ANSWERING REVIEWERS

Dear Editor,

Title: Anti-inflammatory and anti-apoptotic effects of rosuvastatin by regulation of oxidative stress in a dextran sulfate sodium-induced colitis model

Author: Seung Kak Shin, Jae Hee Cho,Eui Joo Kim, Eun-Kyung Kim, Dong Kyun Park, Kwang An Kwon, Jun-Won Chung, Kyoung Oh Kim, Yoon Jae Kim

Name of Journal: *World Journal of Gastroenterology*

Manuscript NO: 33896

Because there is no suggestion of revision in peer-reviewer's comment, I revised the manuscript according to the editor's comments. They are summarized as below.

Step 1. Please revise your manuscript according to the reviewers' comments

COMMENTS TO AUTHORS : Authors tested a hypothesis of presence of protective effect of rosuvastatin in animal DSS induced colitis model and also performed a IEC6 cell line model of another in vitro study. The study showed promising results about protective effects of rosuvastatin by reduction of oxidative stress, reduced apoptosis and decreased inflammation. The study is interesting and could possibly to further investigations for a possible treatment modality.

➔ Because there is no suggestion of revision in peer-reviewer's comment, I revised the manuscript according to the editor's comments.

Editor's comments

1. Please read the core tip then provide the audio core tip:
   Acceptable file formats: .mp3, .wav, or .aiff
   Maximum file size: 10 MB
   To achieve the best quality, don't allow to have the noise.

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2. The format should be like this, please revise others.

➔ We revise the all refererence citations as you suggested.

3. 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.

➔ We add PubMed citation numbers and DOI citation to the reference list as much as possible and list all authors.

Step 2. Please update the manuscript according to the Guidelines and Requirements for Manuscript Revision-Basic Study.

➔ We update the manuscript according to the Guidelines and Requirements for Manuscript Revision-Basic Study.

Step 3. Please provide the scientific research process.

1. What did this study explore?

: We investigated the antioxidant, anti-inflammatory and anti-apoptotic effects of rosuvastatin in a DSS-induced colitis model.

2. How did the authors perform all experiments?

: An acute colitis mouse model was induced by oral administration of 5% DSS in the drinking water for 7 days. In the treated group, rosuvastatin (0.3 mg/kg/day) was

administered orally before and after DSS administration for 21 days. On day 21, mice were sacrificed and the colons were removed for macroscopic examination, histology, and Western blot analysis. In the *in vitro* study, IEC-6 cells were stimulated with 50 ng/mL tumor necrosis factor (TNF)-α and then treated with or without rosuvastatin (2 μM). The levels of reactive oxygen species (ROS), inflammatory mediators, and apoptotic markers were measured.

3. How did the authors process all experimental data?

: The data are presented as mean ± standard deviation. Statistical significance of the difference between experimental groups was assessed using the two-tailed Student's t-test, with a $P < 0.05$ considered statistically significant.

4. How did the authors deal with the pre-study hypothesis?

: In order to obtain the results of the anti-oxidant effects of rosuvastatin, we evaluated the NOX1 and 8-OHdG expression in colon tissue and ROS production measured by confocal microscopy and flow cytometry in vivo and in vitro model. In order to obtain the results of the anti-inflammatory effect of rosuvastatin, we evaluated the the changes of colon length, weight, and colitis severity, the levels of DSS-induced serum inflammatory cytokines in DSS-induced colitis model and inflammatory cytokines such as IL-1β, IL-8, and COX-2 in TNF-α-treated IEC-6 cells. In order to obtain the results of the anti-apoptotic effect of rosuvastatin, we evaluated the protein levels of caspase-3, casepase-7 and PARP in DSS induced colitis model and and protein levels of apoptotic markers in TNF-α-treated IEC-6 cells.

5. What are the novel findings of this study?

: This study demonstrates the possibility of anti-inflammatory effects of rosuvastatin through the regulation of oxidative stress, and is the first to describe the anti-apoptotic effects of rosuvastatin in a DSS-induced colitis model.

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Step 6. Please provide the files related to academic rules and norms.

➔ We provided the file of Institutional Review Board statement, Institutional Animal Care and Use Committee statement, animal care and use statement, conflict-of-interest statement, and data sharing statement.

Step 7. Please provide the approved grant application form(s) or funding agency copy of any approval document(s)/letter(s).

➔ We provide the statement of grant and grant number.

Step 8. Please revise the language of your manuscript.

➔ Because we are non-native speakers of English, we have already received the language editing services from Textcheck.

Step 9. Please sign the Copyright Assignment form.

➔ We added the Copyright Assignment form.

We hope the revised manuscript would better meet the requirements of the World Journal of Gastroenterology for publication.

Sincerely yours,

Yoon Jae Kim, M.D., PhD

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