Author’s response to reviews

Title: Tolerability of inhaled N-chlorotaurine in a pig streptococcal bronchopneumonia model

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Author’s response to reviews: see over
Dear Dr. Marshall, Dear Mr. Appleford-Cook,

thank you and both reviewers very much for the critical review of our manuscript ID 1698033842553480 (Revision 1) and for the valuable comments. We have changed the manuscript again according to the comments of the reviewers and prepared a second revision, which we send for publication in BMC Infectious Diseases.

In the following, you find a point-by-point list of our answers to the comments of the second reviewer with references to the respective lines in the manuscript. All changes are marked with yellow in the revised version. There were no further changes requested by the first reviewer.

We hope that we could answer all comments satisfactorily, and we would be pleased about acceptance and publication in BMC Infectious Diseases. Please do not hesitate to contact us in case of further questions.

Yours sincerely

Markus Nagl
Answers to Reviewer 2:

We are very grateful to the reviewer for the second critical review of our manuscript and for the valuable comments. Here are our answers and references to the respective lines in the manuscript, written in italics. All changes are marked with yellow in the revised version.

Major compulsory revisions

Concern: The experimental model was in the very early phase of infection, and did not simulate broncho-pneumonia as authors stated in Discussion. The model seems to be an acute airway inflammation model rather than pneumonia model.

Answer: This has been changed as suggested, i.e. in the title and on page 20, lines 421-422.

Concern: Distribution of NCT might not be verified. Authors should state the limitation of this study.

Answer: This has been added on page 19, lines 410-413.

Minor essential revisions

1) (Title) This experimental model seems to be an acute airway inflammation model rather than a bronchopneumonia model.

Answer: The title has been changed into “Tolerability of inhaled N-chlorotaurine in an acute pig streptococcal lower airway inflammation model”

2) (page 19 lines 410) This study could not show the antimicrobial activity of NCT in vivo. Authors should discuss on the results. Speculation might cause bias of interpretation.

Answer: We have discussed that in a separate paragraph, page 19, lines 403-417. In our opinion, this is sufficient. We agree with the reviewer that we should omit further speculations in this point. The antimicrobial activity of NCT and its mechanisms have been described and discussed in quite a few other papers. As we clearly stated, the model turned out not to be suited to address this question, and we think that a further discussion would rather cause confusion than be helpful. This remains to be done in further studies on the therapeutic efficacy in the bronchopulmonary system.

3) (page 19 line 402-409) Authors stated that the lack of NCT activity was due to a short half-life of NCT in the lung. It should be noted that homogeneous distribution of NCT in the lung is not verified.

Answer: This has been added in lines 410-413.