Author's response to reviews

Title: A retrospective study of acute pancreatitis in patients with hemorrhagic fever with renal syndrome

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Author's response to reviews: see over
Dear Dr Kochhar:

We would like to express our sincere gratitude to your constructive and positive comments. We have revised the paper accordingly and addressed each of your comments. Our responses are listed below (the corresponding amendments to the manuscript are highlighted in red in the revised text). This manuscript has been edited and proofread by Medjaden Bioscience Limited.

Specific Comments

1. The authors describe 6 cases of hemorrhagic fever with renal failure who were deemed to have acute pancreatitis. I am not sure they have made a case for cause and effect. Even the diagnosis of pancreatitis was questionable in 2 patients with normal enzymes (pain, per se is a common occurrence in HFRF).

According to the Atlanta clinical classification system, acute pancreatitis (AP) is defined by the presence of at least two of the following features: abdominal pain suggestive of pancreatitis (epigastric pain often radiating to the back), with the start of such pain considered to be the onset of AP; serum amylase and lipase levels at three or more times above the normal range; and characteristic findings by computed tomography (CT) and/or magnetic resonance imaging (MRI), or transabdominal ultrasonography (US).

It is true that abdominal pain is a common symptom of Hantavirus infection, but only a portion (n=6) of the patients was diagnosed with AP. Although two of the AP patients showed normal amylase levels, they also presented with the typical abdominal pain suggestive of pancreatitis as well as characteristic CT findings, all of which is line with the diagnostic criteria of AP by the Atlanta clinical classification system. Thus, we are confident in our conclusion that the Hantavirus infection is the etiology of the six AP patients presented in our study.

2. Secondly, they have not excluded other causes of pancreatitis. There is no description of alcohol intake or offending drugs. One patient at least, had gall stones.

We apologize for the confusion; each patient’s medical history has been added to the revised version to help clarify this issue. No patients had a history of alcohol abuse or medications.
The patient with gallbladder stones was initially diagnosed with gallstone-induced SAP in our hospital; however, this diagnosis was insufficient to explain the observed facial flushing, conjunctival injection, polyuria, high fever with headache, and orbital ache.

3. Thirdly, autopsy studies with demonstration of the offending agent would actually clinch the issue. I admit that is not an easy thing to do.

We agree with your opinion, and as such have reviewed the five previously published clinical reports of HFRS complicated with AP, representing 17 patients. Only one of those articles reported autopsy findings for one patient. In our future studies, we will seek to obtain such autopsy information, but like the vast majority of related studies before us, we unfortunately do not have this information available.

4. Why can not the 6 patients be having vascular congestion in pancreas as well in conjunction with other organs. Aren't the authors reading too much in the edema of the gland?

Although two of the patients showed obvious signs of edema of the pancreas, there were no signs of bleeding complications. Thus, we did not take (have ruled out) vascular congestion for these two patients. The treatment guideline of AP does not recommend vascular congestion for AP.

5. Lastly, the report conveys a mistaken idea that these patients need to be treated FOR pancreatitis. I believe the treatment of patients with or without elevated amylase/lipase will remain the same.

We reported two misdiagnosed clinical cases in the article. Both of those patients had been diagnosed with acute pancreatitis initially and then treated with AP therapy. Several days later, these patients were diagnosed with HFRS. We did not emphasize the treatment of AP for patients of HFRS with AP in our Discussion or Conclusions, but we believe that patients with HFRS complicated with SAP benefit from treatments to resolve the pancreatitis.