

December 17, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 14266-review.doc).

Title: Proton pump inhibitor in prevention of low-dose aspirin associated upper gastrointestinal injury: A systematic review and meta-analysis of randomized controlled trials

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 14266

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) the reviewer#1's comment:

1. The number of paper for meta-analysis to get conclusion is too small.

It is true that the number of RCT that meet the inclusion criteria is small, because we only collect high-quality RCTs published in English in our meta-analysis. And some cohort studies, case-control studies and retrospective studies were excluded for bias.

2. There is no new information from this meta-analysis.

PPIs appear to be the most effective strategy in prevention of LDA-associated gastroenterology bleeding, with the less side effects and the convenience of once daily dosing. But there has been no meta-analysis to verify it before. So this paper is the first meta-analysis in this subject.

3. Authors discussed that PPI and H2 RB can be useful for reduce gastrointestinal injury by LDA and/or other anti-coagulant. But main effect of PPI and H2 RB is reduction of acid secretion from gastric mucosa. I suggest that authors need to explain and/or discuss why these drugs can reduce the gastrointestinal injury by anti-coagulant and/or anti-platelet agents.

When gastrointestinal bleeding happens at a gastric PH of <6, the extrinsic and intrinsic coagulation cascade are impaired, and platelet aggregation is virtually abolished. PPI and H2 RB increase the gastric PH by inhibiting gastric acid secretion, make the pepsin inactivation, restrain fibrin thrombolysis, stable the formed blood clots, inhibit platelet depolymerization at the same time, so as to promote the blood coagulation and hemostasis.

4. In discussion, there are a lot of repeated results from references. I suggest that authors need to add new information from their meta-analysis.

Thank you for your kind advice. Improvements have been made in the section of discussion.

(2) the reviewer#1's comment:

1. A lot of grammar and spelling mistakes.

2. Discussion and conclusion can be improved further.

3. Otherwise, good piece of work.

Many grammatical or typographical errors have been corrected and improvements have been made in the section of discussion.

(3) the reviewer#3's comment:

In general, this is interesting and well written review, on an important topic. The data presented confirm and significantly extend the observations already published. The language meets the requirements for publications, however there are few errors in the text (please proofread manuscript and correct errors).

Thank you for your kind advice and many grammatical or typographical errors have been revised.

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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