

## ***Response letter***

January 21, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 15428-review.doc).

**Title:** Hemodynamics and vasoactive substance levels during renal congestion (Effect of renal congestion on hemodynamics in anhepatic phase of orthotopic liver transplantation)

**Author:** Zhong Xin Li, Man Cai Wang, You Cheng Zhang, Jie Mao, Mo Chen, Rui Ni, Feng Xian Wei, Gen Nian Wang, Ling Yi Zhang

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

**ESPS Manuscript NO:** 15428

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

1. Format has been updated
2. Language was edited by AMEditor
3. Revision has been made according to the suggestions of the reviewer and AMEditor

(1) **Title:** “ Effect of renal congestion on hemodynamics in anhepatic phase of orthotopic liver transplantation” **change to** “Hemodynamics and vasoactive substance levels during renal congestion”;

(2) **Running title:** “Role of kidney in anhepatic phase” change to “Li ZX et al. Hemodynamic effects of renal congestion”;

(3) **Author:** “Zhong Xin Li MD, Man Cai Wang MD, You Cheng Zhang MD, PhD, Jie Mao MD, Mo Chen MD, Rui Ni MD, Ai Lin Song MD, Feng Xian Wei MD, Gen Nian Wang MD, Ya Wu Zhang MD, Xiao Dong Xu MD, PhD, Ling Yi Zhang MD” **change to** “Zhong-Xin Li, Man-Cai Wang, You-Cheng Zhang, Jie Mao, Mo Chen, Rui Ni, Feng-Xian Wei, Gen-Nian Wang, Ling-Yi Zhang”;

(4) **Correspondence to:** “Dr. Ling-Yi Zhang, Professor of Medicine, Department of Hepatology, Lanzhou University Second Hospital, Lanzhou 730030, Gansu, China. zhangychmd@126.com” **change to** “Dr. Ling-Yi Zhang, Cuiyingmen 82, Chengguan District, Department of Hepatology, Lanzhou University Second Hospital, Lanzhou 730030, Gansu, China”;

(5) **Abstract: Aim** “To explore the effect of renal vein congestion on hemodynamics, and the correlations between renal vein congestion and the main vasoactive substances in anhepatic phase of orthotopic liver transplantation.” **change to** “To explore hemodynamics and vasoactive substance levels during renal vein congestion that occurs in the anhepatic phase of liver transplantation”;

(6) **Abstract: Method** “Thirty-two New Zealand rabbits were randomly divided into 4 groups. The hepatic pedicle, supra-hepatic vena cava and infra-hepatic vena cava were dissected and ligated in the anhepatic phase group (APH); in the renal vein ligation group (RVL), only renal veins were dissected and ligated; in the renal veins and hepatic pedicle ligation group (RVHP), the hepatic pedicle, supra-hepatic vena cava and renal veins were dissected and ligated, leaving the inferior vena cava open. The hepatic pedicle, supra- and infra-hepatic vena cava of rabbits were all dissected but not

ligated in the sham operation group (SOP). The primary outcomes included hemodynamics parameters (systolic blood pressure, diastolic blood pressure and mean arterial blood pressure) and the level of vasoactive substances (serum bradykinin and angiotensin II). Data were collected at different five time points of 0 min (pre-operation), 10 min, 20 min, 30 min, and 45 min.”

**change to** “New Zealand rabbits received ligation of the hepatic pedicle, supra-hepatic vena cava and infra-hepatic vena cava (anhepatic phase group [APH]; n = 8), the renal vein (RVL; n = 8), renal veins and hepatic pedicle (with the inferior vena cava left open) (RVHP; n = 8), or a sham operation (SOP; n = 8). Hemodynamics parameters (systolic, diastolic, and mean arterial blood pressures) and the level of serum bradykinin (BK) and angiotensin II (ANGII) were measured at baseline (0 min), and 10 min, 20 min, 30 min, and 45 min after the surgery. Correlation analyses were performed to evaluate the associations between hemodynamic parameters and levels of vasoactive substances.”

(6) **Abstract: Result** “In these experimental groups, the arterial blood pressures and angiotensin II level significantly decreased after the operations, and the level of bradykinin increased with time. All of them have no significant changes in the SOP group. Compared between these experimental groups and the SOP group, there are statistically significant differences in arterial blood pressures, angiotensin II level, and bradykinin level at different time points after the operations ( $p < 0.05$ ). There are negative correlations between arterial blood pressures and serum bradykinin concentrations in all experimental groups ( $P < 0.05$ ), while positive correlations are found between arterial blood pressures and serum angiotensin II concentrations ( $P < 0.05$ ).”

**change to** “New Zealand rabbits received ligation of the hepatic pedicle, supra-hepatic vena cava and infra-hepatic vena cava (anhepatic phase group [APH]; n = 8), the renal vein (RVL; n = 8), renal veins and hepatic pedicle (with the inferior vena cava left open) (RVHP; n = 8), or a sham operation

(SOP; n = 8). Hemodynamics parameters (systolic, diastolic, and mean arterial blood pressures) and the level of serum bradykinin (BK) and angiotensin II (ANGII) were measured at baseline (0 min), and 10 min, 20 min, 30 min, and 45 min after the surgery. Correlation analyses were performed to evaluate the associations between hemodynamic parameters and levels of vasoactive substances.”

(7) **Abstract: Conclusion** “Renal vein congestion has an extremely significant impact on the hemodynamic disorders in the anhepatic phase of orthotopic liver transplantation. The mechanisms may be closely related to the changes of serum bradykinin and angiotensin II levels.” **change to** “In the anhepatic phase of orthotopic liver transplantation, renal vein congestion significantly impacts hemodynamic parameters, which correlate with serum BK and ANGI levels.”

(8) **Core tip:** “Hemodynamic disorders remain a focus of most concern in anhepatic phase of orthotopic liver transplantation (OLT). Many factors can contribute to the hemodynamic instability. Although some corresponding measures had been taken, this procedure still has significant morbidity and mortality due to the hemodynamic disorders. Therefore, we presumed there may be some additional elements which implicated in the pathogenesis of hemodynamic disorders in anhepatic phase for patients with OLT. Our study shown that renal vein congestion has an extremely significant impact on the hemodynamic disorders in the anhepatic phase of orthotopic liver transplantation. The mechanisms may be closely related to the changes of serum bradykinin and angiotensin II levels.” **change to** “Hemodynamic disorders remain a focus of concern in the anhepatic phase of orthotopic liver transplantation as they contribute to procedural morbidity and mortality. This study shows that various procedures that cause renal vein congestion significantly reduce hemodynamic measures, which correlate with reduced

angiotensin II and increased bradykinin levels in serum.”

(9) **Introduction:** all the language and order of sentences has been modified according to the editor of AMEditor.

## **MATERIALS AND METHODS**

(10) **Animal:** “Male New Zealand rabbits were obtained from the Animal Center, Lanzhou University, Gansu, China. They were housed under good laboratory practice conditions with a 12-hour light-dark cycle at least 1 week prior to the study.” **change to** “Thirty-two male New Zealand rabbits ( $2.5 \pm 0.2$  kg, 10 weeks) were obtained from the animal center of Lanzhou University, Gansu, China, and individually housed under a 12-h light-dark cycle at least one week prior to the study. Animals were fasted for 12 h and deprived of water 4 h prior to the operation.”

(11) **Experimental procedures:** “Thirty-two young adult male New Zealand Rabbits were maintained in separate cages and were randomly allocated into four groups according to the computer-generated randomization schedules ( $n=8$ , each group). Group 1: the anhepatic phase group (APH); Group 2: the renal veins ligation group (RVL); Group 3: the renal veins and hepatic pedicle ligation group (RVHP); Group 4: the sham operation group (SOP). The specific operations were shown in the part of “experimental procedures” below. In order to avoid the possible bias from the effect of training, all four types of procedures were performed each day, and the sequences of different procedures were randomly arranged by the administrators (administrators and data collectors did not participate in the experiment).” **change to** “Animals were randomly allocated into four groups ( $n = 8$  each): an anhepatic phase group (APH), renal vein ligation group (RVL); renal vein and hepatic pedicle ligation group (RVHP); and a sham operation group (SOP). All four procedures were performed on a given day, in a random sequence, to

eliminate any effect of training by the experimenters. ”

(12) **Hemodynamic monitoring:** “We monitored the hemodynamics by the outcomes of systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MABP). They were monitored continuously with RM 6000 multichannel physiologic recorder (Datex-Ohmeda, USA) through an arterial cannula that was inserted into the right femoral artery [17, 18]. The data of blood pressure were collected at five time points during the procedures (0 min, 10 min, 20 min, 30 min, 45 min) (Figure 1).” **change to** “Systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MABP) were monitored continuously with a multichannel physiologic recorder (RM 6000; Datex-Ohmeda, Madison, WI, United State) through an arterial cannula in the right femoral artery[17,18]. ”

(13) **Vasoactive substances detection:** “The blood samples of the rabbits were collected from external jugular vein at five time points (Figure 1). Blood samples were centrifuged and the serum was then preserved under subambient temperature (-80°C).” **change to** “Blood samples collected from the jugular vein were centrifuged, and the serum was stored at -80°C.”

(14) **Statistical analysis:** “Data were shown as mean value  $\pm$  SD, and different groups were compared using the one-way ANOVA followed by a post-hoc test adjusting for the multiplicity of the comparison (Bonferroni-Dunn, Tukey). The correlation test was analyzed by Spearson correlation analysis.  $P < 0.05$  was considered to have statistical significance. All of the analyses were performed using SPSS software, version 18 (SPSS, Inc., Chicago, IL, USA).” **change to** “Groups were compared using two-way analyses of variance followed by a Bonferroni–Dunn or Tukey’s post-hoc test. Associations between hemodynamic parameters and serum vasoactive substance concentrations were analyzed by Spearman correlation analyses.

Data are shown as mean  $\pm$  SD, and  $P < 0.05$  was considered as statistically significant. All of the analyses were performed using SPSS software, version 18 (SPSS Inc., Chicago, IL, United States). The statistical methods of this study were reviewed by Hu XB from Lanzhou University School of Public Health."

## RESULTS

(15) Add Table 2 to show the correlations between the hemodynamics and vasoactive substances;

(16) All the language and order of sentences has been modified according to the editor of AMEditor.

## DISCUSSION

(16) All the language and order of sentences has been modified according to the editor of AMEditor.

## COMMENTS

(17) It was finished with the help of AMEditor.

## FIGURES

(18) **Figure 2:** Add figure 2C: mean arterial blood pressures

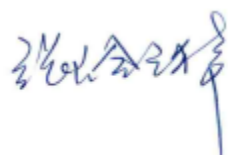
(19) **Figure 3, 4:** delete bar graphs (both graphs show the same data, thus only one depiction should be shown (i.e., line OR bar graph, not both)

4. References and typesetting were corrected

(The DOI of reference 24 did not find in the web of PubMed and crossref.org)

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

Sincerely yours,

A handwritten signature in blue ink, appearing to be 'Zhang Lingyi' in Chinese characters, with a stylized flourish at the end.

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