

Dear Editor-in-Chief:

We would like to thank the reviewers for their helpful comments. We have attached a revised manuscript that incorporates our responses to the reviewers' comments. Detailed responses to the reviewers' comments are provided below.

Sincerely,

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Responses to Reviewer 1

1) This is a very nice review, only a few typo corrections to suggest.

→ We have checked our manuscript carefully, and have corrected any typos within the initial submission.

Responses to Reviewer 2

1) What are the contraindications of pronase premedication?

→ If a patient does not have organic problems such as inability to drink fluids due to severe stenosis in the oropharynx or esophagus, there are no obvious contraindications to use pronase premedication.

2) Is it allowed to use pronase in patients with previous ulcer history?

→ In Korea and Japan, pronase premedication is usually used in routine endoscopy irrespective of a history of ulcers or cancer. Therefore, there is no prohibition to use pronase premedication in patients with a previous history of ulcers.

3) Are there any side effects of pronase premedication?

→ In our study group, we performed three prospective studies using pronase premedication. The patients did not experience any adverse effects except minor complaints such as mild difficulty in drinking the pronase solution due to taste or amount.

4) Is there any data available about pronase provoked ulcer bleeding?

→ As far as we know, there are no data on pronase-provoked ulcer bleeding.

5) When pronase is flushed through the endoscope channel what is the usual and optimal volume?

→ To date, there is no standardized dose and volume of pronase for flushing during endoscopy. Based on our experience, we usually prepare the medication with the same amount of pronase and the same volume of solution used during pronase premedication, and then use 10 to 20 ml of pronase solution during flushing.

Responses to Reviewer 3

1) I have some suggestions: - the introduction is too long - you are better to include some articles about n acetyl cystein - you need to provide a short methodology about how you looked for articles in the scientific engines like pubmed and whatever you used

→ All five authors reviewed the introduction section and concluded that there is no portion of the text that is irrelevant to the discussion. In addition, as stated in the introduction section, we focused only on the role of pronase in increasing the imaging quality of endoscopy. Therefore, if possible, we would like to avoid stating the role of other agents such as n-acetyl cysteine. We hope the reviewer understands our stance.

Regarding the methods used in our study, we added a brief methodology section to the revised text as follows:

METHODS TO IDENTIFY STUDIES

Two reviewers (GH Kim and IK Chung) performed a literature search using PubMed and Embase databases. Key words included pronase, premedication, and endoscopy. Relevant review articles were also investigated and additional studies were identified by searching the bibliography of published articles. We focused on studies that described premedication with pronase to increase imaging quality during endoscopy.