Author's response to reviews

Title: Toxicity after prolonged (more than four weeks) administration of intravenous colistin

Authors:

Matthew E. Falagas (matthew.falagas@tufts.edu)
Michael Rizos (alfa.healthcare@alfahc.gr)
Ioannis A. Bliziotis (i.bliziotis@alfahc.gr)
Kostas Rellos (alfa.healthcare@alfahc.gr)
Sofia K. Kasiakou (s.kasiakou@alfahc.gr)
Argyris Michalopoulos (amichalopoulos@dunant.gr)

Version: 2 Date: 23 November 2004

Author's response to reviews: see over
Athens, November/23/2004

To: Editor, *BMC Infectious Diseases*

Re: Revision of a manuscript

Title: Toxicity after prolonged (more than four weeks) administration of intravenous colistin

Authors: Matthew E. Falagas, M.D., M.Sc., Michael Rizos, M.D., Ioannis A. Bliziotis, M.D., Kostas Rellos, M.D., Sofia K. Kasiakou, M.D., Argyris Michalopoulos, M.D.

Dear Editor,

On behalf of all co-authors I would like to thank you and the reviewers of our paper for their comments. We modified our manuscript based on their suggestions.

**Reviewer 1**

**Major compulsory revisions**

None

**Minor essential revisions**

1. The last 2 sentences on page 5, 1st paragraph of the previous manuscript were rephrased and clarified (page 6, lines 22 – 25 and page 7, lines 1 – 4 of the revised manuscript).
2. Results for continuous variables in Table 1 are presented as median and range.
3. The definitions of the infections were added in the “Methods” section with the appropriate reference (# 9 in the new reference list) (page 4, 2nd and 3rd paragraphs and page 5, 2nd paragraph, lines 1 – 3). In addition, a comment about how the agent of the infection was defined was added (page 5, 2nd paragraph, lines 3 – 4).
4. “Shaded” boxes in the figures represent the distribution of the laboratory values contained between the 25th and 75th percentiles (the interquartile range). The upper edge of the box shows the 75th percentile of the values and the lower edge the 25th.
percentile. Dotted lines, also called whisker lines, extend from the box, down and up, to the minimum and maximum values of the distributions that are not outliers (i.e. that are within 1.5 times the interquartile range); these values of the distribution are shown as “brackets”. Any value, which is an outlier, is drawn as a “horizontal line”. These explanations were added in both figure legends (page 19).

**Reviewer 2**

**Major compulsory revisions**

1. The dosage of intravenous colistin used in this study in mg/kg/day and the dosage adjustments performed in patients with renal impairment were added (page 6, lines 11 – 22).

2. The reported minimum inhibitory concentrations (MICs) of the responsible pathogens, when available, were provided as a separate paragraph in the “Results” section (page 7, 2nd paragraph, lines 1 – 8).

3. The cause of the prolonged administration of intravenous colistin for the treatment of the infections was clarified in the “Results” section (page 6, lines 22– 25 and page 7, lines 1 – 4). It should be emphasized that prolonged (for more than four weeks) treatment was given only in a subset of patients [17 out of 152 (11.2%)] who received colistin in our hospital during the study period, as it is stated in the “Results” section of the paper (page 5, last paragraph of the revised version).

4. The cause for the interruption of intravenous colistin in 4 cases was the attending physicians’ attempts to obtain cultures without the confounding influence of antimicrobial treatment in patients with puzzling continuing symptoms of infection. This was added in the “Results” section (page 6, lines 5 – 11).

5. A comment about the limitation of the retrospective analysis in the ascertainment of colistin associated sensory neurotoxicity was added in the “Conclusions” section as suggested (page 13, 3rd paragraph, lines 2 – 3).

6. Our assessment about the association of colistin therapy with the development of polyneuropathy and/or myopathy was added (page 10, last sentence).

7. The clinical response of the infections to colistin treatment (cure, improvement, and unresponsiveness) was added as a separate paragraph in the “Results” section (page 7, 3rd paragraph, lines 1 – 7).

8. “Shaded” boxes in the figures represent the distribution of the laboratory values contained between the 25th and 75th percentiles (the interquartile range). The upper
edge of the box shows the 75th percentile of the values and the lower edge the 25th percentile. Dotted lines, also called whisker lines, extend from the box, down and up, to the minimum and maximum values of the distributions that are not outliers (i.e. that are within 1.5 times the interquartile range); these values of the distribution are shown as “brackets”. Any value, which is an outlier, is drawn as a “horizontal line”. These explanations were added in both figure legends (page 19).

**Minor essential revisions**

See answer # 8 above.

Sincerely,

Matthew E. Falagas, M.D. M.Sc.
Adjunct Assistant Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts
Scientific Director, Alfa HealthCare, Athens, Greece
Director, Infectious Diseases Clinic, "Henry Dunant" Hospital, Athens, Greece