

Format for ANSWERING REVIEWERS

August 31, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 4532-Review.doc).

Title: Chinese Herbal Medicine Xiangshaliujunzi Decoction treating Diabetic Gastroparesis: A Systematic Review

Author: Jiaxing Tian, Min Li, Jiangquan Liao, Wenke Liu, Xiaolin Tong

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 4532

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

The first review's composition comment on the manuscript and my answer

(1) The authors should refer to the American Motility Task Force on Gastroparesis, which gives a clear practical and treatment guideline on the definition of gastroparesis (Neurogastroenterol motil, 2006, 18(4):264-84)

Answer: Yes, I agree with your comment and have added the reference that gives a clear practical and treatment guideline on the definition of gastroparesis.

(2) Presumably the authors focused on diabetic gastroparesis in this study, did the authors also consider including idiopathic GP?

Answer: This meta-analysis focused on diabetic gastroparesis that were gastric emptying disordered after definitive diagnosis of diabetes. What we evaluated was the condition of whom were diagnosed diabetes. So it didn't include the idiopathic GP.

(3) The authors used gastric emptying time as one of the symptom scores; would the authors please clarify the protocol used in these tests? e.g., 50% emptying time or the standard 4 hr emptying protocol? Do the authors think the type of protocol used would influence the efficacy measure?

Answer: Yes, I agree with your comment and make the corresponding modification. Gastric emptying time is not suitable as one of the symptom scores. What the included studies used was 50% gastric emptying time. We have made the correction in the article.

(4) "Gastric emptying" should be "gastric emptying" unless at start of a sentence or where appropriate.

Answer: Yes, I agree with your comment and make the corresponding modifications.

(5) Abstract - list the version of the Cochrane review standard used Introduction, para 2 - "last option" should be "last options"; "can't" should be "cannot"

Answer: Yes, I agree with your comments and make the corresponding modifications.

(6) Introduction, para 3 - a citation should be provided for the mechanisms of action of XSLJZD Introduction, last para - "XSLJZD for DGP" should be "XSLJZD for treatment of DGP"

Answer: Yes, I agree with your comments. I have added reference to prove the mechanism of XSLJZD and make the corresponding modifications.

(7) Why was acupuncture not included as a conventional treatment option?

Answer: This meta-analysis aims to evaluate the effectiveness of herbs to diabetic gastroparesis. Acupuncture is more like physiotherapy. In our opinion, it is not suitable to compare with herbs. Thus we did not include acupuncture or other physiotherapy in this article.

(8) "Gastric emptying test" and "Gastrointestinal" should be in lower cases unless at start of a sentence or where appropriate; "GI" should only be defined once upon first use; "trail" should be "trial"; "1 researches" should be "1 research study"

Answer: Yes, I agree with your comments and make the corresponding modifications.

(9) Section 2.3 - please provide the Cochrane handbook edition/version number

Answer: Yes, I agree with your comments and have provided the Cochrane handbook edition.

(10) Section 3.1 - "clarified" should be "clarify"; second paragraph, first sentence should end after "473 males and 394 females" Section 3.6 - "1 trails" should be "1 trial"

Answer: Yes, I agree with your comments and make the corresponding modifications.

(11) Discussion, para 3 - "indentify" should be "identify"; "proceed" should be "proceeded"

Answer: Yes, I agree with your comments and make the corresponding modifications.

The second review's composition comment on the manuscript and my answer

We agree with the reviewer's opinion that the researches about herbs treating diabetic gastroparesis are of low quality. Still they could enhance the acknowledge to the effectiveness of herbs. To proceed more strictly controlled clinical researches is our goal.

Gastrointestinal lesions is an complicated disease which caused by many reasons. This meta-analysis focuses on diabetic gastrointestinal disease. The patients we included were gastric emptying disordered after definitive diagnosed of diabetes. Gastrointestinal lesions caused by other reasons was excluded.

The third review's composition comment on the manuscript and my answer

(1) Please follow the guideline of systematic review and meta-analysis.

Answer: We have rewrite the related sections according to guideline of systematic review and meta-analysis.

(2) As for assessing the Cochrane risk of bias, several assessments were inappropriate. 1) Blinding of participants and personnel and blinding of assessors should be separately evaluated. 2) Blinding of participants and personnel should be clearly high risk of bias than unclear. How they can be blinded? 3) What did you judge the item of other sources of bias? Why unclear in Table 2.

Answer: It should be evaluated individually. Blinding of participants and personnel should be clearly high risk of bias than unclear. It is possible to control or adjust for confounders that are known and measured in observational studies. However, it is not possible to adjust for those factors that are not known to be confounders or that were not measured.

(3) Core databases should be searched when conducting rigorous systematic review as Medline, EMBase, Cochrane Central. You need EMBase search.

Answer: We added EMBase search in this revision. But unfortunately we could not find any related research in EMBase.

(4) As for outcomes for testing the clinical effectiveness of Xiangshaliujunzi decoction for diabetic gastroparesis, I am very questionable whether 'clinical effective rate' can be main outcome measure and the conclusion from this doubtful outcome is solid or not. Even the meta-analysis from this outcome makes no sence.

Answer: We agree the reviewers' opinion. We reference the Chinese medicine clinical research guidelines to evaluate the efficacy of diabetic gastroparesis. Since Traditional Chinese Medicine could improve the gastric emptying and syndromes, both of them should be considered in the judgment of efficacy. TCM has advantages in syndrome improvement. The judgment should be improve though,

the evaluation is worth recognition.

(5) As for the decoction of Xiangshaliujunzi, how modified decoction can be considered similar or same one compared original Xiangshaliujunzi decoction?

Answer: The modification is less than 2 herbs in modified decoction. And it is demonstratively established in the article. It is considered similar to original Xiangshaliujunzi decoction in TCM. If the modification is more than 2 herbs, it would be excluded.

(6) Which one is correct? Your inclusion RCTs are 10 or 7? Page 10 explained your inclusion as 7 RCTs, however, your figure 1 and tables showed 10 RCTs for inclusion.

Answer: Thank you for your carefulness. It is my mistake, we actually included 10 researches.

(7) When selecting inclusion criteria, as for controls, other herb treatment seemed not reasonable.

Answer: You are right about this and we rescreen the studies and none of them used other herb treatment in control group. So we rewrote the inclusion criteria section.

(8) Your conclusion is highly positively biased because the results from 10 RCTs which showed high risk of bias and had no solid outcomes were needed to be carefully interpreted with unbiased manners.

Answer: This issue that reviewers raised is very critical and worth thinking. This study is to show the current status of Xiangshaliujunzi decoction treating DGP. On one hand, traditional Chinese medicine for the relief of symptoms is obvious, worthy of recognition. On the other hand, there is a serious shortage in indexes evaluation criteria. What we used in "Chinese medicine clinical research guidelines", use "effective" and "ineffective" as determination of efficacy. Our outcomes are judged by indicators + symptoms two aspects. It may have flaws and differences compared to modern medicine "gold standard", but the efficacy determination combined with symptoms is precisely what the traditional Chinese medicine characteristics. However, for the quality improvement of TCM clinical researches, the continuously thinking and improving of standard determination of the efficacy in traditional Chinese medicine should be stressed. And the importance of clinical indicators and symptoms should be balanced.

(9) Please check abbreviations. Please define it at its first appearance, if defined, please use the defined one. E.g.) XSLJZD, TCM, GI, DPG, (DONE)

Answer: Ok, we have changed that.

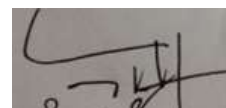
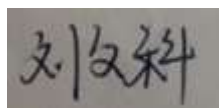
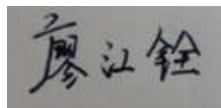
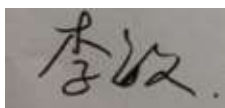
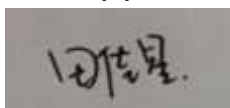
(10) Please check your spelling. E.g) trail -> trial.

Answer: Yes we have checked our spelling.

3 References and typesetting were corrected

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

Sincerely yours,



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