Author's response to reviews

Title: Oral versus intravenous proton pump inhibitors in preventing re-bleeding for patients with peptic ulcer bleeding after successful endoscopic therapy

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Version: 3 Date: 17 April 2012

Author's response to reviews: see over
Dear Editor:

We appreciate the reviewers’ valuable comments for the manuscript entitled “Oral versus intravenous proton pump inhibitors in preventing re-bleeding for patients with peptic ulcer bleeding after successful endoscopic therapy”.

Based on these comments, we have made several revisions to our manuscript, which is resubmitted for your consideration.

The following are point-by-point responses to the comments:

**Reviewer #1’s comment:**

**Major comment**

1. Thank you for these valuable comments. As mentioned in the limitation of the study (please see Discussion, p 11, 2nd paragraph, 2nd and 3rd sentences), we originally plan to include more cases; however, we analyzed at the interim of the study, and found both routes of PPI were equally effective. If more cases were added, the same result would be reached, therefore, we terminated the study and concluded that no evidence of a difference in clinical outcomes between oral and intravenous PPI treatment was found in this study.

2. Thank for the reviewer’s comment. This is an inherent advantage in favor of oral form PPI with possible allowance to leave hospital early. In Table 2, the hospital stay was calculated includes for all patients per protocol. As mentioned in the conclusion section (discussion, p.10 2nd paragraph), the shorter hospital stay of oral PPI maybe an advantage but requires more evidence.

3. The reviewer suggests a discrepancy in the abstract and result. In the abstract, “The mean duration of hospital stay was 1.8 days in the oral group and 3.9 days in the intravenous group (p<0.01).” and in the result “The mean duration of hospital stay was
3.9 days in the ESO group and 1.8 days in the LAN group (p<0.01).” In the study design, the intravenous group received ESO and oral group received LAN. Therefore, there is no discrepancy in the abstract and result. We revised the abstract section to make it more clear.

4. In this study, we aimed to compare the efficacy of different route of PPIs.

Intravenous esomeprazole followed by oral esomeprazole is an established therapy for peptic ulcer bleeding. However, there is no sufficient data about the use of high dose oral esomeprazole. As mentioned in the discussion section, previous study by Laine et al (Gastroenterology 2008; 134: 1836-41) conducted the first study to compare the acid suppression effect of oral and intravenous PPI. Oral lansoprazole is found to have good acid suppression activity. Based on the finding, our hospital’s institutional review board agreed oral PPI as the study drug in this study.

Minor Comments:

1. Thank for reviewer’s comment, we revised the running title.

2. We update the data of Reference 21.

3. We revise some redundant mentions in Figure 1.

Reviewer #2’s comment:

Thank you for the valuable suggestion that future study probably need to be improved with intra-gastric pH study in all patients (IV versus oral PPI) and probably using a similar PPI (for example esomeprazole). As mentioned in the discussion
section (Page 9), many studies had confirmed oral vs intravenous PPI resulted in similar intragastric pH (ref 25, 15, 16). Due to cost benefit and invasiveness, we do not repeat the same experiment.

**Reviewer #3’s comment:**

Thank you for valuable comment.

1. As mentioned in the limitation of the study (please see Discussion, p 11, 2nd paragraph, 2nd and 3rd sentences), we originally plan to include more cases; however, we analyzed at the interim of the study, and found both routes of PPI were equally effective. If more cases were added, the same result would be reached, therefore, we terminated the study and concluded that no evidence of a difference in clinical outcomes between oral and intravenous PPI treatment was found in this study.

2. We agreed the reviewer’s comment that oral LAN and iv ESO are not same drug. In this study, we aimed at comparing the best PPI treatment in oral LAN and ESO form. As mentioned by Reviewer #1 (major comment #2), Lansoprazole in the oral form is evidenced to be effective as intravenous PPI for GI bleeding. Oral lansoprazole (easy to be dissolved in water) is easy to feed to some patients with N-G feeding. The other advantage is that old patients can be fed by mouth holding instead of swallowing the tablet. Therefore, we chose oral Lansoprazole instead of Esomeprazole in this study.

3. We agreed with the reviewer that the short hospital stay can be inherent advantage of this study in favor of oral PPI as commented by Reviewer #1. We mentioned
about the cost associated with oral PPI therapy can be saved in page 9 (3rd paragraph, 2nd sentence). We agreed with the reviewer that one of the important finding of the study is that oral PPI can be cost-saving but more studies are still needed.

*Editor’s comment:*

We have revised the manuscript for your consideration. The structure of the article and figure file was modified according to the journal’s style. Please let me know if further change is required.

We have no financial or other interests in the manufacture or distribution of any device or drug mentioned in this manuscript. All included authors have contributed significantly to this paper and are in agreement with the content of this manuscript. All authors agree to the transfer of copyright to your journal should this manuscript be accepted for publication.

Thank you for the opportunity to resubmit this manuscript for consideration of publication in BMC Gastroenterology. If you have any questions or comments regarding this manuscript, please do not hesitate to contact me by e-mail at buddishtlearning@gmail.com

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