PO Box 2345, Beijing 100023, China
Fax: +86-10-85381893
E-mail: wjg@wjgnet.com www.wjgnet.com

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• BRIEF REPORTS •

Clinical evaluation of four one-week triple therapy regimens in eradicating *Helicobacter pylori* infection

Chuan-Yong Guo, Yun-Bin Wu, Heng-Lu Liu, Jian-Ye Wu, Min-Zhang Zhong

Chuan-Yong Guo, Yun-Bin Wu, Heng-Lu Liu, Jian-Ye Wu, Min-Zhang Zhong, Department of Gastroenterology, Tielu hospital of Tongji University, Shanghai 200072, China
Correspondence to: Dr. Chuan-Yong Guo, Department of Gastroenterology, Tielu Hospital of Tongji University, Shanghai 200072, China. guochuanyong@hotmail.com
Telephone: +86-21-56779971 **Fax:** +86-21-66303983
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Abstract

AIM: To evaluate clinical efficacy of four one-week triple therapies in eradicating *Helicobacter pylori* infection.

METHODS: In this clinical trial, 132 patients with duodenal ulcer and chronic gastritis were randomly divided into four groups, and received treatment with OAC (omeprazole 20 mg + amoxicillin 1 000 mg + clarithromycin 250 mg), OFC (omeprazole 20 mg + furazolidone 100 mg + clarithromycin 250 mg), OFA (omeprazole 20 mg + furazolidone 100 mg + amoxicillin 1 000 mg) and OMC (omeprazole 20 mg + metronidazole 200 mg + clarithromycin 250 mg), respectively. Each drug was taken twice daily for one week. The ^{13}C urea breath test was carried out 4-8 weeks after treatment to determine the success of *H pylori* eradication.

RESULTS: A total of 127 patients completed the treatment. The eradication rate for *H pylori* infection was 90.3%, 90.9%, 70.9% and 65.6%, respectively in OAC, OFC OMC and OFA groups.

CONCLUSION: A high eradication rate can be achieved with one-week OAC or OFC triple therapy. Thus, one-week triple therapies with OAC and OFC are recommended for Chinese patients with duodenal ulcers and chronic gastritis.

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INTRODUCTION

Eradication of *Helicobacter pylori* infection has become a wide clinical practice for *H pylori* related diseases such as peptic ulcers, and considerable clinical efficacy has been achieved over the past two decades[1-6]. However, many short-term (one week) triple therapy regimens include metronidazole and suffer from the problem of metronidazole resistance, which could significantly decreases clinical efficacy[7-11]. Therefore, it is a very important issue to search for anti-*H pylori* regimens that are highly effective in eradicating *H pylori* infection but without drug resistance[12]. The aim of the present study was to evaluate the clinical efficacy of four short-term triple therapy regimens with clarithromycin.

MATERIALS AND METHODS

Selection of patients

Criteria of selection (1) Those aged 18-70 years. (2) Those with duodenal ulcer (DU) or chronic gastritis (CG) confirmed by gastroscopy. (3) Those who were positive for *H pylori* by a rapid urease test (RUT) and positive by serology, silver or Giemsa staining and histological examination.

Criteria of exclusion (1) Patients who had gastric ulcer or severe gastroesophageal reflux disease, and those who had gastric operation history, hemolytic anemia or family history of hemolytic anemia. (2) Patients who were in lactation or pregnancy. (3) Patients who had combined severe diseases of other system that might affect the medical evaluation of this study. (4) Patients who took the drugs included in this study over the past month. (5) Patients who was allergic to the drugs included in this study.

Methods

Drugs Omeprazole (20 mg/cap, Changzhou fourth Pharmaceutical Factory), clarithromycin (250 mg/tab, Hangzhou Chinese-American Eastchina Pharmaceutical Co. Ltd), furazolidone (100 mg/tab, Guangdong Jiangmen Pharmaceutical Factory), metronidazole (200 mg/tab, Shanghai Ensai Pharmaceutical Co. Ltd) and amoxicillin (250 mg/cap, Kunming Baker Norton Pharmaceutical Co. Ltd) were used.

Regimens Patients were randomly divided into four groups, and receive treatment with OAC (omeprazole 20 mg + amoxicillin 1 000 mg + clarithromycin 250 mg), OFC (omeprazole 20 mg + furazolidone 100 mg + clarithromycin 250 mg), OMC (omeprazole 20 mg + metronidazole 200 mg + clarithromycin 250 mg) and OFA (omeprazole 20 mg + furazolidone 100 mg + amoxicillin 1 000 mg), respectively. Each group took the drugs twice a day for 7 d.

Procedures At the entry, clinical symptoms, demographic data and medical history were recorded, and gastroscopy was performed to establish the endoscopic diagnosis and status of *H pylori* infection. During the gastroscopy examination, four biopsy specimens were taken from stomach: one for a rapid urease test (RUT), one for silver or modified Giemsa staining, and two for histological examination. Serum anti-*H pylori* IgG antibodies were also detected. The patients who were intensive positive by the RUT (positive in five minutes) were initially considered to be qualified for the study. Only those patients who were also positive by serology, *H pylori* staining and histological examination were included in the clinical trial. Patients were followed up on the eighth day to check clinical symptoms, side effects and compliance. A ^{13}C urea breath test was carried out 4-8 wk after completion of the therapy.

Definition of *H pylori* eradication *H pylori* eradication was defined when the ^{13}C urea breath test was negative 4-8 weeks after completion of anti-*H pylori* therapy.

Statistical analysis

H pylori eradication rate was the main analytic target. Total eradication rate and its 95% confidence interval of each regimen was calculated and analyzed by intention-to-treat

analysis (ITT) and per protocol (PP), respectively. The significance in the difference of eradication rate between various regimens was tested by Fisher exact probability and Chi-square test. The possible factors affecting eradication rate was analyzed in a logistic regression model. The difference in the incidence of side effects of each regimen was tested by Fisher exact probability test.

RESULTS

Demographic and clinical data

Of the 132 patients enrolled in the study, 127 (96.2%) completed the treatment and five (3.8%) dropped off. The demographic data and the proportion of DU and CG were not significantly different among the groups (Table 1).

Table 1 Comparison between patient age gender and endoscopic diagnostic results of each group

Group	*n*	Male / Female	Age (years)	DU / CG
OAC	33	20 / 13	43.5(18-70)	18 / 15
OFC	33	19 / 14	40.8(20-70)	17 / 16
OMC	33	21 / 12	41.6(19-69)	18 / 15
OFA	33	20 / 13	41.2(20-70)	19 / 14
Total	132	80 / 52	42.0(18-70)	72 / 64

H pylori eradication rates

H pylori eradication rates were significantly different in patients receiving OAC and OFC than in those receiving OMC and OFA ($P<0.05$) (Tables 2 and 3). In the logistic regression model including treatment regimen, age, sex and endoscopes diagnosis, treatment regimens were identified as an independent factor responsible for the difference in the eradication rate (Table 3).

Table 2 *H pylori* eradication rate in each group

Group	Per protocol			Intent to treat		
	n	Eradication rate (%)	Confidence interval (95%)	*n*	Eradication rate (%)	Confidence interval (95%)
OAC	31	90.3	79.8-95.6	33	84.9	80.1-92.3
OFC	33	90.9	78.5-97.3	33	90.9	79.6-95.4
OMC	31	70.9	64.0-81.7	33	66.7	62.5-76.7
OFA	32	65.6	59.9-72.2	33	63.6	60.2-71.6
Total	127	79.5	72.4-82.5	33	76.5	70.5-81.8

Table 3 *H pylori* eradication rate in each group in relation to endoscopic diagnosis

Group	Duodenal ulcer		Chronic gastritis	
	n	Eradication rate (%)	*n*	Eradication rate (%)
OAC	17	88.2	14	92.9
OFC	17	94.1	16	87.5
OMC	16	68.8	15	73.3
OFA	19	57.9	13	76.9
Total	69	76.8	58	82.8

Incidence of side effects

The incidence of side effects varied among the treatment regimens (Table 4). All of side effects were slight. A compliance of >90% was achieved for all the patients who completed the study.

Table 4 Incidence of side effects in each group

Side effects	Incidence of side effects in each group patients (%)				
	OAC (*n*=31)	OFC (*n*=33)	OMC (*n*=31)	OFA (*n*=32)	Total (*n*=127)
Gastroenteric reactions	6.45	9.09	12.9	9.38	9.45
Skin eruption	6.45	0	3.23	6.25	3.94
Headache	6.45	6.06	3.23	0	4.72
Glossitis	0	0	3.23	0	0.79
Weakness	0	0	3.23	0	0.79
Fever	0	3.03	0	0	0.79
Somnolence	3.23	0	3.23	0	1.57

DISCUSSION

In 1990, the 14-d bismuth triple therapy was recommended in the Ninth World Gastroenterology Conference in Sydney. Due to its high incidence of side effects (high than 30%) and poor compliance, this regimen has been replaced with other short-term 7-day triple therapy regimens that are more efficient and had fewer and milder side effects[13-19]. These new regimens include OMC 250 and OAC 500, which achieved *H pylori* eradication rates of more than 90% in the MACH-1 study[20-26]. However, the eradication rates with those regimens decreased due to emergence of metronidazole resistance in *H pylori* over the past few years. It has been reported that prevalence of metronidazole resistant *H pylori* strains has increased to more than 70% in China and other countries[27-31]. This accounts for the failure of *H pylori* eradication with metronidazole triple therapy.

With the wide application of anti-*H pylori* therapy and antibiotic abuse, drug resistance in *H pylori* has becomes an increasingly serious problem and a main reason of poor curative effect. At present[30,31], the resistance to clarithromycin in *H pylori* is diverse in the world. South-north difference existed such as the drugs used to treat other infection before (mainly respiratory infection). There are significant difference in the prevalence of metronidazole resistance between developed and developing countries. High prevalence of metronidazole resistance mainly relates to the wide application in parasite infection, dental infection and gynecological diseases in developing countries. Now there is a tendency that metronidazole resistance in *H pylori* is increasing in the developed countries, probably due to the application of anti-*H pylori* therapy. In spite of wide application of treatment with amoxicillin, amoxicillin resistance in *H pylori* was rare.

In order to overcome the problem of metronidazole resistance and to compare the clinical efficacy of triple therapy regimens containing clarithromycin, we carried out this study. We achieved relatively high eradication rates for the clarithromycin-containing regimens OAC and OFC (90.3% and 90.9%, respectively). On the other hand, the eradication rate was relatively low for the metronidazole-containing regimen OMC and OFA. Taken together, we conclude that OAC and OFC are efficient regimens in eradicating *H pylori* infection. Since the cost of furazolidone in OFC regimen is cheap and the *H pylori* eradication rate of OFC regimen is high, we recommend that this regimen be one of choices for *H pylori* eradication.

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