ANSWERING REVIEWERS

Dear Editor,

ESPS Manuscript NO: 22524

Authors: Zhang et al.

We would like to response the comments one point to point as following:

Response to reviewer 1:

Comment 1:

MAJOR CRITICISMs In this submission Zhang et al. describe a modification of the band ligation technique of hemmorrhoid therapy to by using ESD caps with sclerotherapy. In addition to a novel technique their analysis is rigorous including the use of a post-procedure questionnaire. The images and diagram are also excellent. However there are several important criticisms. 1) The cost of an endoscopic procedure and 12 hours of hospital observation is markedly higher than an outpatient procedure using a disposable anoscope. What would legitimize this increased cost. When would this approach be practical (ie in those undergoing colonoscopy for bleeding or another reason).

Response to comment 1:

Thanks for your deep thinking. This is a pilot observe study on a new interventional therapy. For safety consideration, we request patients to be observed for more 12 hours after the CAES procedure. According to our previous results and clinical records, as a suggestion, there should be not necessary to have the 12 hours of hospital observation. We have highlighted this point in the revised manuscript. Comparing to anoscopy, the advantage of endoscopic procedure is that polypectomy and excision of anal papilla fibroma could be performed if polyps or anal papilla fibroma were found and assessed to be suitable to be resected when peforming the CAES therapy. Besides, our procedure has superiority in that bleeding and other anorectal symptom related colorectal diseases could be better differentiated.

Comment 2:

2) In light of the recent CRE infections of duodenoscopes it would seem that using a sigmoidoscope/colonoscope instead of a disposable anoscope would require scope sterilization and put the patient at very small though possible risk of infectious complications. Addition this would add a lot of cost to the procedure.

Response to comment 2:

That's possible. Further study on the risk of infectious complications is necessary. In the present study, no occurrence of infection in patients was observed.

Comment 3:

3) How can the authors be sure that the adverse event, the patient "who claimed mild tenesmus within four days was "due to an endoscopist who performed this procedure for the first time." It would be better just to note that this was due to subdentate injection causing pain.

Response to comment 3:

That's a good suggestion. It has been highlighted in the text.

Comment 4:

4) Why were the patients observed for 12 hours, often patients return home immediately after such injections.

Response to comment 3:

Only for safety consideration, we request patients to be observed for more 12 hours after the CAES procedure. We need to mention that, based on our pilot study, as a suggestion, there should be not necessary to have the 12 hours of hospital observation.

Response to reviewer 2:

Comment 1:

The authors presented a novel technique for endoscopic treatment of hemorrhoids.

The use of a cap mounted on the tip of an endoscope was useful to stabilize its position for precise injection of a sclerosing agent. Overall, the model is elegant and the results seem promising. I have a few remarks. 1) The small sample size is the main limitation of this study. Please state if the authors are planning to perform a larger prospective study, based on these preliminary results.

Response to comment 1：

Yes, this is a pilot study with small sample size, and further study is ongoing based on the preliminary results.

Comment 2:

2) Did the use of the cap allow to treat all the hemorrhoids in a forward view fashion with no need for retroflection? Please elucidate in the text.

Response to comment 2：

Based on our experience, this CAES technique with the transparent cap is able to treat all hemorrhoids in a forward view fashion. There is no need to have an injection with retroflection of the endoscope and it is impossible for an endoscopist to have retroflection in all cases.

Comment 3:

3) The use of a 15 mm needle is not repeatable in other centers since it was specifically manufactured for the study. Do the authors believe that the same results could be obtained with a standard commercially available needle or not?

Response to comment 3：

I wouldn’t suggest to use the current standard endoscopic injection needle because its short length (eg. 4 or 5 mm), which seems to require more sites for injection and induce more mucosal injury and potential inflammation. Our special designed needle with 15 - 20 mm length should be important for enough submucosal injection with sclerosing agent.

Comment 4:

4) The use of a 15 mm long needle worries me a little. How did the authors make sure that that such a long needle was not penetrating beyond the hemorrhoid itself? I believe there is a risk of injuring deeper tissues or injecting outside of the hemorrhoid on its proximal side.

Response to comment 4：

However, your great thinking on the possible risk should be an important reminder for endoscopists. We have highlighted this in the text. The cap, endoscope, air, long needle, sclerosing agent and endoscopic view should be the key points for endoscopist to perform the CAES. With necessary training, the angle, direction and depth of injection under endoscopic view could be controlled very well, and it would be easy to avoid the risk of injuring deeper tissues or injecting outside of the hemorrhoid.

Comment 5:

5) English language needs improvement.

Response to comment 5：

Thanks. We have polished the manuscript.

Thank you again for publishing our manuscript in the ***World Journal of Gastrointestinal Endoscopy (WJGE)***.

Sincerely yours,

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