Response to Peer-review Report

Dear Editor of WJG

We thank reviewers' comments that we believe improved our manuscript. Below is a point-by-point response to the issues raised.

Response to Reviewer 1

Q1: In the manuscript entitled, "Solutions for submucosal injection: what we choose and how we do it!", the authors present a narrative review aimed to discuss the most commonly used submucosal injection solutions, taking into account their advantages and disadvantages, how and when to perform submucosal injection, and recent developments in this regard. This is an interesting subject, and the manuscript is generally well written. Additional and more specific comments and suggestions, all of which are intended to strengthen the manuscript and many of which can be easily resolved, are provided below

Let me start to thank you for your comments. They were very constructive and helpful.

Q2: Title: - To be perhaps a bit more professional and modest, I would recommend revising the title to something more along the lines of , "Solutions for submucosal injection: what to choose and how to do"

Title was changed to "Solutions for submucosal injection: what to choose and how to do it!" according to the suggestion.

Q3: Abstract: - In the sentence, "Injection provides a lifting up effect of the lesion separating it from the muscular layer, thereby reducing thermal injury and the risk of perforation and bleeding while also facilitates en-bloc resection by improving technical feasibility.", would change the word "facilitates" to "facilitating" -Please be more consistent with the terms submucosa injection, submucosal injection (the latter is preferred). -Instead of "…prevent associated risks", it may be more acceptable to say "prevent associated adverse events". The risk is still there, you cannot prevent it, though you may reduce it.

We made all the recommended changes and tried to keep consistency with the term "submucosal".

Q4: Body of manuscript: -The format of the headings/subheadings makes it a bit difficult to know what goes under what/what is a new section. Please revise based on WJGE style.

We made some changes in the headings and subheadings of the main text by using caps look for the headings adopting the style of other WJG papers.

Q5: Would include Orise gel from Boston Scientific.

We included a brief description of Orise Gel from Boston Scientific in the section "TYPES OF SOLUTION"

Q6: Tables and Figures: -In figure 1, it is unclear how the left hand column is organized. It does not seem to be by size or anatomical order. Please consider re-organizing

In figure 1, the left column is organized by lesions size and/or the need for a more complex endoscopic removal technique

Q7: In the table with the different injectates, please spell out the injectate name wherever possible and write the abbreviation (if a common one) after it, e.g. Hyaluronic acid (HA). There seems to be room in the table to do so.

We made the recommended changes in table 2 by spelling the name of the solutions

Response to Reviewer 2

Let me start to thank you for your commentaries.

Q1: The authors reviewed the details of solutions for submucosal injection, however, a half of manuscript was about the technique of endoscopic treatment. I recommend reconsidering the title of this article.

We made a slight change in the title, but we think that is very difficult to talk about submucosal injection without talking about the techniques in which it is used. Because of that, we included in the title "how to do it". Moreover, in the aims of the work we

propose to explore this topic in a practical way, so we believe to be imperative to explain the different endoscopic removal techniques and when and how to use submucosal injection.

Q2. (Page 5) The authors described submucosal injection was not necessary for ligation-assisted EMR. Was this true?

We report that submucosal injection is **usually not necessary** to perform Ligation-assisted EMR. Although some endoscopists perform submucosal injection prior to ligation-assisted EMR, this step is usually not necessary, which can be based on the following references:

» Khashab MA, Cummings OW, DeWitt JM. Ligation-assisted endoscopic mucosal resection of gastric heterotopic pancreas. *World J Gastroenterol*. 2009;15(22):2805-8.

"…Ligation-assisted EMR may be more operator-friendly than the other EMR techniques. It requires neither saline injection nor snare prepositioning, and the concept of tissue capture is similar to the familiar variceal ligation technique…"

» Kantsevoy, Sergey V. et al. Endoscopic mucosal resection and endoscopic submucosal dissection. Gastrointestinal Endoscopy, Volume 68, Issue 1, 11-18.

"…In ligation-assisted EMR, a standard variceal band ligation device is positioned over the target lesion with or without prior submucosal injection…"

Our personal experience is in the accordance with the above references since we did not experience any complication using band-assisted EMR without SM injection.

Q3. (Page 16) The authors described submucosal injection was needed for coagulation of visible vessels in ESD ulcer. I think it is wrong information.

We reported that: "After complete dissection, coagulation of visible vessels should also be performed with sufficient submucosal lifting". The meaning/message of this affirmation is not that submucosal injection is needed (imperative) for coagulation of visible vessels in ESD ulcer, but that coagulation **should** be done with some residual submucosal lifting. This is especially important to prevent deep thermal injury.

However we rephrased this part of the manuscript in order to clarify the underlying message: "After complete dissection, coagulation of visible vessels should also be performed in gastric ESD, and sufficient submucosal lifting is generally advised in order

to reduce thermal injury to the gastric wall, which could be accomplished with further injection or water jet elevation.

Q4. “Polipectomy” was misspelling

We reviewed the manuscript and made the necessary corrections regarding this.