

June 5, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 10815-Review.doc).

Title: Meta-analysis of the efficacy of probiotics in *Helicobacter pylori* eradication therapy

Author: Rong Zhu, Kan Chen, Yuan-yuan Zheng, Hua-wei Zhang, Jun-shan Wang, Yu-jing Xia, Wei-qi Dai, Fan Wang, Miao Shen, Ping Cheng, Yan Zhang, Cheng-fen Wang, Jing Yang, Jing-jing Li, Jie Lu, Ying-qun Zhou, Chuan-yong Guo

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1

(1) The favourable effects of probiotic in caucasian/non-caucasian populations must be more emphasized because previously unknown. Details of composition of the probiotics used (No. of colony forming units, type of bacteria, Nr. of bacterium species) would have been detailed because there are great differences between the products.

Response:

Thank you for reviewer's suggestion. The favourable effects of probiotic in Asian populations has been emphasized in conclusion. Details of composition of the probiotics used have been detailed.

(2) The reference list is incomplete and did not include/cite all other meta-analysis on the topic. Tables must be rearranged. In the reference list, PMID and doi numbers must be included, some of journal titles are incorrect.

Response:

Thank you for reviewer's suggestion. The reference list is completed. Tables have been rearranged. PMID and doi numbers are included in the reference list. Incorrect journal titles are corrected.

(3) The text of core tip must be corrected.

Response:

Thank you for reviewer's suggestion. The text of core tip have been corrected.

Reviewer 2

(1) Authors should precise the reason why they calculated Odds Ratio while not Risk Ratio. ?

Response:

Thank you for reviewer's suggestion. Odds ratio can be used not only in the retrospective study but also in a prospective study. So we think it is more objective to calculate odds ratio.

- (2) “At present, the standard triple therapy, which consists of a proton pump inhibitor (PPI) and two antibiotics, is regarded as the first-line treatment”. This statement is not completely updated, as the increasing clarithromycin resistances rendered triple therapy ineffective worldwide. Indeed, reference 2 refers to Maastricht II (2000), but the last consensus (Maastricht IV 2012) reports that in areas with high clarithromycin resistances, the first options are sequential or concomitant regimen. ?

Response:

Thank you for review’s suggestion. We updated information and reference about current *Helicobacter pylori* eradication treatment.

- (3) Adverse events: Authors state that they found significant heterogeneity ($I^2 = 85.7\%$; Fig. 4). Therefore, they should perform a sub-analysis according to the probiotic strains. ?

Response:

Thank you for review’s suggestion. Ten studies were divided into two categories according to the probiotic strains: 4 studies with *Lactobacillus* included, another 6 studies without *Lactobacillus* included, significant heterogeneity was also observed. Some factors may lead to heterogeneity, such as the characteristics of patients and the probiotics regimen (species, number of colony forming units, duration of administration, etc.). Therefore, more clinical trials are needed to confirm the results.

- (4) Authors included both 7-day and 14-day lasting triple therapy, so another subgroup analysis is strongly recommended since the eradication rate is significantly different in the two regimens. ?

Response:

Thank you for review’s suggestion. We have divided 14 studies into two categories according to lasting days of triple therapy: ten studies included 7-day lasting triple therapy and four studies included more than 7-day lasting triple therapy. There is no significant difference between studies included 7-day or more than 7-day lasting triple therapy and also has overlapping confidence intervals.

- (5) Authors did not demonstrated that probiotics play a role in *H. pylori* eradication. The OR 1.67 may be explained by the fact that probiotics reduce side effects, so it is more likely that patients received the full therapy, by reducing the number of drop-outs and early treatment interruption. Another possible explanation for their results is that the outcome was affected by antibiotic resistances more than probiotic supplementation. If Authors want to demonstrate that probiotics can eradicate *H. pylori*, they should perform a meta-analysis comparing probiotics alone (without antibiotics) vs placebo. These points have to be discussed in the manuscript. ?

Response:

Thank you for review’s suggestion. Patel A et al. point that no study could demonstrate complete eradication of *H. pylori* infection by probiotic treatment. These probiotic strains are able to improve patient compliance by reducing antibiotic-associated adverse events, increasing the number of patients completing the eradication therapy and resulting in an improved eradication rate.

- (1) In methods section- para 1 the bracket after Streptococcus seems unnecessary. In results section para-3 last line of the page- " patients were divided into two categories according ... is redundant as this statement has already been given somewhere.

Response:

Thank you for review's suggestion. We have removed the unnecessary part.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Chuan-Yong Guo, MD, Professor of Medicine, Department of Gastroenterology, Shanghai Tenth People's Hospital, Tongji University School of Medicine

Fax:

E-mail: guochuanyong@hotmail.com