	0 (0.0%)	1 (1.7%)		
Thyroid disease	**Negative**	56 (96.6%)	58 (100.0%)	57 (98.3%)	58 (100.0%)	0.565*	0.294
	Positive	2 (3.4%)	0 (0.0%)	1 (1.7%)	0 (0.0%)		
Smoking	**Negative**	48 (82.8%)	48 (82.8%)	49 (84.5%)	46 (79.3%)	0.563*	0.905
	Positive	10 (17.2%)	10 (17.2%)	9 (15.5%)	12 (20.7%)		
Concomitant medications	**Negative**	44 (75.9%)	44 (75.9%)	36 (62.1%)	39 (67.2%)	3.857*	0.277
	Positive	14 (24.1%)	14 (24.1%)	22 (37.9%)	19 (32.8%)		
Penicillin allergy	**Negative**	58 (100.0%)	58 (100.0%)	58 (100.0%)	56 (96.6%)	6.052*	0.109
	Positive	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.4%)		

*P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value < 0.01: Highly significant (HS); •: One Way ANOVA test; *: Chi-square test*

Table 2. Examination and treatment outcomes of the studied groups

		Arm 1	Arm 2	Arm 3	Arm 4	Test value	P-value	Sig
		No. = 58	No. = 58	No. = 58	No. = 58			
	Positive	**58 (100.0%)**	**58 (100.0%)**	**58 (100.0%)**	**58 (100.0%)**			
Treatment regimen adherence	**Negative**	3 (5.2%)	3 (5.2%)	13 (22.4%)	9 (15.5%)	11.697*	0.008	HS
	Positive	55 (94.8%)	55 (94.8%)	45 (77.6%)	49 (84.5%)			
Major side effects	**Negative**	57 (98.3%)	58 (100.0%)	58 (100.0%)	58 (100.0%)	3.013*	0.390	NS
	Positive	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			
Minor side effects	**Negative**	58 (100.0%)	56 (96.6%)	55 (94.8%)	55 (94.8%)	3.107*	0.375	NS
	Positive	0 (0.0%)	2 (3.4%)	3 (5.2%)	3 (5.2%)			
Symptoms relief	**Negative**	12 (20.7%)	19 (32.8%)	17 (29.3%)	17 (29.3%)	2.287*	0.515	NS
	Positive	46 (79.3%)	39 (67.2%)	41 (70.7%)	41 (70.7%)			
***H. pylori* stool antigen test result**	**Negative**	34 (58.6%)	29 (50.0%)	29 (50.0%)	25 (43.1%)	2.617*	0.455	NS
	Positive	19 (32.8%)	22 (37.9%)	11 (19.0%)	17 (29.3%)			
	Dropout	5 (8.6%)	7 (12.1%)	18 (31.0%)	16 (27.6%)			

*P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value < 0.01: Highly significant (HS); NA: Not Applicable; *: Chi-square test*

Table 3. Comparison between arm 1 and arm 2 regarding examinations and treatment outcome

		Arm 1	Arm 2	Test value	P-value	Sig.
		No. = 58	No. = 58			
		58 (100.0%)	58 (100.0%)			
Treatment regimen adherence	**Negative**	3 (5.2%)	3 (5.2%)	0.000*	1.000	NS
	Positive	55 (94.8%)	55 (94.8%)			
Major Side effects	**Negative**	57 (98.3%)	58 (100.0%)	1.009*	0.315	NS
	Positive	1 (1.7%)	0 (0.0%)			
Minor Side effects	**Negative**	58 (100.0%)	56 (96.6%)	2.035*	0.154	NS
	Positive	0 (0.0%)	2 (3.4%)			
Symptoms relief	**Negative**	12 (20.7%)	19 (32.8%)	2.157*	0.142	NS
	Positive	46 (79.3%)	39 (67.2%)			
***H. pylori* stool antigen test**	**Negative**	34 (58.6%)	29 (50.0%)	0.950	0.622	NS
	Positive	19 (32.8%)	22 (37.9%)			
	Dropout	5 (8.6%)	7 (12.1%)			

*P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value < 0.01: Highly significant (HS); NA: Not Applicable; *: Chi-square test*

Table 4. Intention to treat and per protocol analysis of *H. pylori* stool Ag test negative patients among treatment-naïve patients

	Arm 1	Arm 2	Test value	P-value	Sig.
Negative *H. pylori* Ag test	ITT: 34 (58.6%)	29 (50.0%)	0.869*	0.351	NS
	PP: 34 (64.2%)	29 (56.9%)	0.578*	0.447	NS

*P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value < 0.01: Highly significant (HS); NA: Not Applicable; *: Chi-square test*

Table 5. Comparison between arm 3 and arm 4 regarding examination and treatment outcome

		Arm 3	Arm 4	Test value	P-value	Sig.
		No. = 58	No. = 58			
	Positive	**58 (100.0%)**	**58 (100.0%)**			
Treatment regimen adherence	**Negative**	13 (22.4%)	9 (15.5%)	0.897*	0.343	NS
	Positive	45 (77.6%)	49 (84.5%)			
Major side effects	**Negative**	58 (100.0%)	58 (100.0%)	NA	NA	NA
	Positive	0 (0.0%)	0 (0.0%)			
Minor side effects	**Negative**	55 (94.8%)	55 (94.8%)	0.000*	1.000	NS
	Positive	3 (5.2%)	3 (5.2%)			
Symptoms relief	**Negative**	17 (29.3%)	17 (29.3%)	0.000*	1.000	NS
	Positive	41 (70.7%)	41 (70.7%)			
***H. pylori* stool Ag test**	**Negative**	29 (50.0%)	25 (43.1%)	1.700*	0.427	NS
	Positive	11 (19.0%)	17 (29.3%)			
	Dropout	18 (31.0%)	16 (27.6%)			

*P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value < 0.01: Highly significant (HS); NA: Not Applicable; *: Chi-square test*

Table 6. Intention to treat and per protocol analysis of *H. pylori* stool antigen test negative patients among treatment-experienced patients.

	Arm 3	Arm 4	Test value	P-value	Sig.
Negative *H. pylori* Ag test	ITT- 29 (50.0%)	25 (43.1%)	0.554*	0.457	NS
	PP -29 (72.5%)	25 (59.5%)	1.534*	0.216	NS

*P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value < 0.01: Highly significant (HS); NA: Not Applicable; *: Chi-square test*

Table 7. Comparison between vonoprazan-based treatment and PPI-based treatment regarding examinations and treatment outcome

		Vonoprazan based treatment	PPI based treatment	Test value	P-value	Sig.
		No.=116	No.=116			
Treatment regimen adherence	**Negative**	16 (13.8%)	12 (10.3%)	0.650	0.420	NS
	Positive	100 (86.2%)	104 (89.7%)			
Major side effects	**Negative**	115 (99.1%)	116 (100.0%)	1.004	0.316	NS
	Positive	1 (0.9%)	0 (0.0%)			
Minor side effect	**Negative**	113 (97.4%)	111 (95.7%)	0.518	0.472	NS
	Positive	3 (2.6%)	5 (4.3%)			
symptoms relief	**Negative**	29 (25.0%)	36 (31.0%)	1.047	0.306	NS
	Positive	87 (75.0%)	80 (69.0%)			
***H. pylori* stool Ag test**	**Negative**	63 (54.3%)	54 (46.6%)	1.866	0.393	NS
	Positive	30 (25.9%)	39 (33.6%)			
	Dropout	23 (19.8%)	23 (19.8%)			

*P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value < 0.01: Highly significant (HS); NA: Not Applicable; *: Chi-square test*

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Guarantor of the article: Prof. Reda Elwakil.

Specific author contributions: RE prepared the protocol of the study and wrote the first draft of the paper. NE, ME, and HMH recruited the participants, supervised the dispensing of medications, and oversaw data collection. YM performed the laboratory work. All authors further contributed to the writing and approval of the manuscript.

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