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RESEARCH ARTICLE

Is tailored therapy based on antibiotic susceptibility effective ? A multicenter, open-label, randomized trial

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Abstract **An effective eradication therapy of *Helicobacter pylori* (*H. pylori*) should be used for the first time. In this study, we assessed whether tailored therapy based on antibiotic susceptibility testing is more effective than traditional therapy. We also evaluated the factors that cause treatment failure in high-resistance areas. For this multicenter trial, we recruited 467 *H. pylori*-positive patients. The patients were randomly assigned to receive tailored triple therapy (TATT), tailored bismuth-containing quadruple therapy (TABQT), or traditional bismuth-containing quadruple therapy (TRBQT). For the TATT and TABQT groups, antibiotic selection proceeded via susceptibility testing using an agar-dilution test. The patients in the TRBQT group were given amoxicillin, clarithromycin, esomeprazole, and bismuth. Successful eradication was defined as a negative ^{13}C-urea breath test at least eight weeks after the treatment ended. Susceptibility testing was conducted using an agar-dilution test. The eradication rate was examined via intention-to-treat (ITT) and per-protocol (PP) analyses. The clarithromycin, levofloxacin, and metronidazole resistance rates were 26.12%, 28.69%, and 96.79%, respectively. Resistance against amoxicillin and furazolidone was rare. The eradication rates for TATT, TRBQT, and TABQT were 67.32%, 63.69%, and 85.99% in the ITT analysis ($P < 0.001$) and 74.64%, 68.49%, and 91.22% in the PP analysis ($P < 0.001$), respectively. The efficacy of TABQT was affected by clarithromycin resistance, and bismuth exerted a direct influence on TATT failure. TABQT was the most efficacious regimen for use in high-resistance regions, especially among clarithromycin-susceptible patients.**

Keywords tailored triple therapy; tailored bismuth-containing quadruple therapy; traditional bismuth-containing quadruple therapy; antibiotic susceptibility testing; eradication rates

Introduction

The eradication of *Helicobacter pylori* (*H. pylori*) has been a popular topic in recent years because this type of bacteria is associated with the risk of developing peptic ulcer, chronic gastritis, and gastric cancer [1–3]. Consensus reports have shown that eradication therapy is the first-line treatment for *H. pylori*-infected patients [4–6]. Increasing antimicrobial resistance is strongly associated with the unsatisfactory eradication rate of *H. pylori* [4–6]. Several studies have reported that the eradication rate for traditional therapy is below 80% in many cities, especially in regions with high incidence of antibiotic resistance [7,8]. Therefore, strategies to improve eradication rates are urgently needed.

Traditional triple therapy containing one proton pump inhibitor (PPI) and two antibiotics (clarithromycin and amoxicillin or metronidazole) is not recommended in several countries [4,7,8]. In China, traditional bismuth-

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containing quadruple therapy is used as the first-line treatment for *H. pylori* infection [4,9–11]. Several studies have investigated *H. pylori* resistance. Overall, antimicrobial resistance exhibits high geographic variation. The global resistance rate for metronidazole ranges from 14.4% to 93.2% [12]. Even cities in the same province demonstrate variations in antibiotic resistance rates over a wide range (e.g., clarithromycin resistance from 12.8% to 22.87% and levofloxacin resistance from 18.8% to 30.68%) [13]. Traditional therapy cannot be applied universally and does not produce eradication rates $\geqslant$ 90% in all regions because antibiotic consumption data and antibiotic adverse reactions are ignored. Successful therapy should be evaluated as having a high eradication rate, such as $\geqslant$ 85% by ITT analysis or $\geqslant$ 90% by PP analysis [14].

Ideally, eradication regimens should be based on the community antibiotic background of *H. pylori*-infected patients [1,4–6,14]. For example, seven-day triple therapy remains valid in regions where clarithromycin resistance is lower than 10% [15,16]. However, in the absence of drug susceptibility testing, the use of this therapy is not recommended when the resistance rate is higher than 15% [17]. A consensus report recommended that future clinical treatment of *H. pylori* infection should be conducted according to antibiotic resistance information obtained by drug susceptibility testing [17]. Patients can take one or more antibiotics depending on the sensitivity of their *H. pylori* stomach isolates (i.e., tailored therapy). However, few studies have examined the efficacy of tailored therapy in clinical treatment, and whether tailored triple therapy (TATT) is effective or not in regions with high levels of antibiotic resistance is unknown. Moreover, factors other than antibiotic resistance that influence the eradication rate in different eradication regimens have not been investigated.

Therefore, we conducted an open-label trial to compare the eradication rates of TATT tailored bismuth-containing quadruple therapy (TABQT), and traditional bismuth-containing quadruple therapy (TRBQT) for 14 days in first-line treatment. We also comprehensively evaluated the factors that might affect the two regimens' efficacies. This study provides a valuable clinical reference in selecting available treatment strategies for *H. pylori* infections.

Materials and methods

Subject selection

This multicenter, parallel, open-label trial was performed on *H. pylori*-positive patients with upper gastrointestinal symptoms from March 2014 to September 2014 from three hospitals in Wenzhou, Zhejiang Province, China. All of the subjects required initial eradication treatment for *H. pylori*, as indicated by a positive ^{13}C-urea breath test and *H. pylori* culture results. The inclusion criteria were as follows: (1) aged 18 to 70 years; (2) patients had abdominal pain, bloating, acid reflux, belching, nausea, vomiting, heartburn, chest pain, hematemesis, melena, etc.; (3) no antibiotics, H2 receptor antagonists, or PPIs have been used in the past month; (4) the ^{13}C-urea breath test is positive; and (5) patients are willing to undergo initial *H. pylori* eradication treatment and willing to cooperate with doctors in a follow-up investigation. The exclusion criteria were as follows: (1) younger than 18 years; (2) severe heart, liver, or kidney dysfunction; (3) pregnant or lactating women; (4) esophageal or gastrointestinal surgery history; (5) psychosis or severe neurosis; and (6) known or suspected allergy to clarithromycin, levofloxacin, amoxicillin, and furazolidone. All patients had a detailed understanding of this study and gave their written informed consent. Moreover, a personal health management strategy was assigned to each patient.

Trial design and procedures

Before enrollment, *H. pylori* infection was diagnosed using a ^{13}C-urea breath test. Patients with positive results underwent endoscopy, and gastric mucosal biopsy samples from the antrum were collected for *H. pylori* isolation. The patients were considered eligible when they had a positive *H. pylori* culture result. Eligible subjects were randomly divided into TATT, TABQT, and TRBQT groups. Each group received 14-day regimens. To ensure allocation concealment, the major researchers in each participating center contacted an independent research assistant to obtain the next allocation number by phone after receiving written informed consent forms from the patients.

Antibiotic susceptibility testing was made available to the three treatment groups. All participants in the TRBQT group were blinded to the antimicrobial susceptibility results. The treatment regimens in the TRBQT group were given twice a day and contained amoxicillin, clarithromycin, esomeprazole, and bismuth potassium citrate (ACEB) or amoxicillin, clarithromycin, esomeprazole, and colloidal bismuth pectin (ACEC).

Antibiotic selection for the TATT and TABQT groups was based on the antibiotic susceptibility test results for *H. pylori*. For example, patients with strains susceptible to clarithromycin were administered amoxicillin and clarithromycin. When the *H. pylori* strains were clarithromycin-resistant but levofloxacin-susceptible, amoxicillin and levofloxacin were administered to the patients. When the strains were resistant to both clarithromycin and levofloxacin, the patients were administered amoxicillin and furazolidone. The major difference between the two regimens was the use of bismuth. Subjects in the TATT group received one triple therapy consisting of amoxicillin, clarithromycin, and esomeprazole (ACE); amoxicillin,

levofloxacin, and esomeprazole (ALE); or amoxicillin, furazolidone, and esomeprazole (AFE) according to the drug susceptibility data. Subjects in the TABQT group were given esomeprazole, two types of sensitive antibiotics, and bismuth potassium citrate or colloidal bismuth pectin. The doses of the drugs used in this study were as follows: 20 mg of esomeprazole, 500 mg of clarithromycin, 200 mg of levofloxacin, 1 g of amoxicillin, 100 mg of furazolidone, and 220 mg of bismuth potassium citrate or 200 mg of colloidal bismuth pectin. All medications were taken twice daily.

Subjects who took less than 80% of the pills during treatment were considered to have poor compliance. All subjects had a personal health management strategy that was designed to record information, including pathological report, antibiotic susceptibility results, therapeutic regimen, and side effects. Additionally, medication reminders were delivered twice (before treatment and a week after treatment). The doctors advised the patients to take their medication on time over the phone.

The eradication outcomes were assessed using a ^{13}C-urea breath test performed at least eight weeks after the treatment ended for all subjects as a follow-up. Negative ^{13}C-urea breath test results with a delta value < 2.5 units were defined as successful eradication of *H. pylori*. Subjects with positive results and a delta value $\geqslant 4$ units were considered to be *H. pylori* treatment failure [18]. Subjects with inconclusive results were assigned to receive another ^{13}C-urea breath test after two weeks until the results became conclusive.

H. pylori culture and antibiotic susceptibility testing

Isolation of *H. pylori* and antibiotic susceptibility testing were carried out at the laboratory at Hangzhou Zhiyuan Medical Inspection Institute. A gastric mucosa biopsy sample was ground, cultured on plates containing Columbia agar (Oxoid) with 5% defibrinated sheep blood, and incubated for 3 d under microaerophilic conditions (5% O_2 and 10% CO_2) at 37 °C. The colonies resembling *H. pylori* were identified by Gram staining and urease, catalase, and oxidase activity testing. Suspensions of *H. pylori*-positive strains were prepared in phosphate-buffered saline (PBS, pH 7.4) at a concentration of 4×10^8 CFU/mL for antibiotic susceptibility testing. Sequentially, the suspensions were inoculated onto Mueller–Hinton agar (Oxoid) plates containing 5% sheep blood and a single antibiotic, which was incubated in the same microaerophilic atmosphere at 37 °C for 3 d [16]. The minimum inhibitory concentration was as follows: clarithromycin $\geqslant 1$, levofloxacin $\geqslant 2$, amoxicillin $\geqslant 2$, furazolidone $\geqslant 2$ μg/mL, and metronidazole $\geqslant 8$ μg/mL [19,20]. Antibiotic resistance was determined according to the status of *H. pylori* growth. A standard *H. pylori* strain (ATCC43504) was used as the quality control.

Statistical analysis

The eradication rates of *H. pylori* in this study were assessed via intention-to-treat (ITT) and per protocol (PP) analyses. All subjects were included in the ITT analysis. Subjects who did not return for a follow-up ^{13}C-urea breath test were classified as treatment failures in the ITT analysis. For the PP analysis, subjects who failed to take at least 80% of their medicine or did not return for a follow-up ^{13}C-urea breath test were excluded. We compared continuous data using the Student's *t* test. A comparison of categorical data among groups was performed using the chi-square test, and 95% confidence intervals were calculated. A *P*-value < 0.05 was considered significant. The SPSS software package (version 19.0; SPSS, Inc., Chicago, IL, USA) was used for all statistical analyses.

Results

Baseline characteristics and prevalence of resistance

From March 2014 to September 2014, gastric mucosal biopsy samples were collected from patients who underwent endoscopy to isolate *H. pylori* strains. In this multicenter study, 467 *H. pylori*-positive patients were enrolled and randomized to receive one of three treatments (Fig. 1). No significant differences were observed in the baseline characteristics of the three treatment groups, including age, male-to-female ratio, and pathological diagnostic results (Table 1). The resistance rates of *H. pylori* were 26.12% (122/467) for clarithromycin, 28.69% (134/467) for levofloxacin, 96.79% (452/467) for metronidazole, and 0% for amoxicillin and furazolidone. The resistance rates were lower in the TRBQT group than in the two other groups for clarithromycin and levofloxacin. However, no significant difference was observed in clarithromycin resistance ($\chi^2 = 3.271$, $P = 0.195$) and levofloxacin resistance ($\chi^2 = 1.717$, $P = 0.424$) among the three treatment groups (Table 1).

Comparative analysis of eradication rates and side effects

As shown in Table 2, the eradication rate of *H. pylori* obtained in the ITT analysis was significantly higher for the patients who received TABQT compared with patients who received TATT ($\chi^2 = 15.142$, $P < 0.001$) and TRBQT ($\chi^2 = 20.719$, $P < 0.001$). The PP analysis showed that *H. pylori* eradication was successful for 91.22% (95% CI, 87.44%–96.34%) of the patients in the TABQT group. However, in the ITT and PP analyses, the eradication rate was lower than 75% for TATT ($\chi^2 = 14.053$, $P < 0.001$) and TRBQT ($\chi^2 = 23.658$, $P < 0.001$). No significant differences in eradication rates were found between TATT and TRBQT

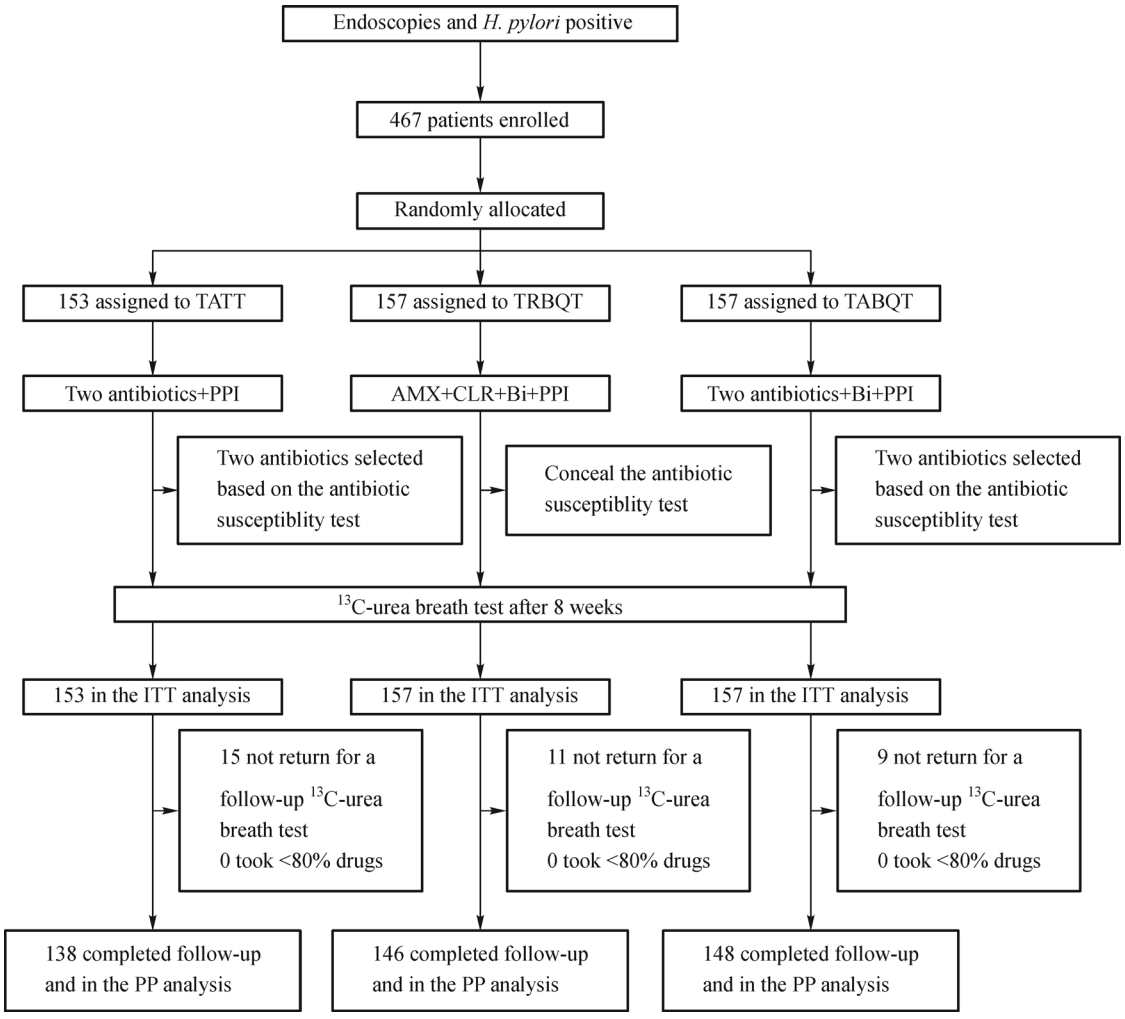

Fig. 1 Trial profile of the study. AMX, amoxicillin; Bi, bismuth; CLR, clarithromycin; ITT, intention-to-treat analysis; PP, per-protocol analysis; PPI, proton pump inhibitors; TABQT, tailored bismuth-containing quadruple therapy; TATT, tailored triple therapy; TRBQT, traditional bismuth-containing quadruple therapy.

groups in the ITT analysis ($\chi^2 = 0.451$, $P = 0.502$) and PP analysis ($\chi^2 = 1.314$, $P = 0.252$). The rate of loss to follow-up for TATT, TRBQT, and TABQT groups was also not significantly different ($\chi^2 = 1.934$, $P = 0.38$). Although most of the side effects were mild, the proportions of diarrhea, bloating, nausea, and vomiting in the three treatments were high (Table 2). Significant differences in bloating were observed between TRBQT and TABQT ($\chi^2 = 6.779$, $P = 0.009$). According to the combined eradication rates and side effects, TABQT was the best treatment choice.

Factors affecting the eradication rates in TABQT and TATT groups

A total of 108 and 113 patients exhibited clarithromycin susceptibility in the TATT and TABQT groups, respectively. However, the eradication rate was higher in the patients treated with TABQT than in the patients treated with TATT ($\chi^2 = 11.839$, $P < 0.001$ in the ITT analysis; $\chi^2 = 11.770$, $P = 0.001$ in the PP analysis; Table 3). For patients susceptible to levofloxacin, TABQT was more effective than TATT, although the difference was not significant (80% vs. 76.19% in the ITT analysis, $\chi^2 = 0.097$, $P = 0.755$; 86.96% vs. 80% in the PP analysis, $\chi^2 = 0.38$, $P = 0.538$). Additionally, TABQT was more effective than TATT for strains resistant to clarithromycin and levofloxacin (84.21% vs. 54.17% in the ITT analysis, $\chi^2 = 4.359$, $P = 0.037$).

For most patients susceptible to clarithromycin, the eradication rate of TABQT was 93.4% in the PP analysis. The efficacy of TABQT was affected by the increasing prevalence of clarithromycin resistance. The eradication rate decreased to 86.96% ($\chi^2 = 1.096$, $P = 0.259$) and 84.21% ($\chi^2 = 1.847$, $P = 0.174$) in the PP analysis, both of which are lower than the acceptable PP cure rate [14].

Table 1 Demographic characteristics of patients and prevalence of antibiotic resistance

	TATT (n = 153)	TRBQT (n = 157)	TABQT (n = 157)	P value
Patient information				
Gender (M/F)	74/79	75/82	84/73	0.537
Age (year, mean, S.D.)	48.10 (11.41)	49.52 (11.88)	49.30 (10.25)	0.492
Pathological diagnosis				
Chronic gastritis	36.6% (56/153)	38.85% (61/157)	38.22% (60/157)	0.915
Chronic gastritis with intestinal metaplasia	18.95% (29/153)	23.57% (37/157)	19.11% (30/157)	0.519
Chronic gastritis accompanied with erosion	14.38% (22/153)	10.19% (16/157)	13.38% (21/157)	0.509
Chronic atrophy gastritis	16.7% (26/153)	15.92% (25/157)	19.74% (31/157)	0.656
Gastric mucosal atypical hyperplasia	11.11% (17/153)	9.55% (15/157)	7% (11/157)	0.45
Other	1.96% (3/153)	1.91% (3/157)	2.55% (4/157)	0.911
Antibiotic resistance rate				
CLR	29.41% (45/153)	21.02% (33/157)	28.03% (44/157)	0.195
LVX	30.72% (47/153)	24.84% (39/157)	30.57% (48/157)	0.424
MTZ	95.42% (146/153)	97.45% (153/157)	97.45% (153/157)	0.507
AMX	0% (0/153)	0% (0/157)	0% (0/157)	
FR	0% (0/153)	0% (0/157)	0% (0/157)	

AMX, amoxicillin; CLR, clarithromycin; F, female; FR, furazolidone; LVX, levofloxacin; M, male; MTZ, metronidazole; S.D., standard deviation; TABQT, tailored bismuth-containing quadruple therapy; TATT, tailored triple therapy; TRBQT, traditional bismuth-containing quadruple therapy.

Table 2 *H. pylori* eradication rates and side effects in the three treatments

Outcomes	TATT	TRBQT	TABQT
Eradication rate			
ITT analysis (%, n/N)	67.32% (103/153)*	63.69% (100/157)*	85.99% (135/157)
PP analysis (%, n/N)	74.64% (103/138) *	68.49%(100/146)*	91.22% (135/148)
Lost to follow-up evaluation (%, n/N)	9.8% (15/153)	7.01% (11/157)	5.73% (9/157)
Side effects (%, n/N)			
Abdominal pain	3.27% (5/153)	3.82% (6/157)	3.18% (5/157)
Bloating	3.92% (6/153)	9.55% (15/157)*	2.55% (4/157)
Nausea and vomiting	3.92% (6/153)	8.92% (14/157)	3.82% (6/157)
Diarrhea	6.53% (10/153)	7.64% (12/157)	6.37% (10/157)
Skin rash	2.61% (4/153)	2.55% (4/157)	3.82% (6/157)
Constipation	3.92% (6/153)	3.18% (5/157)	3.18% (5/157)
Black stool	0.65% (1/153)	0% (0/157)	0% (0/157)
Taste distortion	3.27% (5/153)	1.91% (3/157)	3.18% (5/157)

ITT, intention-to-treat analysis; PP, per-protocol analysis; TABQT, tailored bismuth-containing quadruple therapy; TATT, tailored triple therapy; TRBQT, traditional bismuth-containing quadruple therapy.
* indicates significant differences between TATT and TABQT (P<0.05) and between TRBQT and TABQT (P<0.05).

Table 3 *H. pylori* eradication rates of sensitive antibiotic selection in TATT and TABQT treatments

Antibiotic selection	AMX + CLR	AMX + LVX	AMX + FR
TATT			
ITT analysis (%, n/N)	68.52% (74/108)	76.19% (16/21)	54.17% (13/24)
PP analysis (%, n/N)	76.29% (74/97)	80% (16/20)	61.9% (13/21)
TABQT			
ITT analysis (%, n/N)	87.61% (99/113)*	80% (20/25)	84.21% (16/19)*
PP analysis (%, n/N)	93.4% (99/106) *	86.96% (20/23)	84.21% (16/19)

AMX, amoxicillin; CLR, clarithromycin; FR, furazolidone; ITT, intention-to-treat analysis; LVX, levofloxacin; PP, per-protocol analysis; TABQT, tailored bismuth-containing quadruple therapy; TATT, tailored triple therapy.
* indicates significant differences between the treatment of AMX + CLR from TATT and TABQT (P<0.05) and between the treatment of AMX + FR from TATT and TABQT (P<0.05).

However, the eradication rates were lower than 80% in the TATT group.

For the TATT group, the eradication of TATT was significantly lower than TABQT. The eradication of TATT was significantly lower than TABQT-ACEC (68.52% vs. 85.71% in the ITT analysis, $\chi^2 = 3.941$, $P = 0.047$; 76.29% vs. 93.75% in the PP analysis, $\chi^2 = 4.696$, $P = 0.003$) and TAQBT-ACEB (68.52% vs. 88.46% in the ITT analysis, $\chi^2 = 10.135$, $P = 0.001$; 76.29% vs. 93.24% in the PP analysis, $\chi^2 = 8.812$, $P = 0.003$). The use of bismuth was the main difference between TATT and TABQT. The result suggested that bismuth exerted a direct influence on TATT failure in the region with a high prevalence of resistance. Therefore, TABQT was the most efficacious regimen, especially in areas with high clarithromycin resistance ($> 20\%$).

Discussion

This study obtained several important findings. First, as expected from the consensus report, TABQT is more effective than TRBQT. Second, bismuth availability is necessary in regions with high levels of antibiotic resistance. Without bismuth, TATT has a low eradication rate. No significant differences in eradication rates were detected between TATT and TRBQT. Third, clarithromycin resistance decreases the efficacy of TABQT.

The most common cause of treatment failure in *H. pylori* infection worldwide is increasing antimicrobial resistance [4–6]. China, wherein antimicrobial resistance is typically high, is no exception [21,22]. The resistance rate of metronidazole exceeds 90% in several areas [13]. This situation maybe related to the widespread use of metronidazole in anti-anaerobic treatment in gynecology, stomatology, and surgery and anti-amebic treatment in infectious diseases. Since 1999, bismuth has been used as the second-line treatment to improve eradication rate and reduce antibiotic resistance [9]. Currently, bismuth-containing quadruple therapy is the first-line treatment [4]. However, its efficacy is affected by the geographical area [12,13]. A randomized trial has reported that the eradication rates are higher in areas with low clarithromycin resistance than in areas with high resistance [23]. Our study showed that the resistance rate for clarithromycin was 26.12%. A recent study has also reported that the clarithromycin resistance rate was 20.43% from 2009 to 2015 in Wenzhou, Zhejiang Province, China [13]. One of the reasons for this high resistance is that standard triple therapy has been abandoned. In this study, the efficacy of TATT was only 67.32%. The efficacy of TRBQT was only 68.49%, which is lower than the efficacy previously reported in Shanghai [24]. The clarithromycin resistance rate in Shanghai has been reported to be 18%, and the highest success rate exceeds 90% [24]. Moreover, eradication for patients with clarithromycin resistance was lower than that for patients susceptible to clarithromycin, which had an eradication rate of 93.4% in the PP analysis for the TABQT group (Table 3).

Bismuth potassium citrate, colloidal bismuth pectin, and colloidal bismuth subcitrate are widely available in China [21]. In our study, although the types of bismuth did not significantly affect the eradication rate of *H. pylori* for quadruple therapy, bismuth exerted a direct influence on the failure of the TATT regimen in the region with a high prevalence of resistance (Supplementary Fig. 1). TATT produced poor results, with 67.32% in ITT and 74.64% in PP analyses (Table 2). In other words, clinical treatment based on antibiotic resistance by drugs could be recommended, but this possibility does not ensure that the susceptibility test results will provide the best treatment for *H. pylori* infection. High efficacies should be established based on appropriate therapies according to the community antibiotic background [4–6]. In regions with a low incidence of antibiotic resistance, triple therapy can achieve eradication rates higher than 90%. For example, in a previous work, three types of seven-day triple therapies obtained 90% eradication rates in Yongkang, Zhejiang Province, China [16]. A similar result was obtained in Hong Kong, China, where the resistance rates to clarithromycin and levofloxacin are low [15]. However, in this high-resistance region, triple therapies are likely to be a poor choice. Although the patients selected sensitive antibiotics to eradicate *H. pylori*, the efficacies were all unsatisfactory (Table 3). Therefore, bismuth should be used in high-resistance regions.

Our study showed that the eradication rate of TABQT was significantly higher than the rates obtained for the two other groups (Table 2), especially for clarithromycin-susceptible *H. pylori* patients (Table 3). Several studies have suggested that *H. pylori* clarithromycin resistance is the main reason for treatment failure [25,26]. The lack of susceptibility data has forced doctors to select therapies empirically. Several studies have suggested the use of an alternative antibiotic regimen. In China, the substitution of furazolidone for clarithromycin was recommended in 2005 by the Second Chinese National Consensus Report [10]. A number of randomized studies have reported that the eradication rates of bismuth–furazolidone-containing quadruple therapies are superior to those of non-furazolidone regimens [18,27]. However, we did not fully recommend bismuth–furazolidone-containing quadruple therapies in this study. First, many *H. pylori* patients are still clarithromycin-sensitive although antibiotic resistance is a serious problem. Second, our study showed that the TABQT regimen consisting of clarithromycin, amoxicillin, esomeprazole, and bismuth had a 93.4% eradication rate in the PP analysis for clarithromycin-susceptible patients. Third, from the perspective of adverse effects, furazolidone has significant toxicity, including genotoxicity, hepato-

toxicity, and carcinogenicity [28,29]. Current consensus reports indicate that effective eradication therapy should be used as the first-line treatment regimen [4–6]. Additionally, the cost of endoscopic and antibiotic treatments in Chinese patients is about 500 CNY, and the cost of antibiotic susceptibility testing is about 200 CNY. Compared with the situation in the TRBQT group, more than 20% eradication rate of *H. pylori* was improved by antibiotic susceptibility testing in the TABQT group. Therefore, TABQT might be effective in areas with high resistance. Additionally, clarithromycin resistance was the main reason for the treatment failure of TABQT.

HP treatment should be based on the regional antibiotic resistance background and drug resistance data in combination with tailored treatment under the guidance of antibiotic susceptibility testing from the perspective of safe drug use and economic output ratio. In conclusion, a high *H. pylori* eradication rate was achieved in patients with TABQT according to the antibiotic susceptibility testing. This regimen was effective in curing clarithromycin-susceptible patients. Bismuth should be used in high-resistance regions.

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Compliance with ethics guidelines

Jie Pan, Zhengchao Shi, Dingsai Lin, Ningmin Yang, Fei Meng, Lang Lin, Zhencheng Jin, Qingjie Zhou, Jiansheng Wu, Jianzhong Zhang, and Youming Li declare that they have no conflict of interest. This trial was approved by the Chinese Ethics Committee of Registering Clinical Trials and the clinical trial registration number was ChiCTR-TRC-13004223 (Date of registration: September 29, 2013) and the approved number of ethic committee was ChiECRCT-2013034 (Date of approved by ethic committee: December 2, 2013). Informed consent was obtained from all patients in this article.

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