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CLINICAL TRIAL REPORT

A Modified 14-Day Dual Therapy with Vonoprazan and Amoxicillin Amplified the Advantages Over Conventional Therapies for Eradication of *Helicobacter pylori*: A Non-Inferiority Clinical Trial

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Purpose: The emergence of resistant strains has greatly reduced the eradication rate of *H. pylori* (HP) in conventional bismuth-containing quadruple therapy. Meanwhile, the new 7-day dual therapy with vonoprazan (VPZ) and amoxicillin (AMO) failed to achieve the expected therapeutic effect in China.

Patients and Methods: A total of 256 untreated HP-infected patients are included in this non-inferiority clinical trial. The patients were randomly divided into three groups: 14-day dual therapy group (VPZ 20mg b.i.d + AMO 750mg t.i.d for 14 days, VA14), 14-day modified triple therapy group (VA14 + Jinghua Weikang Capsule 160mg t.i.d, VAC), and conventional bismuth-containing quadruple therapy group for 14 days (BCQ). Eradication rates, drug-related adverse events (AEs), patient compliance, and drug costs were compared among the three groups.

Results: The eradication rates in the BCQ, VA14, and VAC were 78.67, 77.33%, and 86.49% by intention-to-treat analysis, respectively, and 96.72%, 90.63%, and 92.75% by pre-protocol or modified intention-to-treat analysis, respectively. VA14 therapy indicated a non-inferiority eradication rate and advanced safety and economics to BCQ therapy. JWC further improved the eradication rate and reduced the incidence of AEs.

Conclusion: A modified 14-day dual therapy with VPZ and AMO provides satisfied efficacy as the first-line treatment for HP infection in China.

Keywords: vonoprazan, amoxicillin, *Helicobacter pylori*, Jinghua Weikang capsule

Introduction

Helicobacter pylori (HP) infection is the main cause of a variety of gastrointestinal diseases, from chronic active gastritis to fatal gastric adenocarcinoma.[1] Half of the world's population is infected with HP. In China, about 7,000,000 people are infected due to the dietary habit.[2,3] Worse, the increased resistance of antibiotics poses a challenge to the eradication of HP. The latest Sixth Chinese National Consensus Report on *Helicobacter pylori* infection and management, the Maastricht VI consensus, and the Toronto consensus, all strongly recommend that the 14-day quadruple therapy containing bismuth agent as the first-line treatment for HP eradication. However, side effects related to bismuth and multiple-usage of antibiotics, poor compliance, high resistance rates of clarithromycin and metronidazole, and high drug costs are inevitable drawbacks of BCQ therapy. Acid suppressants are indispensable in conventional regimens of HP eradication. It plays dual roles of increasing HP replication to expose HP to antibiotics and enhancing the antibacterial effect of pH-dependent antibiotics (such as amoxicillin).[4,5] Additionally, compared with the high

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resistance rate of HP to clarithromycin (CLA) and metronidazole, the resistance to AMO is still rare in the Asia Pacific region.[6–8] Therefore, further improving the acid inhibiting effect to elevate pH for increasing antibiotic exposure and enhancing the antibacterial effect of AMO may be an effective strategy to breakthrough the current bottleneck of HP eradication.

Vonoprazan (VPZ) is the first clinically available potassium competitive acid blocker.[9] Compared with proton pump inhibitors (PPIs), VPZ shows faster and stronger gastric acid inhibition effect while also undergoing metabolism without CYP2C19 polymorphisms.[10–12] VPZ (20 mg, b.i.d) had pH ≥ 4 and ≥ 5 retention rates of 100% and 99%, respectively, on the seventh day of HP eradication.[13] In addition, VPZ can rapidly turn the intragastric pH to 7 within about 3 hours after the initial dose of 20 mg.[14] This means, when VPZ is used to eradicate HP, the ideal pH condition can be ready from the first day of eradication treatment, so that the antibacterial agent is expected to play a full role in the stomach from the first day. The first clinical usage of VPZ against HP was in Japan. A triple therapy with VPZ 20 mg b.i.d, AMO 750 mg b.i.d, and CLA 200mg b.i.d showed an eradication rate of 92.6%, while that of the control therapy with PPI was 75.9%.[15] Furthermore, another Japanese research indicated that a dose-reduced dual therapy with AMO 500 mg t.i.d and VPZ 20 mg b.i.d provided a similar eradication rate of 92.9% to conventional Japanese triple therapy mentioned above. Thus, this dose-reduced dual therapy can effectively eradicate HP as a first-line treatment in Japan.[16]

Unfortunately, there are regional differences in the HP eradication rate by VPZ combined with AMO. The same strategy of dual therapy with VPZ and AMO even increased AMO doses to 1000mg b.i.d for 10 days was applied in a Chinese random controlled trial (RCT), but only 89.2% eradication rate of HP was achieved, less than the first-line treatment (BCQ) in China.[17] The researchers in this RCT speculated that further extending the time of administration or elevating the frequency of AMO could raise the eradication rate up to 90%. For further proving this speculation and exploring better anti-HP strategies, we designed this RCT and prolonged the treatment time of VPZ+AMO to 14 days (VA14), then compared the eradication rate with Chinese first-line treatment (BCQ). Jinghua Weikang Capsule (JWC) is an anti-HP Chinese patent medicine recommended in the Consensus of Experts Integrating Chinese and Western Medicine in HP Treatment in China at present.[18] It is composed of two main components: Chenopodium ambrosioides L. and Adina pilulifera Chenopodium ambrosioides L. Therefore, we added this non-antibiotic botanical to the dual therapy of VPZ+AMO (VAC) and compared it with the 14-day dual therapy (VA14) and the conventional quadruple therapy (BCQ).

Materials and Methods

Research Design and Ethical Statement

The study is designed as a non-inferiority, single center, randomized controlled clinical trial and registered in Chinese Clinical Trial Registry (https://www.chictr.org.cn/) in July 2020 with a registered number ChiCTR2000034722. This clinical trial is also reviewed and approved by the ethics committee of the Second Affiliated Hospital of Chongqing Medical University (No. 2020–36). Each participant received written informed consent before registration. In addition, the study is carried out in accordance with the Declaration of Helsinki and other relevant regulations.

Sample Size Calculation

For the non-inferiority clinical trial, the sample size is estimated by PASS 2021 software. An acceptable treatment is expected to achieve cure rates of 90% or greater with less side effects.[19] We found the actual difference of eradication rates between the VA14 and BCQ in the pre-experiment to be 0.04. Thus, noninferiority is established if the 95% lower confidence boundary for the difference between the VA14 and BCQ in eradication rates is >-0.1, with a power (1-β) is 0.80, alpha (significance level) is 0.05. Then the sample size is obtained: n=47 persons. In addition, to reduce the error of lost follow-up, an additional 20% will be added on this basis, so 59 cases in each group need to be observed.

Study Population

From July 2020 to July 2022, 256 patients are screened and registered in this research in the Department of Gastroenterology, the Second Affiliated Hospital of Chongqing Medical University. Inclusion criteria: 1) patients who are older than 18 years old, 2) diagnosed as naive HP infection by 13C or 14C urea breath test (UBT), and 3) have not undergone any HP eradication treatment, and 4) have informed consent. Patients are excluded if they have any of the following conditions: 1) pregnant or lactating women; 2) received any antibiotics 4 weeks before initiating study treatment, 3) use of PPIs, histamine H2-receptor antagonists, bismuth, and non-steroidal anti-inflammatory drugs 2 weeks before taking the trial medicine; 3) allergy to any study drug; 4) accompanied by mental diseases or major organic lesions; 5) lack of informed consent.

Administration Plan and Follow-Up

After inclusion, 224 eligible patients are randomly assigned to receive VA14 dual, VAC triplet, and BCQ therapies, with an allocation ratio of 1:1:1. The random allocation sequence is determined by the computer-generated random map. VA14 dual therapy includes VPZ (Takeda Pharmaceutical Company Limited, Hikari plant, Japan) 20 mg b.i.d and AMO (United Laboratories Co., Ltd., China) 750 mg t.i.d for 14 days. VAC triple therapy includes VPZ 20 mg, b.i.d, AMO 750 mg, t.i.d, and JWC (Tianshili Pharmaceutical., Ltd., China) 160 mg, t.i.d for 14 days. The conventional quadruple therapy includes esomeprazole (AstraZeneca Pharmaceutical Co., Ltd., China) 20 mg b.i.d, AMO (United Laboratories Co., Ltd., China) 1000 mg b.i.d, furazolidone (Lisheng Tianjin Pharmaceutical., Ltd., China) 100 mg b.i.d, and 0.6 g bismuth potassium citrate (220 mg of bismuth, Lizhu pharmaceutical factory of Lizhu group, China) b.i.d for 14 days. Schematic diagram of patient selection and study design is shown in Figure 1.

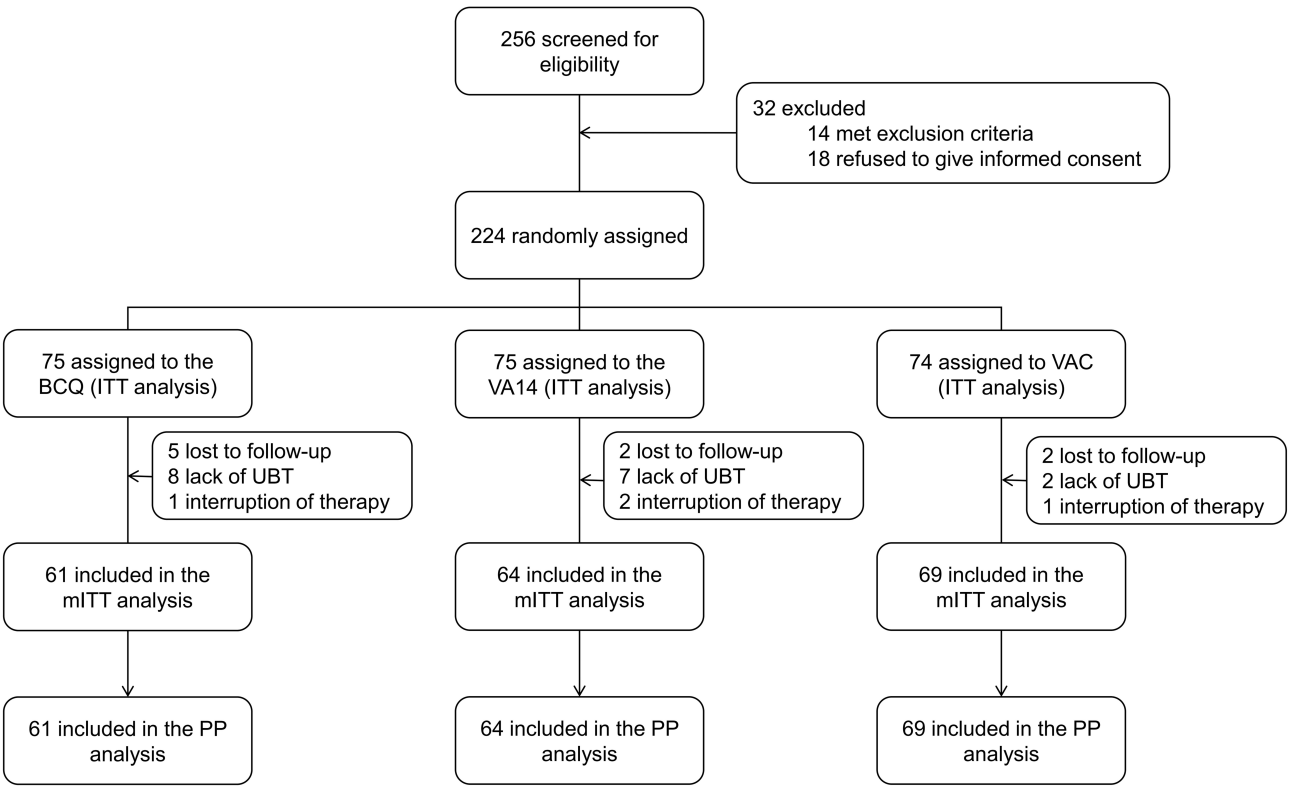

Figure 1 Schematic diagram of patient selection and study design. Of the 256 H. pylori-infected patients assessed for eligibility, 32 were excluded from this study, 14 were ineligible, and 18 refused. A total of 224 study subjects were successfully randomized and allocated to the BCQ group (n=75 of ITT population, n=61 of mITT and PP population), VA14 group (n=75 of ITT population, n=64 of mITT and PP population) and the VAC group (n =74 of ITT population, n=69 of mITT and PP population).
Abbreviations: ITT, intention-to-treat; mITT, modified intention-to treat; PP, per-protocol; UBT, 13C-Urea Breath Test; VA14, vonoprazan+amoxicillin for 14 days, modified dual therapy group; VAC, vonoprazan+amoxicillin+Jinghua Weikang Capsule modified triplet therapy group; BCQ, bismuth containing quadruple therapy group.

Outcome Evaluation

The primary endpoint of this study is the comparison of the eradication rate of HP 4 weeks after treatment among the 3 groups. Diagnosis criterion for HP infection: positive results were obtained by [13C]/[14C]-urea breath test (UBT) before administration. HP eradication standard: the patient stops taking the drug for at least 4 weeks and is negative in the UBT. The secondary end points are drug-induced adverse reactions (AEs), patient compliance, and drug costs among the three groups. During the 14-day eradication treatment, all patients are instructed and required to record their compliance with drugs and adverse events. The researchers asked the patients to evaluate their severity of AEs according to the standard for common terminology of adverse events (CTCAE) v.6.0, using a 1–4 rating system. The compliance is evaluated with the medication possession rate (MPR), which is defined as the proportion of days in treatment period (14 days) that patients take drugs. MPR≥80% is considered compliance, and MPR≤80% is defined as noncompliance. The cost of drugs is calculated according to the Medication Pricing Catalogue 2019 in Chongqing.

Statistical Analysis

SPSS 20.0 and PASS 2021 statistical software are used for data analysis. For the non-inferiority clinical trial, the sample size estimation is operated by PASS 2021. The measurement data conforming to normal distribution are expressed as mean±standard deviation (x±s). Analysis of variance is used for comparison between groups; χ^2 test is used for comparison of counting data between multiple groups and two groups if they meet the χ^2 test requirement. For unqualified counting data, an accurate probability method is used. The data of paired comparison are tested by signed rank sum test. $P<0.05$ meant the difference is statistically significant.

Results

Baseline Demographic and Clinical Characteristics of the Study Subjects

Summary of the baseline demographic characteristics and clinical and laboratory characteristics of the enrolled patients is indicated in Table 1. In general, there is no significant difference in patient demographic characteristics and clinical and laboratory characteristics between the VA14 group, VAC group, and BCQ group ($p>0.05$).

Table 1 Baseline Demographic and Clinical Characteristics of the Study Subjects

	VA14 Group	VAC Group	BCQ Group	p values		
				BCQ vs VA14	BCQ vs VAC	VA14 vs VAC
Gender						
Male	26	31	34	0.182	0.672	0.364
Female	49	43	41			
Age (yr)	45.85±13.97	43.85±15.47	42.67+12.61	0.167	0.608	0.386
BMI (kg/m^2)	25.85±4.80	25.35±5.50	25.48±3.58	0.626	0.867	0.514
Smoking						
YES	32	35	37	0.413	0.804	0.570
NO	43	39	38			
Alcohol drinking						
YES	64	55	52	0.404	0.428	0.094
NO	11	19	13			
Dining Style						
Gather dining	73	74	75	0.155	N.A.	0.157
Individual dining	2	0	0			
PPI usage before trial						
YES	7	5	5	0.547	0.982	0.563
NO	68	69	70			

Notes: VA14, vonoprazan 20 mg b.i.d. + amoxicillin 750 mg t.i.d. for 14 days. VAC, VA14 + Jinghua Weikang Capsule 160 mg t.i.d for 14 days. BCQ, bismuth-containing quadruple therapy, esomeprazole 20 mg b.i.d + AMO 1000 mg b.i.d + furazolidone 100 mg b.i.d + 0.6 g bismuth potassium citrate b.i.d for 14 days.
Abbreviations: BMI, body mass index; PPI, proton pump inhibitor.

Eradication Rates in VA14 Group Show Non-Inferiority to BCQ

All ITT analysis and MITT/PP (no case dropped out after drug-usage) analysis demonstrate that eradication rates (indicated in Table 2) in VA14 group show equivalence and non-inferiority to that in BCQ group. Patients with HP infection could achieve the similar eradication rate by taking only two kinds of drugs (VPZ and AMO, VA14) or three kinds of drugs (VPZ, AMO, and JWC; VAC) as four drugs (esomeprazole, AMO, furazolidone, and bismuth potassium citrate; BCQ). Expect for BCQ, both VA14 and VAC achieve eradication rate >90%. However, even the best result of eradication rate as AMO 1000 mg b.i.d and VPZ 20 mg b.i.d for 10 days in Hu's research only achieve 89.2% eradication rate of HP, less than 90%. These confirm that increasing dosage or administration frequency of AMO (1000 mg b.i.d in Hu's to 750 mg t.i.d in VA14), elongating the course of therapy (10 days in Hu's to 14 days in VA14) could evaluate the eradication rate of HP.[17] In addition, JWC further improved the eradication rate of VA14 numerically, but this improvement failed to reach statistical significance.

VA14 Indicated Advantages of BCQ in AEs, Patient Adherence, and Drug Costs

In regard to adverse effects (AEs), both VA14 and VAC groups show significantly fewer incident rates of AEs (indicated in Table 3, $p<0.05$). Furthermore, comparing with VA14 group, VAC group demonstrates lower incidence of adverse reactions ($p=0.041$). Meanwhile, the significant better compliance was found in comparison between BCQ and VAC

Table 2 Eradication Rates in Each Group

	BCQ Group	VA14 Group	VAC Group	Difference of VA14 from BCQ Group (Adjusted 95% CI for Difference)	P value for VA14 Noninferiority with BCQ (One-Side)	P value for Difference (Two-Sides)		
						BCQ vs VA14	BCQ vs VAC	VA14 vs VAC
ITT	78.67% (59/75)	77.33% (58/75)	86.49% (64/74)	−1.34%	0.0451	0.844	0.209	0.656
95% CI	73.94%±83.40%	72.50%±82.16%	82.52%±90.46%					
MITT/PP	96.72% (59/61)	90.63% (58/64)	92.75% (64/69)	−6.09%	0.0261	0.618	0.317	0.147
95% CI	94.44%±99.00%	86.99%±94.27%	89.63%±95.87%					

Notes: ITT and MITT/PP analyses of eradication rates attained by VA14, VAC and BCQ. VA14, vonoprazan 20 mg b.i.d. + amoxicillin 750 mg t.i.d. for 14 days. VAC, VA14 + Jinghua Weikang Capsule 160 mg t.i.d for 14 days. BCQ, bismuth-containing quadruple therapy, esomeprazole 20 mg b.i.d + AMO 1000 mg b.i.d + furazolidone 100 mg b.i.d + 0.6 g bismuth potassium citrate b.i.d for 14 days.

Abbreviations: CI, confidence interval; ITT, intention to treat; PP, per-protocol; MITT, modified intention-to treat.

Table 3 AEs, Patient Adherence, and Drug Costs in Each Group

	BCQ Group	VA14 Group	VAC Group	p values		
				BCQ vs VA14	BCQ vs VAC	VA14 vs VAC
Adverse events	22.95% (14/61)	9.38% (6/64)	1.45% (1/69)	**0.038**	**0.002**	**0.041**
Nausea	8.20% (4/61)	6.25% (4/64)	1.45% (1/69)	0.944	0.131	0.146
Diarrhea	3.28% (2/61)	0	0	0.144	0.488	N.A.
Dizziness	1.64% (1/61)	1.56% (1/64)	0	0.973	0.469	0.957
Taste distortion	1.64% (1/61)	0	0	0.304	0.286	N.A.
Skin rash	1.64% (1/61)	0	0	0.304	0.286	N.A.
Tongue discolouration	1.64% (1/61)	0	0	0.304	0.286	N.A.
Darkened stool	4.92% (3/61)	0	0	0.073	0.101	N.A.
Others	1.64% (1/61)	1.56% (1/64)	0	0.973	0.286	0.481
Adverse events caused drop-out	0	0	0	N.A.	N.A.	N.A.
Compliance	81.33% (61/75)	85.33% (64/75)	93.24% (69/74)	0.585	**0.029**	0.119
Drug cost (RMB)	317.19	285.06	414.33			

Notes: The bold values indicated p values <0.05. VA14, vonoprazan 20 mg b.i.d. + amoxicillin 750 mg t.i.d. for 14 days. VAC, VA14 + Jinghua Weikang Capsule 160 mg t.i.d for 14 days. BCQ, bismuth-containing quadruple therapy, esomeprazole 20 mg b.i.d + AMO 1000 mg b.i.d + furazolidone 100 mg b.i.d + 0.6 g bismuth potassium citrate b.i.d for 14 days.

group (p=0.029). No case drop-out due to AEs. Drug costs are calculated and compared between the three groups. The cost of the VA14 group is 285.06 RMB, which is lower than those of the BCQ group 317.19 RMB and VAC group 414.33 RMB.

Discussion

Globally, the CLA resistance rate is greater than 15% in HP-infected patients.[4,14] Due to rising CLA resistance rates, eradication rates of HP by PPI-based triple therapy have dropped less than 80% in Europe and the United States.[7,8,20] In China, the situation is even worse, the resistance rates of CLA is 20%–50%, metronidazole is 58%–100%, and levofloxacin is 20%–45%, respectively.[6,21,22] Thus, in the past decade, the eradication rate of HP decrease from 95% to 80% in the worldwide,[6] and from 89% to 78% in China.[13] Fortunately, so far, the resistance to AMO is still rare in the Asia Pacific region, from 0.1% to 22%.[23,24]

Maintaining gastric pH value more than 6 keeps HP in replication, thus increasing the effectiveness of amoxicillin,[25] which means that the anti-bacterial efficacy of AMO is pH dependent. PPIs gradually fail to achieve satisfying intragastric pH control for HP eradication therapy due to their disadvantages such as short elimination half-life, insufficient acid-suppressive capacity, and pharmacokinetic differences between races.[26] Thus, the strategy of improving the effect of anti-acid drugs is thought to become an effective method to breakthrough the bottleneck of HP eradication rate in the Asia Pacific region, especially in China.

A potassium competitive acid blocker, VPZ, can quickly and effectively inhibit gastric acid secretion and elevate the pH value in the stomach. In addition, the rapid increase of pH in the stomach by VPZ may also be helpful to shorten the therapy duration of HP eradication treatment. In the first clinical trial conducted in Japan, the eradication rate of HP by VPZ containing AMO and CLA triple therapy was 92.6%, while the eradication rate of HP containing PPI (such as lansoprazole) regimen was 75.9%.[15] The same clinical results are obtained in patients in the United States and Europe. Research revealed that the VPZ-based triple and dual regimens were non-inferior to the lansoprazole-based triple regimen in eradicating CLA- and AMO-naive HP, and significantly higher eradication rates in subgroups of CLA-resistant strains were observed.[27] Further studies in Japan have shown that the HP eradication rate of VPZ + AMO dual combined therapy (92.9%) is not lower than that of VPZ + AMO + CLA triple combined therapy (91.9%).[11] Therefore, the dual therapy based on VPZ (VPZ 20 mg b.i.d, AMO 500 mg t.i.d, treatment course of 1 week) can effectively eradicate HP infection without the need for double antibiotics, such as CLA. At the same time, it can also reduce the adverse effects of the use of multiple antibiotics on intestinal bacteria and reduce the economic burden of patients.

However, when the same dual strategy was applied in other areas, reports found unsatisfactory HP eradication rate with dual therapy of VPZ+ AMO.[28] Gotoda et al found that the eradication rate of vonoprazan dual therapy did not reach 90% in the treatment of naive patients.[29] In addition, a recent meta-analysis showed that the eradication rate of vonoprazan dual therapy was less than 90%.[30] In China, Hu et al increased the dose of AMO to 1000 mg b.i.d even t.i.d for 7 or 10 days. Nevertheless, the eradication rate of dual regiment is still lower than 90%, which could be achieved by conventional BCQ strategy.[17]

How to improve VPZ-AMO strategy to challenge conventional BCQ strategy in China becomes a burning issue. First, increasing the frequency of administration of AMO seems to be a better way to improve the eradication rate of HP in VPZ-AMO strategy than simply increasing the dose of AMO. The bactericidal effect of AMO depends on the percentage of time above the minimum inhibitory concentration (MIC) (%T>MIC), rather than the maximum concentration/MIC or AUC (area under the blood concentration time curve)/MIC.[31] Since the plasma half-life of AMO is short,[32] theoretically, the bid dose of AMO seems inappropriate. It is reasonable to give AMO t.i.d or q.i.d to make %T>MIC longer.[33] Secondly, prolonging treatment course may also be a potential strategy to improve HP eradication rate of VPZ-AMO strategy. The eradication therapy course was set at 1 week because that VPZ 20 mg could reduce the intragastric pH to 7 within 3–4 hours[10] and generally, HP strains sensitive to amoxicillin cannot survive for 1 week on the agar plate containing AMO. Therefore, if sufficient pH conditions are provided in the stomach, 1 week is enough for AMO to play a satisfactory role. However, report showed the 7-day VPZ-AMO strategy failed to achieve an acceptable eradication rate. We speculate that it is related to the severity of HP infection and drug resistance, unhealthy diet habits, and poor compliance in China. Based on these, Hu's research prolonged the VPZ-AMO therapy to 10 days and increase the dosage

of AMO. The eradication rate of HP did increase significantly, but it was still lower than the level of more than 90% which BCQ achieved.[17] Thirdly, some non-antibiotic Chinese botanicals with proven effectiveness, Jinghua Weikang Capsule, for example, are likely to be useful in improving HP eradication rates in VA programs.

In our research, we further prolong the VA therapy to 14 days and used a compromised AMO dose but a higher frequency of 750 mg t.i.d (VA14). To evaluate the eradication rate of VA14, we compare it with that of conventional BCQ therapy which is still the standard therapy and achieves the highest eradication rate of HP in current situation in China. We do not organize a 7-days therapy group with same doses of VPZ-AMO for rigorous demonstration because this has been confirmed ineffective and unethical. The 14-day VPZ-AMO strategy (VA14) we designed shows that the eradication rate of HP is equivalent to that of the conventional BCQ therapy in the non-inferiority test. This result is consistent with the results of Gao et al 14-day VA therapy, but Gao's study used a higher dose of AMO, up to 3000 mg daily.[34] On the other hand, the incident rates of AEs, compliance, and cost schemes in VA14 group are also lower than those of BCQ therapy. However, the compliance of VA14 group was not superior to that of BCQ group, which may be related to the same administration time and doubts about new drugs.

For further improving the therapeutic effect, we combine a wildly used non-antibiotic and anti-HP Chinese patent medicine JWC with VA14 as a modified triple therapy (VAC). JWC has also been proved to protect gastric mucosa from inflammatory response induced by HP via nuclear factor-κB signaling pathway and has bactericidal activity against antibiotic resistant HP.[35,36] Although the eradication rate is not significantly improved in the VAC group with the addition of JWC compared with VA14, the incidence of adverse effects is significantly reduced, and the difference is statistically significant. This may be related to the fact that JWC had been reported to reduce the inflammatory response of the gastric mucosa. The VAC group also showed significantly higher medication adherence, which may be related to its ability to significantly reduce adverse drug reactions and the relative acceptance of proprietary Chinese medicines in the Chinese population.

Inevitably, our research has some deficiencies. First, the sample size of single-center research is small, which may lead to potential sampling selection bias. Further research is needed to increase the sample size to demonstrate the efficacy of VA14 and the role of JWC in improving the eradication rate of HP and reducing the incidence of AEs. Second, the 24-hour intragastric pH value is not detected during the whole treatment process. Therefore, we cannot directly evaluate whether gastric acid secretion is successfully inhibited. Third, we did not perform subgroup analysis of AMO dose or frequency of dosing or duration time of treatment. Therefore, the identification of specific factors for the improvement of HP eradication rate is ambiguous.

Conclusion

In conclusion, our results prove that, in the anti-HP therapy of VPZ combined with AMO, prolonging the administration time, and increasing the administration frequency of AMO can improve the eradication rate of HP. Furthermore, compared with the conventional BCQ therapy, dual therapy of VPZ and AMO for 14 days is also effective, and cheaper and safer. JWC can further increase the efficiency and decrease adverse effects of VA regimen. Our research supports the suggestion of recommending VA therapy for 14 days as an alternative first-line treatment for HP eradication in China.

Abbreviations

VPZ, vonoprazan; HP, *Helicobacter pylori*; AMO, amoxicillin; VA14, 14-day dual therapy group (VPZ 20 mg b.i.d + AMO 750 mg t.i.d for 14 days); VAC, 14-day modified triple therapy group (VA14 + Jinghua Weikang Capsule 160 mg t.i.d, VAC); BCQ, bismuth-containing quadruple therapy group for 14 days; AEs, adverse events; CLA, clarithromycin; PPI, proton pump inhibitors; RCT, random controlled trial; JWC, Jinghua Weikang Capsule; RMB, Chinese Yuan; MIC, minimum inhibitory concentration; t.i.d, ter in die; b.i.d, bis in die; q.i.d, quater in die.

Data Sharing Statement

The data that support the findings of this study are available upon reasonable request from the first author Juan LI, 305265@hospital.cqmu.edu.cn. The data are not publicly available due to privacy or ethical restrictions.

Ethics Approval and Informed Consent

This clinical trial is reviewed and approved by the ethics committee of the Second Affiliated Hospital of Chongqing Medical University (No. 2020-36). Each participant received written informed consent before registration. In addition, the study is carried out in accordance with the Declaration of Helsinki and other relevant regulations.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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