

Format for ANSWERING REVIEWERS



Jan 21, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6512-review.doc).

Title: Efficacy of ilaprazole in the treatment of duodenal ulcer: a meta-analysis

Author: Xi-Qing Ji, Jun-Feng Du, Gang Chen, Guang Chen, Bo Yu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6512

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

(1) This is a good review of "the state of art" through a meta-analysis study of this new PPI drug (Ilaprazol).

Answer: Thank you very much for your comments.

(2) Efficacy of a new PPI, ilaprazole in the treatment of duodenal ulcer: a meta-analysis by Xi-Qing et al.
Comments : This meta-analysis evaluated the efficacy of a new PPI- ilaprazole in the treatment of duodenal ulcer. It concluded that ilaprazole is a highly effective and safe PPI in the treatment of duodenal ulcer. Ilaprazole could be recommended as a therapy for acid related disorders. Major Criticisms:

1. The main drawback of the study is that meta-analysis is based on a small number of trials (only four valid studies) and that too from a single region and some from the same group of authors. One of the trials included is an abstract and not a full published study.

Answer: Thank you very much for your comments. These were indeed the limitations of this meta-analysis. Ilaprazole is currently only approved in Asian countries, the trials included in this study all come from Asian countries, and thus further trials are needed in western populations in the future.

2. It is not clear how the articles were included and then how they selected the five mentioned publications.

Answer: The detailed literature search and study selection criteria were described in the method section.

3. How the author has taken the details from the study by Song j et al if it in an abstract format? If the details are not published then it may not appropriate for the study to be included.

Answer: The information in the abstract was sufficient to judge to include the study.

4. Although the I2 statistics shows a good homogeneity between the trials it may be irrelevant when the number is very small and some belong to the same authors.

Answer: Thank you very much for your comments. We agree with your view. Thus, we further conducted sensitivity analysis.

5. "Meta-analysis showed no difference was found between the ilaprazole and other PPIs of 4w-healing rate. (89.7% vs 87.0%, RR 1.02, 95%CI: 0.98-1.06, Z=1.00, P=0.32). Meta-analysis indicated that the rate of side effects in the ilaprazole group was lower than that in the control group, but the difference was not significant." In spite of these results which has shown no difference between ilaprazole and other PPIs (most of the other studies mentioned have used omeprazole) how did the authors conclude that "ilaprazole is a highly effective and safe PPI in the treatment of duodenal ulcer. Ilaprazole could be recommended as a therapy for acid related disorders". It would be more appropriate to conclude that it is comparable to omeprazole in efficacy and side effects. There is no particular evidence from this MA as to why it should be recommended over the existing PPIs.

Answer: Thank you very much for your comments. In this meta-analysis, we just concluded that "ilaprazole is a highly effective and safe PPI in the treatment of duodenal ulcer." We did not say "Ilaprazole is better than other PPIs or could be recommended over the existing PPIs" throughout the manuscript.

6. The article by Zhou et al (2009) appears to be published in a journal which is not available on the PubMed. Hence accessing the article was difficult.

Answer: The article was published in Chinese not English, and thus it was not available on the PubMed. However, it could be searched in the Chinese Literature Data (<http://med.wanfangdata.com.cn/searchcenter/ALLsearchInformation.aspx?infoQuery=zhxhnjzz98200909008>).

7. Overall it appears that the MA is premature to draw conclusions for the comparison of efficacy between ilaprazole vis-a-vis other PPIs. It would be more appropriate to wait for the publication of other trials especially from other parts of the world on the efficacy of ilaprazole so as to be included in a MA to draw authentic conclusions.

Answer: Thank you very much for your comments. We agree with your opinion. We have revised the conclusion as "Ilaprazole could be recommended as a therapy for acid related disorders, especially in Asian populations."

(3) We have carefully examined this new manuscript. This is a meta-analysis of published randomized controlled trials of ilaprazole evaluating its efficacy in duodenal ulcer healing and tolerability compared with other proton pump inhibitors. This analysis of 5 randomized controlled trials shows that ilaprazole has comparable (but not superior) efficacy to other proton pump inhibitors. The authors must be very clear that their results demonstrate equivalency and not superiority. This manuscript requires minor language polishing. In our minor comments:

1. In summary (abstract): under "results": second line: please consider deleting "was found" to improve the grammatical correctness of the sentence.

Answer: Thank you very much for your comments. We have deleted the words.

2. In Background: 1st line: please consider substituting "but was" with "has been"; 2nd paragraph: 1st sentence: consider using "preclinical research" in place of "some preclinical researches"; 6th line: substitute "with" with "to have"; 3rd paragraph last line: substitute "and" with "with".

Answer: We have revised them as required.

3. In Materials and Methods: 1st paragraph 5th line: substitute "searching terms" with "search term".

Answer: We have revised them as required.

4. In Results: 1st paragraph 5th line: please consider a change in this sentence to “Four were published in English and the other was published in Chinese”; 7th line: would change to “All trials were of high quality except one”. Would use “are” in place of “were”. Under “Meta-analysis” line 4: would delete “was found”. Under “Sensitivity analysis”: 1st line: would add “with” after “dose 10mg/d”. 2nd paragraph line 2-3: would delete “was found”.

Answer: We have revised them as required.

5. In Discussion: 2nd paragraph: line 4: would substitute “as” with “of”. 3rd paragraph, line 2: would add: “the fact” after “due to”.

Answer: We have revised them as required.

(4) To compare the efficacy and tolerance of ilaprazole compared with other PPIs in the treatment of duodenal ulcer. Study: Electronic databases including Medline, Embase, Cochrane controlled trials register, Web of Science, PubMed, Chinese Biomedical Literature Database (updated to July 2013), and manual searches were conducted. A meta-analysis of randomized controlled trials comparing the efficacy and tolerance of ilaprazole and other PPIs in the treatment of duodenal ulcer was performed. The study is well organized; results and their discussion are very detailed. The references, which include 28 items, are accurately selected and relevant. I believe that the manuscript should be accepted for publication.

Answer: Thank you very much for your comments.

3 References and typesetting were corrected.

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

Sincerely yours,

Bo Yu, MD,

Department of General Surgery,

General Hospital of Beijing Command of People's Liberation Army,

Beijing 100700, China

E-mail: yubobeizong@126.com