

## ANSWERING REVIEWERS



August 25, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12975-review.doc).

**Title** Effect of pronase as mucolytic agent on imaging quality of magnifying endoscopy

**Author:** Gwang Ha Kim, Yu Kyung Cho, Jae Myung Cha, Sun-Young Lee, Il-Kwun Chung

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 12975

Dear Editor,

We have enclosed our revised manuscript, "Effect of pronase as mucolytic agent on imaging quality of magnifying endoscopy", in Word format (12975-review.doc), which we resubmit for your further consideration for publication as an original article in *World Journal of Gastroenterology*. We revised our initial manuscript (ESPS Manuscript # 12975) according to the reviewers' suggestions.

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

1. We have updated the format of the manuscript.
2. We provided point-by-point responses to the comments of reviewers in this letter and revision has been made according to the suggestions of the reviewer.
3. References and typesetting were corrected

### **Reviewer 1**

The study characteristics/logistics should be clearly stated, not only for presentation improvement, but to assist any future attempts for systematic reviews/meta-analyses.

Although inter observer agreement -or indeed disagreement- between only 2 persons (endoscopists/reviewers etc) is not that solid, your manuscript would be greatly enhanced by some Kappa stats. Please consider combining table 2 and 3 to one. Good luck with your submission.

**Answer:** Thank you for your detailed review and kind suggestion.

1. According to your suggestion, we combined table 2 and 3
2. I agree with your opinion. When we were designing the study, we did not include the kappa statistics, so, it cannot be presented at this time. Instead, we did several methods to minimize the inter-observer variability.

① Frequent study meetings were held where the endoscopists were provided with standardized images to aid in the assessment of gastric mucosal visibility grades.

② To coincide with the mucosal visibility grade level, we compared the other endoscopist's grade of the endoscopic picture randomly sampled through the study meetings. But we did not do it for all endoscopic pictures; we cannot present kappa statistics now.

③ Mainly two experienced endoscopists (YK Cho and GH Kim) conducted the study. We enrolled the 58 patients and 84 patients in each hospital. The random number was assigned in each hospital. So number of group A and group B in each hospital were same; When we analyzed all data separately according to the hospital enrolled, the all results of conventional endoscopic visibility, magnifying endoscopic visibility in stomach and esophagus, number of water flush were similar to final result even

though the superiority of visibility in conventional endoscope is more prominent. The only large difference was procedure time, it usually depends on endoscopist. So we expressed it as median (range) value.

## **Reviewer 2.**

Authors concluded that premedication with the proteolytic enzyme promise improved the quality of magnifying endoscopic images and required fewer water flushes to achieve satisfactory endoscopic viewing.

Although this paper is an interesting topic, this paper needs several additional changes which I feel addressing.

**Answer:** Thank you for your detailed review and kind suggestion.

1. Authors showed a significant difference in the median visibility score of magnifying endoscopy between group A and B. However, no significant difference in the endoscopic procedure time was observed between two groups. In addition, most of patients needed less than four water flushes to clean up their stomach.

When we interpret their results, oral premedication with promise is useful for having better mucosal visibility during conventional endoscopy. If they evaluate in the magnifying endoscopy, the endoscopists should directly use water flushes with pronase to the lesions which were needed magnifying observation.

- ① The previous data (reference No.22; **Bhandari P et al.** Use of gascon and pronase either as a pre-endoscopic drink or as targeted endoscopic flushes to improve

visibility during gastroscopy: a prospective, randomized, controlled, blinded trial.

*Scand J Gastroenterol* 2010; **45**:357-361) shows endoscopic flush of mucolytics to

targeted area was not effective as pre-endoscopic drink. So we did not do

endoscopic flush

- ② We did conventional endoscopic observation at first, then, magnifying endoscopic observation was followed. Because the procedure time largely depends on endoscopist, especially, when it comes to magnifying endoscopic observation, it was dependent on observation more than on mucosal state. So we primarily analyzed mucosal visibility grade and number of water flush.

- ③ We added your opinion in the Discussion section

“Third, endoscopic flush to the lesion when magnifying observation can be better method to confine its effect on magnifying endoscopy. But we used pre-endoscopic drinking considering previous study [22] that endoscopic flush of mucolytics to targeted area was not effective as pre-endoscopic drinking. So, it may be possible its effect on conventional observation would reach the magnifying observation, even though most of flushed water was suctioned before switch to magnifying observation.”

2. Two experienced endoscopists evaluated the mucosal visibility grade during endoscopy. As described in the discussion section, intra or inter observer variability may exist. Authors should show the inter- and intra-observer agreement of the endoscopists.

3. Authors described that this study was designed as a prospective, randomized, double blind study in the method section. They should explain how the studied patients were randomized.

When we were designing the study, we did not include the kappa statistics. So, it cannot be suggested at this time. Instead we did several methods to minimize the intra-observer variability.

- Frequent study meetings were held where the endoscopists were provided with standardized images to aid in the assessment of gastric mucosal visibility grades.

Especially, to coincide with the mucosal visibility grade level, we compared the other endoscopist's grade of the endoscopic picture randomly sampled through the study meetings. But we didn't do it for all endoscopic pictures. We cannot present kappa statistics now.

- We planned to enroll the patients competitively in two hospitals. When we designed the study, the number of patients aimed was 80 at each considering drop out. The random number was assigned in each hospital. We enrolled the 58 patients and 84 patients in each hospital. Number of group A and group B in each hospital were same.

We added it to the Method section "We planned to enroll the patients competitively in two hospitals. The random number was assigned in each hospital"

- When we analyzed all data separately according to the hospital enrolled, the all results of conventional endoscopic visibility, magnifying endoscopic visibility in stomach and esophagus, number of water flush were similar to combined results. The only large

difference was procedure time, it usually depends on endoscopes. So we expressed it as median (range).

Thank you for the opportunity to resubmit our manuscript, and hope you will find it worthy of publication in *World Journal of Gastroenterology*.

Sincerely yours,

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