Author's response to reviews

Title: Simvastatin decreases the level of heparin-binding protein in patients with acute lung injury

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Author's response to reviews: see over
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To the Editor,

BMC Pulmonary Medicine

Please find our revised manuscript entitled “Simvastatin decreases the level of heparin-binding protein in patients with acute lung injury” by McAuley and co-authors.

We would like to thank the reviewers for their advice and comments which have helped us to improve the discussion section of the manuscript. We have provided a detailed point-by-point reply to the reviewers.

**Reviewer:** Jeffrey R Jacobson.

We were pleased to read that “this is a brief report but represents important and novel findings that may ultimately have significant clinical impact.”

**Minor point 1:** We would like to thank the reviewer for providing us literature sources to help us improve the discussion section of the manuscript. We have now added a paragraph (last paragraph of the discussion section) in which we discuss in detail how statins can impair activation of the beta2 integrins LFA-1 and Mac-1 and thereby prevent adhesion-dependent release of HBP. Accordingly, we have added 4 additional references (19-22).

**Minor point 2:** We have addressed this point in the discussion and revised the last sentence in the results section of the abstract to clarify it was the reduction in HBP that was associated with survival, not simvastatin treatment. We have now discussed the limitations of our study in relation to the relatively small size sample population. We have now clearly stated that simvastatin treatment was not associated with ICU survival (see discussion section).

**Reviewer:** Arzu Topeli

**Minor comments:**

We have now changed the scale in Figure 2 as asked for by the reviewer. We agree that this change helps to better compare the concentrations of HBP in survivors and non-survivors over time.

In Figure 3, we have shown the effect of simvastatin on HBP levels in ALI patients over time. In the simvastatin-treated group, we included data from both survivors and non-survivors. Because our study
involved a relatively small size population, we feel providing a table with HBP concentration for survivors (placebo and statins-treated) and non-survivors (placebo and statins-treated) will not be meaningful as the size of the population within each group would be too small to warrant proper interpretation.

**Major comments:**

While we agreed these data would be interesting, we are unable to make correlations between plasma levels of HBP and other physiological parameters as the size of the population in this study is too small. This limits the interpretation of the data as we have now stated in the discussion section. However we will plan to undertake this as part of subsequent larger studies.

We do hope that this revised version is now of sufficient scientific quality to be published in BMC Pulmonary Medicine.

Sincerely Yours

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