

## Format for ANSWERING REVIEWERS

August 25, 2012

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 14183-review.doc).

**Title:** Endoscopic cyanoacrylate injection for the treatment of gastric varices in children

**Author:** Seak Hee Oh, Seung Jin Kim, Kang Won Rhee, Kyung Mo Kim

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

**ESPS Manuscript NO:** 14183

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

### 1) Reviewer No 2917470

**Question 1:** The authors mentioned that one patient developed abdominal pain and distension following the procedure, what is the possibility of this symptoms? Could it be self-limited embolism, any CT scan of the abdomen (or other investigations was performed to clarify the cause of this event?

**Answer 1:** Thank you for your kind comments about the possibility of self-limited embolism. We agree that the possibility of embolism can be ruled out by further investigations, such as CT scan. The patient had only X-ray of the chest and abdomen. The abdominal distension was observed right after the procedure and relieved soon without any complications. On the clinical context, we believe that it was just because of too much air-inflation into the bowel during the procedure. However, your comment is very important and I will consider it on the next cohort study.

**Question 2:** Because the procedure was done without fluoroscopy, the risk of embolization could be high. Does the author recommended to have this procedure done under fluoroscopic monitoring or just probing technique is enough?

**Answer 2:** Our strategy to minimize the risk of embolism is using repeated injection with small volume by experienced pediatric endoscopists. According to recent reports, intravariceal injection can be observed and felt, when the needle is penetrating the variceal wall. We believe that the procedure can be available without simultaneous monitoring by fluoroscopy, therefore, we think that fluoroscopy does not have to be essential. Instead, we strongly recommend that the procedure must be performed in the PICU, where intensivist closely checks patient's condition. It is because children with variceal bleeding are clinically unstable and gastric bleeding is generally much severe compared to esophageal bleeding.

**Question 3:** Do all the enrolled patients underwent chest x-ray?

**Answer 3:** Yes. All the patient had X-ray of the chest and abdomen. This was mentioned in the

Method.

**Question 4:** Asymptomatic embolization from histoacryl injection was also mentioned in the adult, how about in the children?

**Answer 4:** We think self-limited asymptomatic embolism will be one of important issues for the long-term outcome. Hopefully we design next cohort study to evaluate this. Thank you for the suggestion.

**Question 5:** Is there any patient had re-bleeding within 2 weeks after the procedure? And what is the cause of early re-bleeding?

**Answer 5:** In our study, there was no case of early rebleeding. The shortest re-bleeding free duration was 1 month after the procedure. This was mentioned in the Result: "Eleven patients (52.4%) developed rebleeding events, with the mean duration of hemostasis being  $11.1 \pm 11.6$  months (range: 1.0–39.2 months)." The cause of rebleeding was simply rebleeding from GOV.

#### **Reviewer No. 1438500**

Thank you for your kind questions about my manuscript. I hope my answers and revised manuscript suit you.

**Question 1:** Concentration of cyanoacrylate (Histoacryl) mixed Lipiodol noted in page 5: Each injection consisted of 0.1–0.5 mL of 0.5 mL N-butyl-2-cyanoacrylate mixed with 0.5 or 0.8 mL Lipiodol (cyanoacrylate:Lipiodol=1:1 or 1:1.16). Is this a standard concentration in your institute? It seems to be low concentration. Usually we use cyanoacrylate:Lipiodol=1:1-2:1?

**Answer 1:** Thank you for your kind correction. There was a mistake in describing the ratio of the mixture. The correct cyanoacrylate : Lipiodol ratio is 1:1 or 1:1.6. This is a standard concentration in my institution and these concentrations have been applied to both adult and children. Also these concentration have been used in previous studies on adult patients according to ASGE committee<sup>[1,2]</sup>. However, we know that data is limited in pediatric group.

**Correction 1:** Each injection consisted of 0.1–0.5 mL of 0.5 mL N-butyl-2-cyanoacrylate mixed with 0.5 or 0.8 mL Lipiodol (cyanoacrylate:Lipiodol=1:1 or 1:1.6).

**Question 2:** As the subjects/patients are children, height and body weight should be added in the text and Table. Furthermore, condition of concomitant esophageal varices should be described briefly.

**Answer 2:** I fully agree with your suggestion. We reviewed patient's record again and added more detailed information in Method. In our study, all children have GOV type 1 and type 2, which means all children carried esophageal varices together. A brief description of esophageal varices was added in the Method.

#### **Correction 2:**

The mean height and weight of the children were  $120 \pm 26$  cm and  $21 \pm 14.4$  kg, respectively. Esophageal varices of higher than grade 2 were noted among 16 (76.1%) children with GOV.

#### **Reviewer 12969**

We appreciate your kind comments.

**Question 1.** EVO may also be useful for GOV type 1 in pediatric patients, but the authors may have to compare the two types of gastric varices in terms of the injection volume, efficacy, and safety.

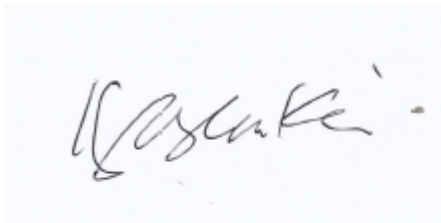
**Answer 1:** Thank you for your kind reviewing our study. Definitely, I agree with your opinion. However, the number of cases in the study was too small to compare those factors in Type 1 and Type 2 GOV. I hope I can have an opportunity to compare two methods in the near future and have an honor to present a new result to your prestigious journal "World Journal of Gastroenterology".

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

**Kyung Mo Kim**

A handwritten signature in black ink, appearing to read 'K. Mo Kim', on a light blue background.

Department of Pediatrics, Asan Medical Center Children's Hospital,  
University of Ulsan College of Medicine,  
388-1 Pungnap-Dong, Songpa-Gu, Seoul 138-736, South Korea.

[kmkim@amc.seoul.kr](mailto:kmkim@amc.seoul.kr)

**Telephone:** +82-2-30103380      **Fax:** +82-2-4733725