World Journal of Gastroenterology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.3748/wjg.v21.i39.11179

World J Gastroenterol 2015 October 21; 21(39): 11179-11184
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Clinical Trials Study

Effects of daily telephone-based re-education before taking medicine on *Helicobacter pylori* eradication: A prospective single-center study from China

Chun-Hua Wang, Sheng-Tao Liao, Jun Yang, Chun-Xia Li, Ying-Ying Yang, Ran Han, Dong-Feng Chen, Chun-Hui Lan

Chun-Hua Wang, Jun Yang, Chun-Xia Li, Ying-Ying Yang, Dong-Feng Chen, Chun-Hui Lan, Department of Gastroenterology, Daping Hospital, the Third Military Medical University, Chongqing 400042, China

Sheng-Tao Liao, Cadet Brigade, the Third Military Medical University, Chongqing 400042, China

Ran Han, Department of Gastroenterology, Guizhou Aerospace Hospital, Zunyi 563000, Guizhou Province, China

Author contributions: Lan CH designed the research; Wang CH, Yang J, Li CX and Yang YY performed the research; Han R and Chen DF contributed new reagents or analytic tools; Wang CH and Liao ST analyzed the data; Liao ST and Lan CH wrote the paper.

Supported by National Natural Science Foundation of China, No. 81171526 and No. 81472006.

Institutional review board statement: The study was reviewed and approved by Daping Hospital, Third Military Medical University Institutional Review Board.

Clinical trial registration statement: This study is registered at http://www.chictr.org.cn/showproj.aspx?proj=4382. The registration identification number is ChiCTR-TRC-14005193.

Informed consent statement: All study participants or their legal guardian provided informed written consent prior to study enrollment.

Conflict-of-interest statement: Chun-Hua Wang, Sheng-Tao Liao, Jun Yang, Chun-Xia Li, Ying-Ying Yang, Ran Han, Dong-Feng Chen, and Chun-Hui Lan have no conflicts of interest or financial ties to disclose.

Data sharing statement: No additional data are available.

Correspondence to: Chun-Hui Lan, MD, Department of Gastroenterology, Daping Hospital, the Third Military Medical University, No. 10 Changjiang Branch Road, Chongqing 400042, China. tiandaochouqin99@hotmail.com
Telephone: +86-23-68757616
Fax: +86-23-68757616

Received: March 5, 2015
Peer-review started: March 12, 2015
First decision: April 24, 2015
Revised: May 15, 2015
Accepted: August 29, 2015
Article in press: August 29, 2015
Published online: October 21, 2015

Abstract

AIM: To investigate the effects of daily telephone-based re-education (TRE) before taking medicine for the eradication of *Helicobacter pylori* (*H. pylori*) on the compliance and the eradication rate in a Chinese patient population.

METHODS: A prospective, physician-blinded, randomized, controlled clinical study was conducted. The patients were randomly assigned to receive TRE every day before taking medicine (TRE group) or no TRE (control group). The patients in the TRE group received regular instructions before taking medicine for the eradication of *H. pylori* during the entire course

of treatment through telephone calls. The patients in the control group received detailed instructions at the time of seeing a doctor for the guidance. The primary outcome was the *H. pylori* eradication rate after treatment. The secondary outcomes included the clinical remissions after treatment, adverse events, compliance, and patients' satisfaction.

RESULTS: A total of 140 patients were randomized, 70 to the TRE group and 70 to the control group. As the primary outcome, the *H. pylori* eradication rates in the TRE and control groups were 62.7% and 71.2% in per protocol analysis (P = 0.230), and 52.9% and 52.9% in intention-to-treat analysis (P = 0.567), respectively. As the secondary outcomes, there were no significant differences in the patients' satisfaction between the two groups (good, 79.7% *vs* 76.9%; fair, 13.6% *vs* 19.2%; poor, 6.7% *vs* 3.9%, for the TRE group and control group, respectively; $P > 0.05$ for all); the rates of adverse effects were 15.2% and 63.5% in the TRE and control groups, respectively ($P < 0.001$); the compliance rates in the TRE and control groups were 85.7% and 74.3%, respectively (P = 0.069).

CONCLUSION: Daily TRE before taking medicine had no significant impact on the patients' compliance, satisfaction, or *H. pylori* eradication, but reduced the rate of adverse events.

Key words: *Helicobacter pylori*; Eradication; Telephone re-education; Compliance; Adverse events

Core tip: Compliance is an important factor affecting *Helicobacter pylori* (*H. pylori*) eradication. The present study is the first attempt to evaluate the telephone re-education (TRE) in *H. pylori* treatment in China. The daily TRE neither improved the eradication rate nor the patients' compliance or satisfaction, but decreased adverse effects. Meanwhile, adverse effects may not be the main reason for poor compliance. Our results suggest that compliance is not the important reason for a decreased *H. pylori* eradication rate in China.

Wang CH, Liao ST, Yang J, Li CX, Yang YY, Han R, Chen DF, Lan CH. Effects of daily telephone-based re-education before taking medicine on *Helicobacter pylori* eradication: A prospective single-center study from China. *World J Gastroenterol* 2015; 21(39): 11179-11184 Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i39/11179.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i39.11179

INTRODUCTION

Helicobacter pylori (H. pylori) is a pathogen that infects more than 50% of the human population, resulting in high healthcare costs worldwide[1]. Although some of the *H. pylori*-positive individuals may remain asymptomatic through their life span, the infection can cause chronic gastritis in almost 100% of infected individuals, even resulting in severe diseases, such as atrophic gastritis, peptic ulcer disease, and gastric cancer[2]. Recently it has been revealed that poor compliance is often seen in patients undergoing treatment for the eradication of *H. pylori*[3]. Poor compliance and bacterial resistance are two major factors that cause the eradication rates of *H. pylori* to decrease to an unacceptable level ($\leqslant$ 80%)[4,5].

Compliance in *H. pylori* treatment has a great influence on treatment failures in antibiotic-sensitive patients and on the development of antibiotic resistance[6]. Multiple factors such as complexity and duration of the treatment can affect the patients' compliance. Several methods had previously been tried to enhance patients' compliance with instructions for *H. pylori* treatment, but the results are inconsistent. Adjuvant treatment (especially with probiotics) can improve the compliance[7].

Taking phone interview on the last day of therapy and returned pill counting can improve patients' compliance, but attempts to increase compliance may have no impact on the treatment outcomes[8]. The doctor-patient relationships, including the relations with pharmacists and nurses, can also play an important role in improving compliance and eradication of *H. pylori*[9]. In addition, structured aftercare and follow-up often help improve the compliance and subsequent *H. pylori* eradication rate[10,11].

China is among the countries with a high prevalence of *H. pylori* infection with a rate of 50%-80%. Several factors may affect the compliance of *H. pylori* treatment in Chinese patients such as lack of detailed guidance on drug administration, lack of detailed instruction or consultation from gastrointestinal doctors due to busy schedule, misunderstanding of or concerns over the side effects of Western medicine, and preference of use of traditional Chinese medicine due to the belief of having fewer adverse effects[12]. Therefore, there is an urgent need for improving the compliance of *H. pylori* treatment in China.

Telephone re-education (TRE) is often used to improve treatment compliance[6], but has not been well studied in China. We hypothesized that compliance of *H. pylori* infected patients and *H. pylori* eradication rate could be improved by TRE every day before taking medicine, reminding the patients of the detailed information related to the time and dose of medicines, answering the patients' questions, and comforting and encouraging them to continue the treatment. The purpose of the present study was to evaluate the effects of the intervention with TRE on the rate of *H. pylori* eradication and on other clinically relevant outcomes, such as the clinical symptoms after treatment and treatment-related adverse effects.

MATERIALS AND METHODS

Patients

The present study employed a prospective, physician-blinded, randomized, controlled single-center study design, and was conducted in consecutive outpatients at the Department of Gastroenterology of Daping Hospital, Chongqing, China, from September 2014 to November 2014. The study protocol and informed consent form were reviewed and approved by the Ethics Review Committee of Daping Hospital, Third Military Medical University, Chongqing, China [Approval No. (2014) 06], and the study was registered with the Chinese Clinical Trial Register (ChiCTR-TRC-14005193). Each of the patients provided written informed consent before enrolment to the trial.

Patients were randomized to either a TRE group or a control group at the time of first clinical visit, by using a computer generated random number kept in a sealed opaque envelope. At least two telephone numbers for each of the patients or their relatives living together were recorded for the TRE. All patients were instructed not to tell physicians and/or investigators about their preparation method and when they received instructions in any time of the study (before, during and after the procedure)

The inclusion criteria were as follows: (1) outpatients aged 18-60 years with chronic gastritis or gastroduodenal ulcer; (2) confirmed diagnosis of *H. pylori* infection by at least one of the following methods: ^{13}C-urea breath test, histology, rapid urease test or bacterial culture; (3) an indication of *H. pylori* eradication treatment; and (4) ability and willingness to participate in the study.

The exclusion criteria were as follows: (1) advanced chronic disease that would not allow the patient to complete follow-up or attend visits; (2) allergy to any of the drugs used in this study; (3) previous gastric surgery; (4) pregnancy or breastfeeding (female participants with childbearing potential were required to use medically accepted contraception for the duration of the study); (5) alcohol or drug abuse; (6) previous *H. pylori* eradication treatment; and (7) taking antibiotics or bismuth salts within two weeks before the study.

Intervention

The patients in the TRE group received detailed instructions at the time of seeing a doctor for the guidance of clinical medication and reexamination at four weeks after the treatment. The detailed instructions of rational drug use and periodic review were given by another doctor through telephone call every day before taking medicine. The 10-d treatment was the triple therapy, including esomeprazole (AstraZeneca Pharmaceutical Co, London, United Kingdom; Lot H20046379; 20 mg/12 h), amoxicillin (Zhuhai Union Pharmaceutical Co. ltd., Zhongshan, China, H44021351; 1 g/12 h), and clarithromycin (Shanghai Abbott Laboratories Co. Ltd., Shanghai, China, J20050067; 500 mg/12 h). Symptom relieving drugs including gastric mucosal protective drugs, cardiovascular drugs, and other medications were allowed to be used in both groups when needed. At four weeks after treatment, the patients received telephone calls to schedule reexamination through ^{13}C-urea breath test to confirm eradication.

The patients in the control group received detailed instructions at the time of seeing a doctor for the guidance of clinical medication and reexamination at four weeks after treatment. The treatment plan was identical as that in the TRE group.

Trial outcomes

The primary outcome was the eradication of *H. pylori* at four weeks after treatment. The eradication of *H. pylori* was confirmed by the ^{13}C-urea breath test. The secondary outcomes included the compliance, clinical symptom remission after treatment, adverse events, and patients' satisfaction. The satisfaction of the patients were evaluated and recorded using a ten-point scale (poor, 1-4; fair, 5-7; good, 8-10) based on questionnaire in a physician-blinded fashion.

Calculation of sample size

The sample size calculation was performed by assuming a 25% difference in the rate of *H. pylori* eradication after treatment. The rate of standard triple therapy in China was about 75%. We calculated that at least 116 patients were needed for the study by using a significance level (α) of 0.05 and a power of 80% with a two-tailed test. However, from our previous experience, approximately 20% of patients may withdraw from the trial or be lost to follow-up. We estimated that a total of 140 patients would be sufficient to detect a significant difference in the primary outcome.

Statistical analysis

The intention-to-treat (ITT) and per-protocol (PP) analyses were used to assess the primary outcome. Categorical variables were analyzed using χ^2 tests or Fisher's exact test, as appropriate. Continuous variables were expressed as mean ± SD and analyzed using Student's *t*-test. Analyses were performed with SPSS software V.19.0 for Windows. A P value < 0.05 was considered statistically significant.

RESULTS

Patients' characteristics

We screened 286 outpatients with *H. pylori* infection; 146 of them were excluded (82 met exclusion criteria and 64 were unwilling to participate in the study); 140 were randomized to the TRE group (n = 70) or the control group (n = 70). Eleven subjects in the TRE group and 18 in the control group withdrew from the

Table 1 Baseline characteristics of the patients included in this study *n* (%)

Characteristic	TRE group (*n* = 70)	Control group (*n* = 70)	*P* value
Sex (M/F)	25/45	28/42	1.000
Age (yr)	42.9 ± 10.7	45.9 ± 9.2	0.098
BMI (kg/m^2)	23.1 ± 4.0	23.7 ± 3.7	0.677
Grade of education			0.199
Elementary school or no education	5 (7.1)	9 (12.9)	
Higher than elementary school	65 (92.9)	61 (87.1)	
Residence			0.604
Country	8 (11.4)	8 (11.4)	
City	62 (88.6)	62 (88.6)	
Digestive tract hemorrhage	5 (7.1)	3 (4.3)	0.529
Family gastric cancer history	4 (5.7)	2 (2.9)	0.340
Endoscopy results			
Chronic gastritis	55 (71.2)	59 (84.3)	0.257
Peptic ulcer	14 (20.0)	10 (14.3)	0.251
Helicobacter pylori infection	70 (100.0)	70 (100.0)	

Values are expressed as mean ± SD, % or *n* (%). BMI: Body mass index; TRE: Telephone re-education; M: Male; F: Female.

Table 2 Effects of telephone re-education on the symptoms after treatment of *Helicobacter pylori* eradication *n* (%)

Symptom	TRE group (*n* = 59)	Control group (*n* = 52)	*P* value
Pain	14 (23.7)	10 (19.2)	0.367
Burning sensation	3 (5.1)	5 (9.6)	0.290
Acid reflux	4 (6.8)	3 (5.8)	0.571
Nausea and vomiting	3 (5.1)	1 (1.9)	0.358
Belching	2 (3.4)	3 (5.8)	0.440
Abdominal distension	8 (13.6)	2 (3.8)	0.071
Poor appetite	1 (1.7)	1 (1.9)	0.720

TRE: Telephone-based re-education.

study or were lost to follow-up for various reasons including a busy schedule, remission of symptoms and stopping medication in treatment process, unsatisfying efficacy, giving up treatment, adverse events, and others. There was no significant difference in the number of patients lost in the follow-up between the two groups (11 *vs* 18, *P* = 0.069). Finally, 59 in the TRE group and 52 in the control group completed the treatment for the eradication of *H. pylori*.

The baseline characteristics of the patients in both groups were well balanced (Table 1), with no significant differences between the two groups.

Outcomes of treatment

In the PP analysis of the primary outcome, the *H. pylori* eradication rates of the TRE and control groups were 62.7% (37/59) and 71.2% (37/52) (*P* = 0.230), while in the ITT analysis, the rates were 52.9% (37/70) and 52.9% (37/70) (*P* = 0.567), respectively.

There were no significant differences in the symptoms after treatment between the two groups (*P* > 0.05 for all; Table 2). The rate of adverse effects in the TRE group was significantly lower than that of the control group (*P* < 0.001; Table 3). The taste disorder was significantly lower in the TRE *vs* the control group (6.8% *vs* 53.8%, *P* < 0.001)

Table 3 Effects of telephone re-education on the adverse events after *Helicobacter pylori* treatment *n* (%)

Adverse event	TRE group (*n* = 59)	Control group (*n* = 52)	*P* value
Skin rash	2 (3.4)	0 (0.0)	NS
Headache	1 (1.7)	0 (0.0)	NS
Sore throat	0 (0.0)	2 (3.8)	NS
Taste disorder	4 (6.8)	28 (53.8)	< 0.001
Diarrhea	2 (3.4)	3 (5.8)	0.44
Total	9 (15.2)	33 (63.5)	< 0.001

NS: Not significant; TRE: Telephone-based re-education.

Table 4 Satisfaction of patients included in this study *n* (%)

	TRE group	Control group	*P* value
Satisfaction			
Good	47 (79.7)	40 (76.9)	0.452
Fair	8 (13.6)	10 (19.2)	0.290
Poor	4 (6.7)	2 (3.9)	0.401

TRE: Telephone-based re-education.

The compliance rate in the TRE group (84.3%) was slightly higher; however non-significant than that of the control group (74.3%, *P* = 0.069). The results of patients' satisfaction are shown in Table 4. There was no significant difference in patients' satisfaction between the two groups (*P* > 0.05).

DISCUSSION

The triple therapy as a traditional standard care is widely used in China, but the eradication rate is decreasing due to various reasons such as drug resistance, poor compliance, high bacterial loads, and genic polymorphisms of cytochrome P450 proteins 2C19 (CYP2C19)[2,13-15]. Therefore, the standard triple therapy does not reach the acceptable threshold of 80% eradication rate in most contexts[5,16]. Most studies have focused on the antibiotic resistance. In fact, improving compliance is relatively simple and less costly compared with other measures to improve the therapeutic outcome. The improvement in compliance can be accomplished through education. In the present study, the *H. pylori* eradication rates in the TRE and control groups were 62.7% and 71.2% (PP), and 52.9% and 52.9% (ITT), respectively.

Failure to comply with the anti-*H. pylori* therapy (AHT) requirements by the patient often results in treatment failure[6,17]. In a previous study, patients with good compliance had a higher AHT effectiveness rate (96%) than those with low compliance (69%)[17]. The major reason for poor compliance was the development of an adverse event during the course

of AHT[18], and the adverse events were found to be different with different AHT regimens[19]. In our study, the rates of adverse effects were 15.2% and 63.5% in the TRE and control groups, respectively. The reasons for the difference may be a result of telephone follow-up every day, including timely resolve, comfort and relief of the symptoms among the TRE patients. The studies with a seven-day AHT regimen have shown a 41% frequency of adverse effects, which provoked cessation of therapy in 3%-10% of the patients[20]. If the treatment time is prolonged to 10-14 d, the development of adverse effects can be seen in more than half of the patients[21].

In order to improve the compliance of *H. pylori* eradication, detailed instructions of rational drug use and periodic review were provided by telephone call every day before taking medicine. A follow-up telephone call after initiation of therapy in a previous study suggested that although adverse effects were common between enhanced compliance program and control groups, most patients were able to complete 60% or more of the two-week regimen[20]. There was no statistically significant difference between the two test groups in the number of patients taking more than 60% of the medications, and the number of patients taking more than 90% of the medications; an enhanced compliance program further improved the percentage of medications taken[22].

However, similar studies found that the enhanced compliance had no impact on the treatment outcome and adverse effects were very common[8].

In the present study, TRE every day before taking medicine could not significantly improve the compliance or the *H. pylori* eradication rate. No statistically significant differences were found between TRE and control groups regarding the symptoms after treatment; however, the adverse effects in the TRE were significantly fewer than those in the control group. The results indicated that adverse effects might not be the major reason for poor compliance and less effectiveness in the eradication of *H. pylori*.

Although adverse effects are common in standard therapies, they are rarely severe. In our study, the adverse effects included taste disorder, diarrhea, skin rash, headache and sore throat. The most common adverse events reported in most studies are diarrhea, nausea, and vomiting. Using the standard first-line triple therapy, a multi-center study has found that the overall rate of adverse events was 53.3%[23]. The evidence supporting concurrent administration of probiotics to lessen the side-effects of triple therapy is still equivocal. While Kim *et al*[24] found that probiotics had no effect on the side-effect profile, but increased the rates of eradication, another study revealed that probiotics reduced side-effects and did not affect the eradication rate[25]. In our study, the adverse effects in the TRE group were significantly less than that of the control group, but the *H. pylori* eradication rates were similar between the two groups. Although the compliance increased in the TRE group, it was non-significant compared to the control group. Moreover, there were no differences in the satisfaction of patients between the two groups. It seems that the patients neither recognized the difference nor acknowledged the effects of the TRE. It is possible that daily telephone calling was exaggerated and perhaps made the patients feel uncomfortable. The effectiveness and acceptance of TRE may be dependent on the type of disease and the intervention. For instance, in a study conducted in China, it has been reported that TRE one day prior to colonoscopy improved the compliance, quality of bowel preparation, and the polyp detection rate[26]. Our results suggested that TRE may not be the best way to improve compliance in *H. pylori* treatment and that modifications of the TRE intervention may be required or other better approaches are needed.

In conclusion, the present study represented the first attempt to evaluate the TRE in *H. pylori* treatment in China. Although the daily TRE did not improve the *H. pylori* eradication rate, compliance, or patients' satisfaction, it decreased adverse effects. Meanwhile, adverse effects may not be the main reason for poor compliance. Our results may help develop an effective plan for improving compliance and therapeutic outcome of *H. pylori* therapy.

COMMENTS

Background

Compliance with therapy is one of the most important factors in *Helicobacter pylori* (*H. pylori*) eradication. The effects of telephone re-education (TRE) daily before taking medicine for *H. pylori* treatment on the compliance and the *H. pylori* eradication rate have not yet been studied in China.

Research frontiers

Most studies have mainly focused on the antibiotic resistance in the treatment of *H. pylori* eradication. Improving compliance is a relatively simple and less costly approach to improving the therapeutic outcome, compared with other measures. The improvement in compliance can be accomplished through effective patient education program.

Innovations and breakthroughs

In the present study, an innovative TRE program was developed and evaluated in patients undergoing *H. pylori* treatment in China. The most important findings were that daily TRE before taking medicine reduced the rate of adverse events, but had no significant impact on the patients' compliance, satisfaction, or *H. pylori* eradication rate.

Applications

The results from the present study suggest that compliance is not the main reason for a decreased *H. pylori* eradication rate in China. Additionally, adverse effects may not be the main reason for poor compliance. These results would help develop a more effective plan for improving compliance and therapeutic outcome of *H. pylori* therapy in China.

Terminology

Daily TRE: The detailed instructions of rational drug use and periodic review were given to the patient by physicians through telephone call every day before taking medicine.

Peer-review

The authors conducted a new study to investigate the effects of daily TRE program before taking medicine on the compliance and the eradication rate

in patients with the treatment for eradication of *H. pylori*. It is believed that this is the first study of this kind in China. The authors provided sufficient data to support their conclusion that daily TRE before taking medicine had no significant impact on the patients' compliance, satisfaction, or *H. pylori* eradication, but reduced the rate of adverse events. The research is interesting and the study design and the results are clearly presented. Future large-scale studies should be conducted to develop an effective way to improve the outcome of *H. pylori* eradication therapy in China and other countries as well.

REFERENCES

1 **Hunt RH**, Xiao SD, Megraud F, Leon-Barua R, Bazzoli F, van der Merwe S, Vaz Coelho LG, Fock M, Fedail S, Cohen H, Malfertheiner P, Vakil N, Hamid S, Goh KL, Wong BC, Krabshuis J, Le Mair A. Helicobacter pylori in developing countries. World Gastroenterology Organisation Global Guideline. *J Gastrointestin Liver Dis* 2011; **20**: 299-304 [PMID: 21961099]

2 **Malfertheiner P**, Megraud F, O'Morain CA, Atherton J, Axon AT, Bazzoli F, Gensini GF, Gisbert JP, Graham DY, Rokkas T, El-Omar EM, Kuipers EJ. Management of Helicobacter pylori infection--the Maastricht IV/ Florence Consensus Report. *Gut* 2012; **61**: 646-664 [PMID: 22491499 DOI: 10.1136/gutjnl-2012-302084]

3 **McNicholl AG**, Marin AC, Molina-Infante J, Castro M, Barrio J, Ducons J, Calvet X, de la Coba C, Montoro M, Bory F, Perez-Aisa A, Forné M, Gisbert JP. Randomised clinical trial comparing sequential and concomitant therapies for Helicobacter pylori eradication in routine clinical practice. *Gut* 2014; **63**: 244-249 [PMID: 23665990 DOI: 10.1136/gutjnl-2013-304820]

4 **Wermeille J**, Cunningham M, Dederding JP, Girard L, Baumann R, Zelger G, Buri P, Metry JM, Sitavanc R, Gallaz L, Merki H, Godin N. Failure of Helicobacter pylori eradication: is poor compliance the main cause? *Gastroenterol Clin Biol* 2002; **26**: 216-219 [PMID: 11981460]

5 **Gisbert JP**, Calvet X. Review article: the effectiveness of standard triple therapy for Helicobacter pylori has not changed over the last decade, but it is not good enough. *Aliment Pharmacol Ther* 2011; **34**: 1255-1268 [PMID: 22017749 DOI: 10.1111/j.1365-2036.2011.04887.x]

6 **O'Connor JP**, Taneike I, O'Morain C. Improving compliance with helicobacter pylori eradication therapy: when and how? *Therap Adv Gastroenterol* 2009; **2**: 273-279 [PMID: 21180555 DOI: 10.1177/1756283x09337342]

7 **Manfredi M**, Bizzarri B, Sacchero RI, Maccari S, Calabrese L, Fabbian F, De'Angelis GL. Helicobacter pylori infection in clinical practice: probiotics and a combination of probiotics + lactoferrin improve compliance, but not eradication, in sequential therapy. *Helicobacter* 2012; **17**: 254-263 [PMID: 22759324 DOI: 10.1111/j.1523-5378.2012.00944.x]

8 **Henry A**, Batey RG. Enhancing compliance not a prerequisite for effective eradication of Helicobacter pylori: the HelP Study. *Am J Gastroenterol* 1999; **94**: 811-815 [PMID: 10086671 DOI: 10.1111/j.1572-0241.1999.00856.x]

9 **Al-Eidan FA**, McElnay JC, Scott MG, McConnell JB. Management of Helicobacter pylori eradication--the influence of structured counselling and follow-up. *Br J Clin Pharmacol* 2002; **53**: 163-171 [PMID: 11851640 DOI: 10.1046/j.0306-5251.2001.01531.x]

10 **Talley NJ**, Fock KM, Moayyedi P. Gastric Cancer Consensus conference recommends Helicobacter pylori screening and treatment in asymptomatic persons from high-risk populations to prevent gastric cancer. *Am J Gastroenterol* 2008; **103**: 510-514 [PMID: 18341483 DOI: 10.1111/j.1572-0241.2008.01819.x]

11 **Fock KM**, Katelaris P, Sugano K, Ang TL, Hunt R, Talley NJ, Lam SK, Xiao SD, Tan HJ, Wu CY, Jung HC, Hoang BH, Kachintorn U, Goh KL, Chiba T, Rani AA. Second Asia-Pacific Consensus Guidelines for Helicobacter pylori infection. *J Gastroenterol Hepatol* 2009; **24**: 1587-1600 [PMID: 19788600 DOI: 10.1111/j.1440-1746.2009.05982.x]

12 **Liu X**, Cheng H, Gao W, Dong X, Hu F. [Efficacy and safety of 14-day amoxicillin and furazolidone-based quadruple rescue regimen for eradication of Helicobacter pylori: a retrospective study]. *Zhonghua Yi Xue Za Zhi* 2014; **94**: 567-571 [PMID: 24762682]

13 **Chey WD**, Wong BC. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. *Am J Gastroenterol* 2007; **102**: 1808-1825 [PMID: 17608775 DOI: 10.1111/j.1572-0241.2007.01393.x]

14 **Monés J**, Gisbert JP, Borda F, Domínguez-Muñoz E. Indications, diagnostic tests and Helicobacter pylori eradication therapy. Recommendations by the 2nd Spanish Consensus Conference. *Rev Esp Enferm Dig* 2005; **97**: 348-374 [PMID: 16004527 DOI: 10.4321/S1130-01082005000500007]

15 **Hu FL**, Hu PJ, Liu WZ, De Wang J, Lv NH, Xiao SD, Zhang WD, Cheng H, Xie Y. Third Chinese National Consensus Report on the management of Helicobacter pylori infection. *J Dig Dis* 2008; **9**: 178-184 [PMID: 18956598 DOI: 10.1111/j.1751-2980.2008.00342.x]

16 **Graham DY**, Fischbach L. Helicobacter pylori treatment in the era of increasing antibiotic resistance. *Gut* 2010; **59**: 1143-1153 [PMID: 20525969 DOI: 10.1136/gut.2009.192757]

17 **De Francesco V**, Ierardi E, Hassan C, Zullo A. Helicobacter pylori therapy: Present and future. *World J Gastrointest Pharmacol Ther* 2012; **3**: 68-73 [PMID: 22966485 DOI: 10.4292/wjgpt.v3.i4.68]

18 **Graham DY**, Lew GM, Malaty HM, Evans DG, Evans DJ, Klein PD, Alpert LC, Genta RM. Factors influencing the eradication of Helicobacter pylori with triple therapy. *Gastroenterology* 1992; **102**: 493-496 [PMID: 1732120]

19 **Maev IV**, Andreev DN, Kucheryavyi YA, Dicheva DT. Host Factors Influencing the Eradication Rate of Helicobacter Pylori. *WASJ* 2014; **61**: 134-140

20 **Hudson N**, Brydon WG, Eastwood MA, Ferguson A, Palmer KR. Successful Helicobacter pylori eradication incorporating a one-week antibiotic regimen. *Aliment Pharmacol Ther* 1995; **9**: 47-50 [PMID: 7766743 DOI: 10.1111/j.1365-2036.1995.tb00350.x]

21 **Fallone CA**. Treatment of Helicobacter pylori infection. *Minerva Gastroenterol Dietol* 2003; **49**: 1-9 [PMID: 16481966]

22 **Lee M**, Kemp JA, Canning A, Egan C, Tataronis G, Farraye FA. A randomized controlled trial of an enhanced patient compliance program for Helicobacter pylori therapy. *Arch Intern Med* 1999; **159**: 2312-2316 [PMID: 10547171 DOI: 10.1001/archinte.159.19.2312]

23 **Misiewicz JJ**, Harris AW, Bardhan KD, Levi S, O'Morain C, Cooper BT, Kerr GD, Dixon MF, Langworthy H, Piper D. One week triple therapy for Helicobacter pylori: a multicentre comparative study. Lansoprazole Helicobacter Study Group. *Gut* 1997; **41**: 735-739 [PMID: 9462204 DOI: 10.1136/gut.41.6.735]

24 **Kim MN**, Kim N, Lee SH, Park YS, Hwang JH, Kim JW, Jeong SH, Lee DH, Kim JS, Jung HC, Song IS. The effects of probiotics on PPI-triple therapy for Helicobacter pylori eradication. *Helicobacter* 2008; **13**: 261-268 [PMID: 18665934 DOI: 10.1111/j.1523-5378.2008.00601.x]

25 **Cremonini F**, Di Caro S, Covino M, Armuzzi A, Gabrielli M, Santarelli L, Nista EC, Cammarota G, Gasbarrini G, Gasbarrini A. Effect of different probiotic preparations on anti-helicobacter pylori therapy-related side effects: a parallel group, triple blind, placebo-controlled study. *Am J Gastroenterol* 2002; **97**: 2744-2749 [PMID: 12425542 DOI: 10.1111/j.1572-0241.2002.07063.x]

26 **Liu X**, Luo H, Zhang L, Leung FW, Liu Z, Wang X, Huang R, Hui N, Wu K, Fan D, Pan Y, Guo X. Telephone-based re-education on the day before colonoscopy improves the quality of bowel preparation and the polyp detection rate: a prospective, colonoscopist-blinded, randomised, controlled study. *Gut* 2014; **63**: 125-130 [PMID: 23503044 DOI: 10.1136/gutjnl-2012-304292]

P- Reviewer: Cheng H, Eren B, Murad HAS, Suzuki H
S- Editor: Yu J **L- Editor**: Wang TQ **E- Editor**: Wang CH

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com

ISSN 1007-9327