

Dear Dr. Editorial Board,

We are very honored to have the opportunity to publish a paper in your journal. We revised our paper based on peer review and the science editor. The detailed modifications are as follows.

**To reviewer #1:**

The Authors should explain more in depth the reasons for which the combination of the two drugs is superior to PPIs alone, which are powerful inhibitors of gastric acid secretion and were used at a dosage higher than those which are usual in Asiatic countries. In particular, the benefit of the addition of aluminium gel is difficult to understand in esophageal ulcers, because it should adhere to esophageal mucosa and this is not easy to occur - there are some spelling errors throughout the text.

Response: Thank you very much for this valuable feedback. (1)The mucosal protective agent APG neutralises and buffers gastric acid to increase the intragastric pH, which promotes the formation of blood clots through the formation of a colloidal protective film. This film combines with the ulcer face formed after surgery, which protects against the corrosive effects of stomach acid, stimulates mucosal epithelial cells to secrete mucus, and promotes epithelial cells to undergo autonomous repair. The protective film formed on the surface provides a high-affinity binding site for oral preparations of PPIs and promotes their absorption. Theoretically, this exerts a complementary effect with the PPI preparation. (2)APG is thick and flows slowly down the wall of the tube when taken. APG is more likely to adhere to the surface of the surface is not smooth, so it is very easy to adhere to the ulcerative surface of the esophagus.

**To reviewer #2:**

In my opinion, a major review is needed for considering your paper suitable for being published. Although English is not my mother tongue, I strongly suggest a deep language edition of all the text, starting by the Title. In the third paragraph of the Introduction, ref 12 is about endoscopic, not surgical treatment. Authors should clarify that use of ETAI is mainly for gastric varices, and its use in esophageal varices is marginal. Also, a description of EG varices classification such as Sarin's should be described and used for the rest of the paper (Methods and Results). A mention to similar studies or data about aluminum phosphate gel would improve the Introduction. For Methods section, there is no mention of the

use of endoscopy in patients with suspected re-bleeding. Use of B-blocker is named here but not summarized in the Results section. No mention of the use of PPI double dose. For the statistical analysis, a logistic regression to undermine factors associated with rebleeding would enhance the value of the study. Varices size and location following Sarin classification is missing. The results section lacks key data in the description of both groups, such as the varices size, the prevalence of the use of ETAI or banding or the use of B-blockers in both groups. I suggest removing gastric varices patients from the analysis since their number is too small to warrant statistical analysis, and physiology of these varices is sometimes different to esophageal. Also, no mention to endoscopic management of rebleeding. Discussion section misses a briefing of the main results, and paragraphs one and two include information already described in the introduction. Authors should make comments on some important topics not covered by this manuscript such as the use of double dose PPI, use of APG in other similar lesions, the role of TIPS, explain why there is the same mortality rate if mortality is enhanced by rebleeding. Limitations such as the absence of endoscopy description in rebleeding, not using a placebo and low PPI dose should be commented on besides the short follow up and the retrospective nature of the study.

Response: Thank you very much for this valuable feedback. (1)We have translated and polished the article again. (2)References 12 are endoscopic, and the use of the word “surgery” is a translation error, we have corrected it. (3)Because the number of cases of gastric fundus varicose vein hemorrhagic disease was relatively small, we eliminated it according to your suggestion. (4)We performed endoscopy on all patients with rebleeding. It was described again in the manuscript. (5)We added a summary of the use of the nonselective beta-blocker (propranolol) to the manuscript. (6)A double dose of PPI was not used in the study. (7)Several articles on the factors of rebleeding have been published, and we have cited them in the paper. (8)The data in the result part are supplemented. (9)The discussion section has been revised. (10)There was no significant statistical difference in the death rate, which may be attributed to the timely return to hospital of all patients with early rebleeding.

### **To the science editor:**

1 Scientific quality: The invited manuscript describes "Effects of Aluminium Phosphate Gel Combined with Proton Pump Inhibitors that Prevent Early Re-haemorrhage after Treatment of Gastroesophageal Varix Haemorrhage". The topic is within the scope of the World Journal of Gastroenterology. (1) Classification: Grade C, Grade D; (2) Summary of the Peer-Review Report: (04718369): In my opinion, a major review is needed for considering your paper suitable for being published. Although English is not my mother

tongue, I strongly suggest a deep language edition of all the text, starting by the Title. In the third paragraph of the Introduction, ref 12 is about endoscopic, not surgical treatment. Authors should clarify that use of ETAI is mainly for gastric varices, and its use in esophageal varices is marginal. Also, a description of EG varices classification such as Sarin's should be described and used for the rest of the paper (Methods and Results). A mention to similar studies or data about aluminum phosphate gel would improve the Introduction. For Methods section, there is no mention of the use of endoscopy in patients with suspected re-bleeding. Use of B-blocker is named here but not summarized in the Results section. No mention of the use of PPI double dose. For the statistical analysis, a logistic regression to undermine factors associated with rebleeding would enhance the value of the study. Varices size and location following Sarin classification is missing. The results section lacks key data in the description of both groups, such as the varices size, the prevalence of the use of ETAI or banding or the use of B-blockers in both groups. I suggest removing gastric varices patients from the analysis since their number is too small to warrant statistical analysis, and physiology of these varices is sometimes different to esophageal. Also, no mention to endoscopic management of rebleeding. Discussion section misses a briefing of the main results, and paragraphs one and two include information already described in the introduction. Authors should make comments on some important topics not covered by this manuscript such as the use of double dose PPI, use of APG in other similar lesions, the role of TIPS, explain why there is the same mortality rate if mortality is enhanced by rebleeding. Limitations such as the absence of endoscopy description in rebleeding, not using a placebo and low PPI dose should be commented on besides the short follow up and the retrospective nature of the study. (00004403): The study is interesting and the results favour the use of PPI + antacid against PPI alone. The sample size of the two treatment arms is large, but the retrospective design reduces the clinical meaning of the trial. \_ the Authors should explain more in depth the reasons for which the combination of the two drugs is superior to PPIs alone, which are powerful inhibitors of gastric acid secretion and were used at a dosage higher than those which are usual in Asiatic countries. - In particular, the benefit of the addition of aluminium gel is difficult to understand in esophageal ulcers, because it should adhere to esophageal mucosa and this is not easy to occur - there are some spelling errors throughout the text. (3) Format: There are 3 tables and 1 figure; (4) References: A total of 27 references are cited, including 6 references published in the last 3 years; (5) Self-cited references: There are 0 self-cited references; (6) References recommendations: The authors have cited proper references. 2. Language evaluation: Classification: Grade A and Grade A. 3 Academic norms and rules: The authors provided the Non-Native Speakers of English Editing Certificate. Biostatistics Review Certificate. Institutional Review Board Approval Form or Document. 4 Supplementary comments: This is an invited manuscript. The authors declare no conflict of interest. This study supported by Natural Science Foundation of Guangdong Province of China, No.2018A0303130278. The topic has not previously been published in the World Journal of Gastroenterology. 5 Issues raised: The references should be updated. 6 Re-Review: Required. 7. Recommendation: Conditional acceptance.

Response: We sincerely appreciate this valuable feedback. We have revised the questions raised by the review and added references. We will upload all provide original pictures in a PowerPoint. All pictures are not reused and are not published elsewhere.

We sincerely hope that this revision will meet the expectations of the science editor and reviewer. Please feel free to contact us if further modifications are required.

Thank you very much!

Sincerely,

Zheng-Lei Xu, MD