Dear Dr. Ma,

Thank you very much for your correspondence and advice on our manuscript (Manuscript #17413), entitled “Effects of daily telephone-based re-education before taking medicine for *Helicobacter pylori* eradication”. We also thank the reviewers for their constructive and positive comments, and suggestions. We have revised the manuscript accordingly and all amendments are highlighted in yellow in the revised manuscript. In addition, our point-by-point responses to the comments are listed in the following pages.

We hope that our responses and revisions meet your and the reviewers’ expectations and the manuscript is acceptable for the publication in your journal.

Look forward to hearing from you soon.

Yours sincerely,

Chun-hui Lan

Responses to Reviewers' Comments

First of all, we express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer 2

THE WHOLE TEXT

Please reduce it Helicobacter pylori should be in italic.

Response: Thanks for your suggestion. The correction has been made in the revised manuscript.

TITLE

Please add: a prospective single-center study from China. Please use on Helicobacter

Response: Thanks for your insightful suggestion. The correction has been made to the title.

ABSTRACT

There were no significant differences in the symptoms after treatment were found between the TRE and control groups ….; No significant differences in the symptoms and satisfaction of patients after treatment were observed between the two groups. The underlined sentences are the same, please just add (and satisfaction of patients) in the first sentence. Also the authors didn't mention the percentage of satisfaction.

Response: The two sentences have been modified in the abstract in the revised manuscript (Page 2, Lines 42-43)

Core tip

This study is the first attempt to … However, the daily TRE did not improve the H. pylori eradication rate, the compliance, or patients' satisfaction, it decreased adverse effects (please rephrase as follows: The daily TRE neither improved the eradication rate nor the patients' compliance or satisfaction, however it decreased adverse effects). Our results suggest that the most important reason that caused a deceased H. pylori eradication rate is likely an antibiotic resistance (it is not tested in the study), but not compliance.

Response: The sentence has been rephrased in the core tip (Page3, Lines 59-60). Meanwhile, the last

sentence in core tip has been revised (Page 3, Lines 62-63).

INTRODUCTION

1. Transfer Multiple factors such as complexity and duration of the treatment can affect the patients' compliance [6] from line 95 to line 78.

Response: Thanks for your rearrangement.

2. Line 80: 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 and lactoferrin) has often improved the compliance and the eradication rates [7]. According to the mentioned reference (see below), only probiotics improved compliance. No improvement in eradication. Thus please correct this sentence. CONCLUSIONS: Probiotics associated with ST provide optimum therapeutic compliance compared with the placebo and, despite the need to take a larger number of tablets, they should be taken into consideration as an adjuvant to therapy for H. pylori infection. The addition of LF to the PB did not bring about any further improvements in compliance. As compared with the placebo, the eradication rate of ST did not improve by adding LF + PB or by using PB alone.

Response: Thanks for your constructive suggestion. The correction has been made in the revised manuscript (Page 4, Line 81).

3. Line 110: please add a reference

Response: a reference has been added.

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(8):567-571. [PMID: 24762682]

MATERIALS AND METHODS

1. Line 137: please rephrase

Response: The sentence has been rephrased in the revised manuscript (Page 6, Lines 134-136).

2. Regarding Inclusion criteria: confirmation of diagnosis should come before indication of therapy, thus please rearrange as shown.

Response: Thanks for your rearrangement.

3. Line 181: How the scale of satisfaction was calculated? Based on questionnaire? if yes, what were the questions & was this questionnaire validated or not?)

Response: Yes, the scale of satisfaction was calculated based on questionnaire and this questionnaire has been applied in many studies.

RESULTS

1. Nothing is new in Figure 1 (just repetition of the aforementioned text), thus please delete it.

Response: Figure 1 has been deleted.

2. Table 4 is confusing because percentage of compliance is calculated out of n=70 while percentages of satisfaction were calculated out of n= 59 & n= 52 for the TRE and control groups respectively. Thus please delete compliance from the table.

Response: Thanks for your constructive suggestion. The compliance has been deleted from the table and the sentences have been revised (Page 9, Lines 228-231)

DISCUSSION

1. Line 269: Please rephrase to be clearer. 2. Line 269: The underlined is exactly copy & paste from Lee et al., 1999 (see below) RESULTS: There was no statistically significant difference between the 2 groups in the number of

Response: Thanks for your constructive suggestion. The sentence has been rephrased in the revised manuscript (Page 10, Lines 267-268).

Replies to Reviewer 3

This study was well designed and the results might be interesting for the readers of WJG. The followings are the comments for improvement.

Major

The rate of taste disorder in control group (54%) is extremely high compared to previous reports. Taste disorder is subjective and difficult to evaluate. The way of asking might have a problem. It should be clarified how and when the answer was collected. If this high rate is incontrovertible, the reasons should be explained with other references in discussion.

Response: Thanks for your constructive suggestion. All the adverse events were calculated based on the questionnaire after treatment. Although taste disorder was subjective and difficult to evaluate, we used the same method for its evaluation. There was significant difference in this subjective feeling between the two groups. These results indicated that daily telephone-based re-education may have a psychological effect to patients.

Minor

1, "H.pylori" should be italic.

Response: Thanks for your great suggestion. The correction has been made in the revised manuscript.

2, Are there patients who stopped medication due to taste disorder in each group? If yes, it should be compared with discussion.

Response: No, there patients who stopped medication mainly due to forgetting to take medicines. However, there might be other reasons, including a busy schedule, remission of symptoms, unsatisfying efficacy, giving up treatment, and others.

3, In discussion, "These results suggested that the TRE group would have more patients to continue to the therapy, due to fewer side effects" is not correct because the compliance rate was not statistically different in both groups.

Response: Thanks for your constructive suggestion. The sentence has been deleted in the revised manuscript.

Replies to Reviewer 4

1. They did not describe the number of patients to be used to calculate the PP and ITT eradication rates.

Whether the lost patients were included to calculate the ITT rate?

Response: Thanks for your insightful suggestion. Correction has been added (Page 9, Lines 218-220). Yes, all the lost patients were included to calculate the ITT rate.

2. They did not describe how to evaluate the compliance of patients. Whether the lost patients should be regarded as poor compliance? Whether the number of patients lost in TRE group less than the control was related to TRE?

Response: The compliance was defined by the numbers of reexamination *H. pylori* infection after treatment. Yes, the lost patients were regarded as poor compliance. 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), which may have no significant impact on the patients' compliance.

3. Suggest comparing the compliance of the failure patients between the two groups.

Response: Thanks for your constructive suggestion. There was also no significant difference in the compliance of the failure patients between the two groups.