Format for ANSWERING REVIEWERS

February 2, 2015

Dear Editor,

Please find enclosed the edited manuscript in word format (13416-Review.doc).

Title: Landiolol, an ultra-short-acting β1 selective blocker, is useful for managing supraventricular tachyarrhythmias in patients with sepsis

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Name of Journal: *World Journal of Critical Care Medicine*

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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:

Response for the first reviewer (reviewer No. 2723778)
The original comments of the first reviewer are as follows.
Comment: 1) In Material and Methods-Study design and Patients Selection is stablished: "Patients were divided into 2 groups: those treated with landiolol (landiolol group) and those not treated with landiolol (control group) to control HR of supraventricular tachyarrhythmias". What was the selection criteria for Landiolol administration? Particularly, define better the control group
Response: Because this is the historical cohort study, the drug for managing tachyarrhythmia was selected by intensivists or primary doctors. Therefore drug selection (landiolol or others) was totally dependent on intensivists or primary doctors examining the patient then. We additionally described some comments according to drug selection bias in Discussion section as one of limitations (page 12 line 18-page 13 line 6).

Comment: 2) In Table 1, are there any significant differences? If not, please write down.
Response: There are some differences in infected site. As you suggest, we added those differences in Table 1 and Results section (page 7 line 17-page 8 line 3).

Comment: 3) In Results, it lacks the duration of Landiolol perfusion.
Response: Mean duration of landiolol administration was 80.7±78.5hr. We added that in Results section (page 9, line 7).

Comment: 4) How were choosed and titrated the drugs in the control group,
Please, list the drugs used in the control group and the number of patients treated with each one.
Response: As I described in response to comment 1), the drugs for managing tachyarrhythmia

was selected by intensivists or primary doctors in the control group. We added the drug and number of patients list in Table 2.

Comment: 5) In Results, "The conversion rate to sinus rhythm was approximately 25.6% in the landiolol group but 0% in the control group (Figure 1, $p < 0.05$)". approximately? This difference is huge and it merits a paragraph in the Discussion, adding your opinion about drugs in the control group were not able to stop the SVT.
Response: As you suggested, we removed "approximately" word in Results section (page 8 line 12-14). We also added the merit of landiolol for the conversion rate in Figure 1 legend and Discussion section (page 12 line 2-6). And we noted our opinion why drugs in the control group were not able to stop the SVT in Discussion section (page 12, line 14-17).

Comment: 6) Disclosure of interest is mandatory
Response: We added disclosure of interest (page 14, line 10-11).

Response for the second reviewer (reviewer No. 502780)
The original comments of the second reviewer are as follows.
Comment: 1) The drug I salary in use for SVT 10 years ago what is your novel massage of this study.
Response: One of our novel messages was high conversion rate to sinus rhythm immediately after landiolol administration. We added that message in Discussion section (page 12, line 2 -6).

Comment: 2) The cardia index is reduced in your patients in comparison to control group in need the pre administration values to be included in table 2'.
Response: Cardiac index indicated in Table 2 is pre-administration value. Landiolol was administrated in more hemodynamically unstable patients, such as lower systolic blood pressure and lower CI, than control group. We additionally explained that in **Discussion** section (page 13, line 3-6).

Response for the third reviewer (reviewer No. 502932)
The original comments of the third reviewer are as follows.
Comment: 1) The paper should describe how patients were selected to receive landiolol, as opposed to control treatment. Were there some selection biases which might have affected the results observed?
Response: Because this is the historical cohort study, the drugs for managing tachyarrhythmia was selected by intensivists or primary doctors. Therefore drug selection (landiolol or others) was totally dependent on intensivists or primary doctors examining the patient then. We additionally described some comments according to drug selection bias in Discussion section as one of limitations (page 12, line 18-page 13, line 6).

Comment: 2) What was the duration of treatment with landiolol in those patients who received drug?
Response: Mean duration of landiolol administration was 80.7±78.5hr. We added that in Results section (page 9, line 7).

Comment: 3) Was significant bradycardia seen in any treated patients?
Response: We have never seen significant bradycardia in any treated patients. We additionally

described some comments according to bradycardia in Results section (page 9, line 7-8).

3 References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Critical Care Medicine*.

Sincerely yours,

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