Author's response to reviews

Title: Outcome of infections due to pandrug-resistant (PDR) Gram-negative bacteria

Authors:

Matthew E. Falagas (matthew.falagas@tufts.edu)
Ioannis A. Bliziotis (i.bliziotis@alfahc.gr)
Sofia K. Kasiakou (s.kasiakou@alfahc.gr)
George Samonis (alfa.healthcare@alfahc.gr)
Panayiota Athanassopoulou (alfa.healthcare@alfahc.gr)
Argyris Michalopoulos (amichalopoulos@hol.gr)

Version: 3 Date: 18 March 2005

Author's response to reviews: see over
Athens, March/17/2005

To: Editor, BMC Infectious Diseases  
Re: Revision of a manuscript

Title: Outcome of infections due to pandrug-resistant (PDR) Gram-negative bacteria

Authors: Matthew E. Falagas, Ioannis A. Bliziotis, Sofia K. Kasiakou, Panayota Athanasopoulou, Argyris Michalopoulos

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**

1. The objective of the study was added in the introduction, as suggested (page 3, 2nd paragraph, lines 13-16 of the revised manuscript).

2. The methods used to define susceptibility for colistin were further described in the “Methods” section (page 5, 3rd paragraph, lines 5-14 of the revised manuscript).

3. Decisions regarding the site of the infections and the responsible pathogens were based on the guidelines from the Centres for Disease Control and Prevention and were added in the “Methods” section with the appropriate reference cited (page 4, 2nd – 3rd paragraphs, page 5, 1st – 2nd paragraphs, and reference # 13 of the revised manuscript).

4. A comment about the difficulty in evaluating the effect of the infection and of the treatment on the patients’ outcome was added in the “Discussion” section, as a limitation of the study (page 12, 2nd paragraph, lines 3-5 of the revised manuscript).
Minor essential revisions
1. We substituted “garamycin” with “gentamicin”, as it was suggested (page 6, 2nd paragraph, line 5 of the revised manuscript).
2. We deleted repeated information from Table 1 (page 16, column 2, heading: “Age/gender” and column 3, heading: “Reason of admission/comorbidity” of the table of the previous version of the manuscript). However, we added 1 additional column based on the 2nd reviewer’s comments (Table 1, page 16, column 8 of the revised manuscript).

Discretionary Revisions
The comment about the inability to evaluate the origin of the pandrug-resistant isolates, since molecular typing was not performed, was added in the “Discussion” section, as a limitation of the study (page 12, 2nd paragraph, lines 1-3 of the revised manuscript).

Reviewer 2
Major compulsory revisions
1. Detailed information about the formulation of colistin used and the specific dosage regimens administered in each patient was added in the “Results” section (page 5, 4th paragraph, line 8 and page 6, 1st paragraph) and in Table 1 (page 16, column 8 of the revised manuscript).
2. NCCLS was substituted with CLSI as it was suggested (page 11, 3rd paragraph, line 1 of the revised manuscript).
3. Although the focus of the paper is not the mechanisms of resistance to colistin, we did not modify this part of the discussion section, based on the 1st reviewer’s comment that found it very interesting.
4. We deleted repeated information from Table 1 (column 2, heading: “Age/gender” and column 3, heading: “Reason of admission/comorbidity” of the table of the previous version of the manuscript).
5. The statement that “there is generally agreement in the results obtained from agar dilution and broth microdilution methods regarding the in vitro susceptibility testing of colistin sulfate” was based on the paper of *J Clin Microbiol*. 2001 Jan;39(1):183-90 by Gales et al. (reference # 27). We agree that more work is
needed for the correct interpretation of cut-off points of the in vitro susceptibility testing using various microbiological techniques.

6. The fact that colistin sulfate, rather than methanesulfonate, is used for the breakpoint values of the in vitro susceptibility testing is mentioned on page 11, 3rd paragraph, lines 7-9).

**Minor essential revisions**

1. The suggested change was made (page 10, 3rd paragraph, and page 11, 1st paragraph of the revised manuscript).
2. The pH value “5.8” was changed to “5.8” (page 11, 1st paragraph, line 11 of the revised manuscript).

**Discretionary Revisions**

In vitro data such as fractional inhibitory concentrations of the combinations of the antimicrobial agents were not performed.

Sincerely,

Matthew E. Falagas, M.D. M.Sc.
Adjunct Assistant Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts
President, Board of Trustees, Alfa Institute of Biomedical Sciences, Athens, Greece
Director, Infectious Diseases Clinic, "Henry Dunant” Hospital, Athens, Greece