Author's response to reviews

Title: Influence of Ketotifen, Cromolyn Sodium, and Compound 48/80 on the survival rates after intestinal ischemia reperfusion injury in rats

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Author's response to reviews: see over
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Title: Influence of Ketotifen, Cromolyn Sodium, and Compound 48/80 on the survival rates after intestinal ischemia reperfusion injury in rats (MS: 3896324981826408)
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In the present study, the authors evaluate the effect of mast cell stabilizer, H2 blocker or mast cell degranulator on intestinal recovery and survival rate after intestinal ischemia-reperfusion in a rat model.

Major concerns:
1. A limitation of this study is that it is more illustrative than quantitative. Effect of described factors on intestinal recovery as well as on lung histology was only illustrative. The intestinal mucosal parameters (like mucosal weight, mucosal DNA and protein content, villus height, crypt depth, enterocyte proliferation, enterocyte apoptosis etc) were not measured. Most of the pictures do not provide any important information and should be omitted.

The main object in this paper was to observe the survival rate after administrated with Ketotifen, Cromolyn Sdium(CS), and Compound 48/80(CP), so we selected some parameters according to the reference (Kalia N, Brown NJ, Wood RF, Pockley AG: Ketotifen abrogates local and systemic consequences of rat intestinal ischemia-reperfusion injury. Journal of gastroenterology and hepatology 2005, 20(7):1032-1038). It would be better if the parameters as the reviewer indicated were detected. We deleted the figure of ultrastructure of intestinal mucosa since we didn’t have enough money to detect the parameters as the reviewer indicated.

2. In my opinion, the paper suffers from insufficient data to fully examine the hypothesis or to draw conclusions. The conclusion that IR and treatment with CS and kotifen affect liver is based on evaluation of ALT and AST as well as their effect on myocard is based on evaluation of LDH and CK. This is not enough.

Although the evaluation is not enough, it can reflex the injury of liver and myocard partly.

3. It is very difficult to explain a discrepancy between unchanged intestinal injury score and 50% mortality rate after 75 min of ischemia.

We detected the intestinal injury score in the survival rats of at the 3rd day after intestinal ischemia, the intestinal mucosa is one of the best recovered organs according to the report(Chang JX, Chen S, Ma LP, Jiang LY, Chen JW, Chang RM, Wen LQ, Wu W, Jiang ZP, Huang ZT: Functional and morphological changes of the gut barrier during the restitution process after hemorrhagic shock. World J Gastroenterol 2005, 11(35):5485-91). That can explain why there were unchanged intestinal injury score in the 3rd after 75 min of ischemia.

Minor concerns
Abstract
1. This is well-written.

Introduction
This section is generally well-written with logical development. A few changes suggested.
1. "Cordeiro and his colleagues" change to "Cordeiro and colleagues"

Done
2. The statement: "The effects of administration of mast cell… on IIRI…” is unclear. Do the authors mean on intestinal recovery following IIRI or in preventing damage caused by IIRI?
It means in preventing damage caused by IIRI.

Methods
1. Study design should be concentrated in one place. The statement that 48 rats are divided into IV groups is described in one section, the other statement about 120 rats that were divided into 5 groups are described in the other section.
Change made as indicated by the reviewer

2. Provide please reference for Chiu's method.
Done

Discussion
The Discussion is a little rambling. Nevertheless, the overall message of the paper is important although the manuscript has insufficient data to fully draw the final conclusions.
1. Statement that intestinal mucosa is one of the best recovered organs in 24 hours after IIRI is doubtful. The recovery requires usually 48-72 hours.
Intestinal mucosa is one of the best recovered organs according to the report(Chang JX, Chen S, Ma LP, Jiang LY, Chen JW, Chang RM, Wen LQ, Wu W, Jiang ZP, Huang ZT: Functional and morphological changes of the gut barrier during the restitution process after hemorrhagic shock. World J Gastroenterol 2005, 11(35):5485-91), and we found the Chiu’s score were the same in the 3rd day after ischemia in different groups.
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions
Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests

Reviewer's report
Version: 1 Date: 24 March 2008
Reviewer: Saburo Horikawa
Reviewer's report:
Major Compulsory Revisins
This article is of considerable interest and potential importance in demonstrating therapeutic strategies for intestinal ischemia and reperfusion injury. This experiment is well designed and conducted, however, the manuscript is not adequately arranged.
Major points.
1. In "Results" section, figures (Figure 3, 4, 5 and 6) are not adequately arranged as seen in completed manuscript. It is difficult to estimate the significance of the results described by authors in the text.
We arranged the images in one panel

2. In "Materials and Methods" section, the subsection of "Immunohistochemical detection of tryptase in intestine" exists. Which section can we find the figure or interpretation of the result? We added the figure of immunohistochemical detection of tryptase in intestine

Minor points.

3. In page 7, first paragraph.
Concerning to the description of "The surviving rats---- after 75 min intestine ischemia", sham-operated group does not undergo a 75 min ischemia.
The sentence was replaced by the description of “The surviving rats and states after operation”

4. In addition, there are several (many) misspellings and wrong use of a term. For example, Cromolun Sdium (Cromolyn Sodium) et al. Please carefully check the manuscript.
Change made as indicated by the reviewer

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests.