

May 28, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 10445-review.doc).

Title: The Characteristic and Clinical Outcome of Nonsteroidal Anti-Inflammatory Drug-Induced Acute Hepato-nephrotoxicity among Chinese Patients

Author: Yali Cao, Zhigang Tian, Fang Wang, Wenge Li, Danying Cheng, Yanfang Yang, Hongmei Gao

Name of Journal: *World Journal of Gastroenterology*

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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

Major comments: (1) Abstract. "The risk factors of NSAIDs induced acute hepato-nephrotoxicity, including age older than 60 (57.1%), a high prevalence of alcohol use (71.4%) and positive hepatitis B virus (HBV) markers (85.7%), increased extracellular volume depletion (71.4%) and RAAS inhibitor combined using (57.1%)." These findings are obtained by the comparison between combined ALI-AKI with mere ALI and with mere AKI, separately. Thus the authors should separately describe the results.

Response: We thank the reviewer for the nice recommendation. We separately described the results according to your suggestions. Please see page 3, line 14-19.

(2) Results. "patients with mere AKI (n=124) and ALI (n=96)". The characteristics of these patients should be shown in Tables. Especially the causes of injury are to be demonstrated. NSAIDs induce ALI or AKI is better for the purpose of comparison. They should also mention how they selected these patients.

Response: We really appreciate the reviewer for the good suggestions of this point. Actually, the patients with mere AKI and ALI included in this study for comparison are induced by NSAIDs. We mentioned the selected criteria in the methods part, page 7, line 1-3. As for the results part, we rephrased the statement very clearly to "we performed the comparison between the patients with NSAIDs induced combined hepato-nephrotoxicity and patients with NSAIDs associated mere AKI (n=124) and ALI (n=96), respectively." Please see page 10, line 3-4.

(3) Discussion. "Female sex showed slight predominance in this analysis" This comment is inappropriate, since F/M is only 3/4.

Response: Thanks the reviewer point out the drawbacks of discussion section. This comment is not correct and we deleted this sentence.

(4) Discussion. "elderly age, decreased effective circulating volume, RAAS inhibitor combined using". This finding is obtained by the comparison between combined ALI-AKI with mere ALI. The authors should describe about the results of comparison between combined ALI-AKI with mere AKI.

Response: Yes, this is another great recommendation. We change the sentence to "However, in situations in which renal perfusion may be diminished, including what we have demonstrated in this study by the comparison between NSAIDs induced combined ALI-AKI and mere ALI, elderly age, decreased effective circulating volume, RAAS inhibitor combined using," Please see page 12, line 2-3.

(5) Discussion. In the end of Discussion, there should be conclusion.

Response: This is, yet again, an excellent suggestion by this reviewer. We added the conclusion in the

end of discussion. Please see page 14, line 10-15.

Minor comments (1) Patients selection. "volume depletion". How did the authors diagnose volume depletion? Please describe the criteria.

Response: Estimates of volume depletion were obtained from the accurate history in the medical records as reported by the patients and physical examination. Usually, the accurate history and physical examination can help to determine both the presence and etiology of volume depletion. The history can identify a source of fluid loss.

(2)Table 2. Creatinine should be shown in mg/dL as in KDIGO.

Response: Thank you for your suggestion. Creatinine was shown in mg/dL. Please see Table 2.

3 References and typesetting were corrected

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

Sincerely yours,

Wenge Li, MD, PhD
Department of Nephrology
China-Japan Friendship Hospital
No. 2 Yinghua Street, Chaoyang District,
Beijing, 100029, China.
Fax: +86-10-84206174
E-mail: yalicao050501@hotmail.com