Microbes and Infectious Diseases 2023; 4(2): 506-513

Microbes and Infectious Diseases

Journal homepage: https://mid.journals.ekb.eg/

Original article

Efficacy of vonoprazan-based triple therapy for cure of *H. pylori* infection among patients attending GIT outpatient clinic at Suez Canal University Hospital

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ARTICLE INFO

Article history:
Received 2 February 2023
Received in revised form 5 March 2023
Accepted 8 March 2023

Keywords:
Vonoprazan
Helicobacter pylori
Triple therapy
Eradication
Cure

ABSTRACT

Background: Treatment of *Helicobacter pylori* (*H.pylori*) became mandatory for prevention and cure of most upper gastrointestinal complaints. Despite the varieties in available therapeutic options, achieving a high eradication rate is very challenging. Currently, vonoprazan based protocols are being introduced, and they provide promising outcomes. We aimed at studying vonoprazan efficacy and safety for cure of *H.pylori* among Egyptian patients. **Methods**: In a prospective cohort study, we included 300 patients who tested positive for *H. pylori* to receive vonoprazan-based triple therapy for two weeks. Then, we assessed the cure rate, improvement of symptoms and side effects. **Results**: We found that vonoprazan-based triple therapy achieved a cure rate of 90%. There was a remarkable improvement in all presenting symptoms after complete cure with this regimen. Few adverse effects were observed, not exceeding 9.3% of patients. Most common side effects were nausea (4.3%), burping (2.6%) and bloating (1.3%). **Conclusions:** vonoprazan-based triple therapy is effective and safe for cure of *Helicobacter*.

Introduction

Helicobacter pylori (*H. pylori*) disease is becoming a debilitating and chronic infection as it invades the gastric mucosa and causes gastritis. Chronic inflammation caused by *H. pylori* in the gastric mucosa can lead to atrophic gastritis, gastroduodenal ulcer, mucosa-associated lymphoid tissue (MALT) lymphoma, gastric adenocarcinoma, and even idiopathic thrombocytopenic purpura. These conditions can be prevented and treated by *H. pylori* eradication [1, 2].

With the increasing number of strains of *H. pylori* with antibiotic resistance, eradication became extremely challenging. One common example for such difficulty is resistance to clarithromycin, which delays *H. pylori* eradication. To overcome this, eradication regimens that use combination of drugs, higher doses of drugs, and longer treatment durations (10-14 days) have been recommended [2, 3].

After a long era of using proton pump inhibitors (PPIs) based protocols, it has been reported that triple therapy with vonoprazan offers a higher rate of eradication than that of PPIs. Vonoprazan is a

DOI: 10.21608/MID.2023.191490.1459
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potassium-competitive acid blocker (PCAB) that was firstly tried and prescribed by Japanese scientists in early 2015 for treatment of *H pylori* eradication [**4**].

There are multiple studies that investigated and compared the efficacy of vonoprazan versus PPI that favored vonoprazan based therapies. But, to the best of our knowledge, none of these studies assessed the efficacy and safety of vonoprazan triple therapy for eradication of *H. pylori* among Egyptian patients.

Aim

In this study, we aimed at assessment of efficacy including symptoms improvement and cure rate, in addition to evaluation of the adverse events of vonoprazan triple therapy in treatment of *H pylori*.

Material and Methods

This was a prospective cohort study for assessment of efficacy of vonoprazan-based triple therapy in cure of *H. Pylori* infection. It was conducted on patients attending GIT outpatient clinic at Suez Canal University Hospital at Ismailia governorate. This study was approved by the institutional review board of Faculty of Medicine, Suez Canal University, Ismailia, Egypt. Before start of study, we also gained informed consent from all patients.

We included 300 patients who tested positive for *H. P*ylori infection was confirmed by stool antigen, urea breath test or histopathology during endoscopy. We included both naïve and treatment experienced patients who are over 18 years old from both genders. We excluded patients with allergy or contraindication to treatment.

Before receiving treatment, we collected baseline data from patients including demographic data, history of present illness and any co-morbid conditions. All patients received treatment course for two weeks of vonoprazan-based triple therapy and it included: vonoprazan 20 mg twice daily + amoxicillin 1 gm twice daily + metronidazole 500 mg twice daily.

After a follow-up period of four weeks, all patients were assessed for cure of *H. pylori* by *H. pylori* stool antigen, improvement of symptoms after treatment, and occurrence of adverse events. Cure of *H. pylori* infection was determined based on a negative test of *H. pylori* stool antigen after four weeks of starting treatment.

All statistical analyses were performed using the *SPSS* statistical package for social science version 25. Descriptive statistics were applied in numerical form (mean, SD or percentages) to describe the quantitative variables. Associations between variables were tested for significance by using Chi-square test for categorical variables, and the Student (t) test/ paired t test for continuous variables with normally distributed data.

Results

In this study, we included 300 patients who tested positive for *H pylori*. Approximately equal number of both genders was involved. Their mean age was 38. Most of them lived in urban residences. We found that only 38.4% of patients were unemployed, while the majority of them had jobs. Around one fifth of the participants were smokers. Regarding co-morbid conditions, hypertension was the most prevalent among patients, followed by diabetes mellitus. While few patients had ischemic heart disease, chronic obstructive pulmonary disease, renal failure, chronic liver disease, and heart failure. Around three fourths of patients did not receive any treatment for *H pylori* before **(Table 1)**. The remaining 27% patients who received treatment for *H. pylori* before enrolling to our study were categorized based on the received regimen into 7 groups as shown in **table (2)**.

Concerning the symptoms the patients presented with, epigastric pain on the top of the list, followed by heartburn, early satiety and nausea. The least common manifestations were hematemesis, tenesmus, and melena. There was a remarkable improvement in all presenting symptoms after use of vonoprazan **(Table 3)**. The cure rate of *H. pylori* after use of vonoprazan was 90% **(Figure 1)**.

It is worth mentioning that the cure rate with naïve patients was higher than in those who experienced previous PPI based treatment; 92.7 and 82%, respectively; *p* 0.01) **(Figure 2)**.

Regarding the presenting symptoms before and after treatment, it was noticed before treatment the majority of patients either responders or non-responders had no difference in prevalence of symptoms, except for colic which was more prevalent among non-responders.

On the other hand, after treatment there was a significant difference between responders and non-responders regarding almost all symptoms except for hematemsis, melena and constipation where no difference was found. It was noticed that after treatment the prevalence of some symptoms was higher among non-responders than responders except for colic where it was higher among responders. While responders witnessed a decrease in all symptoms after treatment, surprisingly, non-

responders were different. For example, some symptoms did not disappear such as vomiting, heartburn and hiccups. There were also some symptoms which became more prevalent than before treatment such as nausea, bloating, burping and diarrhea. The remaining symptoms became less prevalent after treatment **(Table 4)**.

The incidence of different adverse effects of vonoprazan was low (9.3%). For instance, nausea occurred in only 4.3% of patients. The rest of adverse effects (burping, bloating, diarrhea, and tenesmus) affected only 15 patients **(Table 5)**.

Table 1. Patients' characteristics.

	N= 300	%
Age **(mean ± SD)**	38.6 ± 11.5	
Gender		
Male	152	50.7
Female	148	49.3
Residence		
Urban	213	71
Rural	87	29
Occupation		
Employer	90	30
Worker	70	23.3
Farmer	25	8.3
Unemployed	115	38.4
Smoking		
Yes	52	19.3
No	248	82.7
Co-morbid conditions		
Diabetes	57	19
Hypertension	69	23
COPD	15	5
IHD	21	7
Heart failure	3	1
Renal failure	12	4
CLD	6	2
Treatment status		
Naïve	219	73
Experienced	81	27

Data are presented as frequency and percent, unless otherwise indicated. Abbreviations: COPD; chronic obstructive pulmonary disease, IHD; ischemic heart disease, CLD; chronic liver disease.

Table 2. Regimen for previous *H. pylori* TTT.

Regimen	N= 82	%
1 – PPI + Amoxicillin + clarithromycin	25	8.3
2 – PPI + Amoxicillin + Metronidazole	18	6
3 – PPI + clarithromycin + Metronidazole	17	5.7
4 – PPI + Amoxicillin + Nitazoxanide	7	2.3
5 – PPI + Amoxicillin + clarithromycin + Metronidazole	6	2
6– PPI + clarithromycin + Quinolone	5	1.7
7– PPI + Amoxicillin + Quinolone	3	1

Data are presented as frequency and percent, unless otherwise indicated. Abbreviations: PPI; proton pump inhibitor.

Table 3. Comparison of symptoms before and after treatment.

	Before	After	*p* value
Nausea	156 (52)	65 (21.7)	**<0.001****
Vomiting	52 (17.3)	10 (3.3)	**<0.001****
Heart burn	201 (67)	46 (15.3)	**<0.001****
Hicough	71 (23.7)	17 (5.7)	**<0.001****
Epigastric pain	229 (76.3)	22 (7.3)	**<0.001****
Globus sensation	93 (31)	18 (6)	**<0.001****
Early satiety	191 (63.7)	35 (11.7)	**<0.001****
Hematemesis	15 (5)	0 (0)	**<0.001****
Melena	5 (1.7)	0 (0)	**0.02***
Tenesmus	9 (3)	2 (0.7)	**0.03***
Bloating	113 (37.3)	28 (9.3)	**<0.001****
Burping	77 (25.7)	23 (7.7)	**<0.001****
Colic	102 (34)	29 (9.7)	**<0.001****
Diarrhea	33 (11)	14 (4.7)	**0.002***
Constipation	45 (15)	15 (5)	**<0.001****

Data are presented as frequency and percent, unless otherwise indicated.

Table 4. Comparison of symptoms between responders and non-responders.

		Responders N =270	**Non-responders** N=30	***p* value**
Nausea	**Before**	141 (52)	15 (50)	0.4
	After	37 (14)	28 (93)	<0.001**
Vomiting	**Before**	46 (17)	6 (20)	0.4
	After	4 (2)	6 (20)	<0.001**
Heart burn	**Before**	180 (67)	21 (70)	0.4
	After	25 (9)	21 (70)	<0.001**
Hiccough	**Before**	63 (23)	8 (27)	0.4
	After	9 (3)	8 (27)	<0.001**
Epigastric	**Before**	207 (77)	22 (73)	0.4
Pain	**After**	7 (2.6)	15 (50)	<0.001**
Globus	**Before**	81 (30)	12 (40)	0.1
Sensation	**After**	8 (3)	10 (33)	<0.001**
Early satiety	**Before**	172 (64)	19 (63)	0.5
	After	18 (7)	17 (57)	<0.001**
Hematemesis	**Before**	13 (5)	2 (7)	0.4
	After	0 (0)	0 (0)	-
Melena	**Before**	4 (2)	1 (4)	0.4
	After	0 (0)	0 (0)	-
Tenesmus	**Before**	9 (3)	0 (0)	0.3
	After	0 (0)	2 (7)	0.01*
Bloating	**Before**	103 (38)	10 (33)	0.3
	After	14 (5)	14 (47)	<0.001**
Burping	**Before**	70 (26)	7 (23)	0.4
	After	8 (3)	15 (50)	<0.001**
Colic	**Before**	86 (32)	16 (53)	0.01*
	After	17 (6)	12 (4)	<0.001**
Diarrhea	**Before**	29 (11)	4 (13)	0.4
	After	9 (3)	5 (17)	0.008*
Constipation	**Before**	42 (16)	3 (10)	0.3
	After	14 (6)	1 (4)	0.5

Data are presented as frequency and percent, unless otherwise indicated.

Table 5. Adverse effects of vonoprazan based therapy.

	N = 300 (%)
Nausea	13 (4.3)
Burping	8 (2.6)
Bloating	4 (1.3)
Tenesmus	2 (0.6)
Diarrhea	1 (0.3)
Total	28 (9.3)

Data are presented as frequency and percent.

Figure 1. Cure rate.

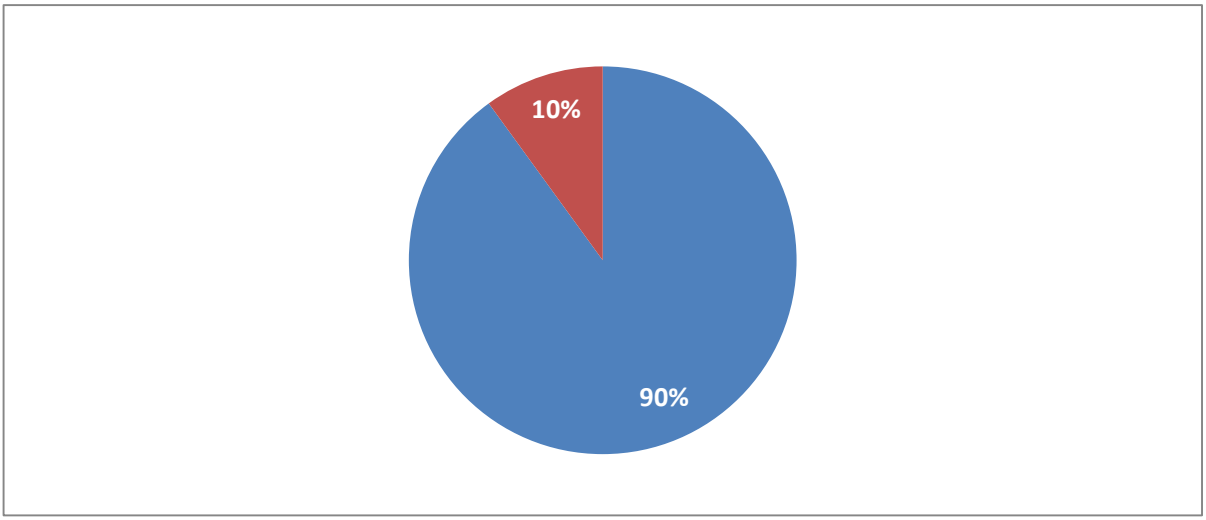
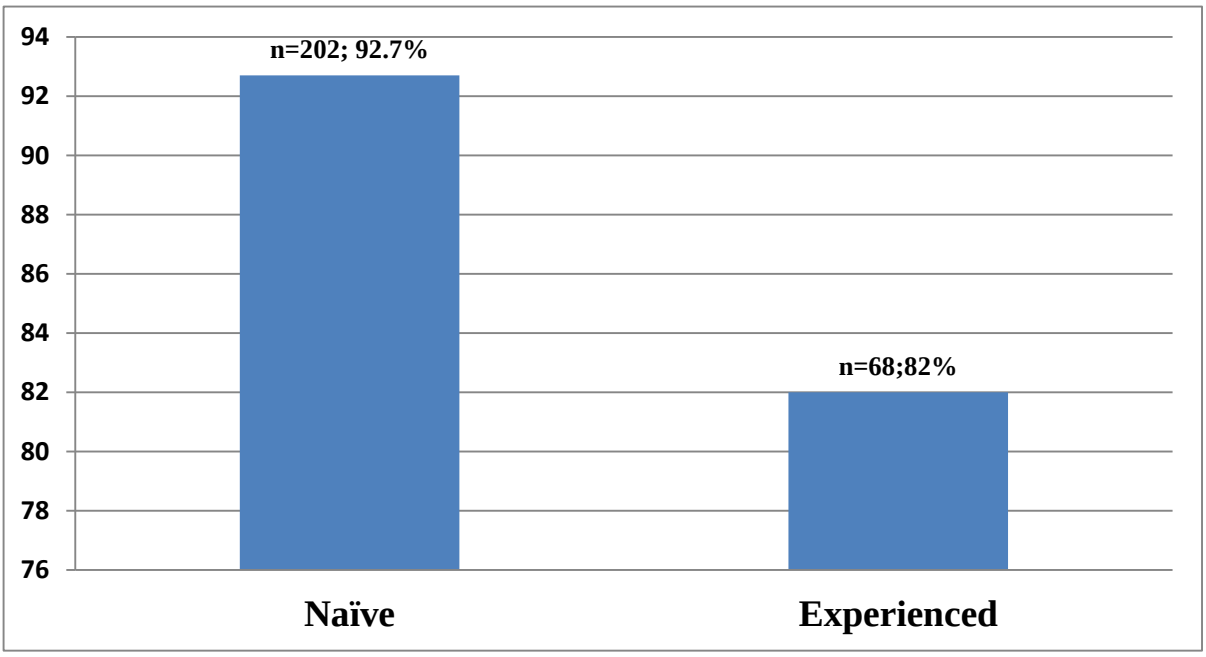


Figure 2. Cure rate according to treatment status.



Discussion

Vonoprazan was introduced in Japan and other few countries since 2015; however, it was just introduced to the Egyptian market by early 2022. Thus, this study is promising and valuable, as it is the first study to investigate the role of vonoprazan triple therapy for H pylori cure in Egypt.

We found that triple therapy with vonoprazan had a 90% cure rate, which is considered satisfactory and effective**. Katayama et al.** found a quite comparable but lower eradication rate (87%) when used a similar regimen. In contrast to our regimen, they used a lower dose of metronidazole; 250 mg twice daily instead of 500 mg twice daily [5]**.** This lower dose might justify the lower eradication rate. But there are studies which used the exact same regimen with same doses and reported a higher eradication rate. For instance, Ono et al included 13 patients into trial of vonoprazan-based triple therapy, using metronidazole; 250 mg twice daily, which produced eradication rate of 92.3%. Yet it is a study with a small sample size to deduce such a conclusion based on it [6].

There is a debate on the effectiveness of clarithromycin over metronidazole when used in the triple therapy with vonaprazan. **Katayama et al.** reported that using clarithromycin in the triple therapy yielded a similar eradication rate as we found (90.6%) [5]**.** Also, **Murakami et al.** found that a similar eradication rate (90.9%) with the vonoprazan-based triple therapy (vonoprazan, 20 mg; amoxicillin, 750 mg; and clarithromycin, 200 or 400 mg, twice daily) [7]. **Tanabe et al.** reported an eradication rate of 94.4% with vonoprazan 20 mg, amoxicillin 750 mg, and clarithromycin 200 or 400 mg, twice a day for 7 days as first line treatment and 97.1% for second line treatment (with vonoprazan 20 mg, amoxicillin 750 mg, and metronidazole 250 mg, twice a day for 7 days [8].

What might explain the superiority of metronidazole over clarithromycin in triple therapy is that metronidazole resistance is less prevalent. Additionally, metronidazole sensitivity has a minimal effect on eradication rate [9]**.**

Surprisingly, **Okubo et al.** confirmed that vonoprazan -based triple therapy with clarithromycin was highly effective among clarithromycin resistant (CAM-R) patients as well with a comparable eradication rate; 91.6% among clarithromycin sensitive (CAM-S) versus 89.4% among CAM-R with no statistically significant difference [10]**. Furuta et al**. concluded that dual therapy with only vonoprazan and amoxicillin is just as effective as triple therapy; 92.9% and 91.9%, respectively. Which made it clear that neither clarithromycin nor metronidazole as a second antibiotic contributes that much to the eradication rate of *H pylori* [11]**.**

Noticeably, non-responders witnessed an increase in prevalence of some symptoms. This might be justified by persistence of original symptoms due to failure of eradication, in addition to occurrence of side effects due to the regimen. Regarding adverse effects of vonoprazan triple therapy, we found that few cases were affected (9.3%), with nausea as the most common side effect. This is similar to **Okubo et al.** study as they reported the percent of total adverse effects of vonoprazan-based triple therapy was 8.4%. But, conversely, they found that heartburn and diarrhea were the most commonly reported side effects. Additionally, they reported one case of dysgeusia and one had rash 10**.** In a meta-analysis by **Jung et al.**, they claimed that pooled rate of any side effects of vonoprazan triple therapy was 8.1% **[**12] **.** In contrast to previous studies, **Furuta et al.** study reported a higher incidence of adverse effects reaching 25% [11]. Also **Murakami et al.** reported a much higher incidence of adverse events of vonoprazan triple therapy, as a first line therapy, than most of the studies in the literature (34%). In their study the most common side effects was diarrhea (12.5%), followed by nasopharyngitis (5.5%), and dysgeusia (4%) [7] .

Our patients did not witness that high incidence of diarrhea as our treatment regimen did not include clarithromycin which is known for its ability to increase peristalsis.

In conclusion, vonoprazan triple therapy is effective in cure of *H pylori* among the Egyptian patients as perceived by the high cure rate. It is also a safe regimen that elicited such few adverse effects even when used for two weeks. After such a success, it is highly recommended to investigate the feasibility of using vonoprazan based triple therapy for shorter duration. This would reduce the financial cost for eradication therapy, and also reduces the incidence of adverse events to the minimum. We highly encourage gastroenterologists to replicate the Japanese experience of using vonoprazan based protocol for a successful eradication of *H. pylori*.

Conflicts of interest

The authors report no conflicts of interest

Financial disclosure

None to declare. The study is self-funded by the authors.

Contributors

All authors have participated in the concept and design, analysis and interpretation of data, drafting, revising and preparation of the manuscript. All authors have approved the manuscript.

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