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Dear Editor,

Please find the edited manuscript in Word format (file name: ESPS Manuscript NO 10152_edited.doc).

Title: Clinical, endoscopic characteristics of drug-induced esophagitis

Author: Su Hwan Kim, Ji Bong Jeong, Ji Won Kim, Seong-Joon Koh, Byeong Gwan Kim, Kook Lae Lee, Mee Soo Chang, Jong Pil Im, Hyoun Woo Kang, Cheol Min Shin

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 10152

Thank you for allowing the revision of our manuscript NO 10152.
We revised our manuscript according to the editor's and reviewers' suggestions. The changes by the editor's comments were written in **blue** color. The changes by the reviewers' comments were written in **red** color.

Changes by editor's comments

Comment 1>
Title/Running title should be no more than 10~12 words/60 bytes. Please revise it.

Reply : Our title consists of 6 words. Because it is less than 10 words, we didn't change the title. But, our title is followed by running title, which is confusing. Editor also advised us to reposition the running title in comment 3. So, we changed the position of running title as the editor suggested.

Comment 2>
Please provide the postcode of the city.

Reply : Postcodes were already written in the addresses. We highlighted the postcode in blue color for you to find it easily.

Comment 3>
Please add a running title at here.

Reply : Running title was repositioned as the editor suggested.

Comment 4>
Please add 5-10 key words that could reflect content of the study mainly from Index Medicus.

Reply : We added more key words as below. We also used semicolon according to guideline.

Key Words : drug; esophagitis; endoscopy; pathology; symptoms; kissing ulcers

Comment 5>
Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.

Reply : We inserted core tip as you suggested.

Comment 6>
Please provide all authors abbreviation names and manuscript title here (After the "core tip").

Reply : We added authors abbreviation names and manuscript title as you suggested. We also changed the order of abbreviation name from "first name-surname" into "surname-first name" For example, we changed SH Kim into Kim SH.

Comment 7>
Please write the COMMENTS section at here. See the format in the attachment (Highlighted contents).

Reply : We added comments according to your comments.

Comment 8>
Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please revise throughout. The author should provide the first page of the paper without PMID and DOI.

Reply : We added PubMed citation numbers and DOI citation to the reference list and listed all authors according to your comments. Because reference 19 has no PMID or DOI citation, we provide the first page of reference 19 in PDF file.

Changes by reviewers' comments

Comment 1>
Most of cases of drug induced esophagitis is situated at middle esophagus. Please explain the reason why most of drug induced esophagitis is situated at middle esophagus. I understand that reflux esophagitis is situated lower esophagus due to decreased LES.

Reply: Thank you very much for your valuable comments. We corrected it as below.

(Discussion section : 1st paragraph, line 19)

Because the middle third of esophagus is subject to compression by the aortic arch or enlarged left atrium, drug-induced esophagitis is commonly located in the mid-esophagus.

Comment 2>
In page 7, drug induced esophagitis have abrupt-onset chest pain. Please explain the reason why drug induced esophagitis's patients are suffering from abrupt-onset chest pain?

Reply : Thank you very much for your valuable comments. We corrected it as below.

(Discussion section : 1st paragraph, line 25)

According to Kikendall, the typical drug-induced esophagitis patient presents with the sudden onset of odynophagia, dysphagia or retrosternal pain.[10] Based on this report, Abid et al.'s study was performed with patients who experienced acute onset of esophageal symptoms of less than 3 days' duration.[6] According to Boyce, symptoms of drug-induced esophagitis can develop within hours to 10 days after medication.[11] After being lodged in the esophagus, injurious pills release noxious contents damaging esophageal wall.[10] Thus, it is postulated that this damage of esophageal wall gives rise to the abrupt-onset symptoms of drug-induced esophagitis.

Comment 3>

In page 5, "the proportion of antibiotics as a cause of drug-induced esophagitis was higher among the younger group than in the elderly group." But in page 8, drug induced esophagitis is predominantly found among elderly patients. A study showed that the esophageal transit time was significantly longer in elderly subjects than the younger subjects. Please explain above data.

Reply : Thank you very much for your valuable comments. We corrected it as below.

(Discussion section : 3rd paragraph)

There are reports that drug-induced esophagitis is predominantly found among elderly patients as they are more likely to spend time in the recumbent position, consume more medications including alendronate or NSAIDs, have more esophageal motility problem or cardiac enlargement with mid-esophagus compression, and are less aware of the drug instructions.[11] A study showed that the esophageal transit time was significantly longer in elderly subjects than the younger subjects.[18] However in our study, the proportion of antibiotics was higher in younger group than in elderly group. According to literature, antibiotics was the commonest or second commonest cause of drug-induced esophagitis.[6, 9] In our study, antibiotics was the commonest causative drug. In contrast to NSAIDs, anti-hypertensive drugs and bisphosphonates, which are frequently prescribed for elderly patients, antibiotics are commonly prescribed in young patients to treat acne, urinary tract infections or pelvic inflammatory disease.[11] Our study showed that the predominant causative drugs were different between age groups.

Comment 4>

From the point of histological finding in your data, there is no difference between reflux esophagitis and drug induced esophagitis. But kissing ulcer is typical endoscopic finding

of drug induced esophagitis in your data. Please explain the reason why kissing ulcer is a typical endoscopic finding in drug induced esophagitis.

Reply : Thank you very much for your valuable comments. We compared histopathologic features between reflux esophagitis group and drug-induced esophagitis group. However, with regard to kissing ulcers, there was no control group. In our study, kissing ulcers were observed in 43.6% of the patients diagnosed with drug-induced esophagitis. Thus, we did not state that kissing ulcers are typical finding of drug-induced esophagitis. We only suggested that kissing ulcers might be helpful in diagnosing drug-induced esophagitis.

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

Sincerely yours,

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