Author's response to reviews

Title: Discrepancy between Effects of Carbapenems and Flomoxef in Treating Nosocomial Hemodialysis Access-Related Bacteremia Secondary to Extended Spectrum Beta-lactamase Producing Klebsiella pneumoniae in Patients on Maintenance Hemodialysis

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Author's response to reviews: see over
April 23, 2012

Roselle Pangilinan on behalf of
Dr. Silvia F. Costa
BMC Infectious Diseases
BioMed Central
236 Gray’s Inn Road
London WC1X 8HB
United Kingdom

Re: MS: 5953918475798609
Discrepancy between Effects of Carbapenems and Flomoxef in Treating Nosocomial Hemodialysis Access-Related Bacteremia Secondary to Extended Spectrum Beta-lactamase Producing Klebsiella pneumoniae in Patients on Maintenance Hemodialysis

Dear Ms. Pangilinan and Dr. Costa:

Enclosed please find the revised copy of our manuscript for consideration for publication in the BMC Infectious Diseases.

We thank the reviewers for the helpful comments and suggestions. We have modified the manuscript accordingly, and we hope to have addressed all your concerns.

Please do not hesitate to inform us of any remaining errors or concerns in the revised manuscript.
Thank you for your consideration.

Yours sincerely,

Chih-Chao Yang, MD
Reviewer One(Giovanni Battista Orsi)

Major compulsory revisions

1. **ABSTRACT**: Results, last paragraph: the results of multivariate analysis should be presented all together.
   
   **Response**: We have made this modification, which is as follows:
   
   “Multivariate analyses revealed that flomoxef use, PBS, and catheter-dependent HD > 30 days were independently associated with increased mortality (OR, 3.52; 95% CI, 1.19–58.17, OR, 2.92; 95% CI, 1.36–6.26 and OR, 5.73; 95% CI, 1.21–63.2, respectively).”

2. **INTRODUCTION**: 2nd paragraph: “Risk factors setting”: the English needs to be improved.
   
   **Response**: We have revised the English in the manuscript.

3. **INTRODUCTION**: 3rd paragraph: The use of cephamycins is not universal but limited in some countries.
   
   **Response**: We have made the necessary modifications to this paragraph:
   
   “Unfortunately, the use of cephamycins is not universal but limited in some countries. In addition, many controversies about optimal treatment exist…”

4. **MATERIALS AND METHODS**: Why the study included 57 patients but the analysis and conclusions were carried out only on 42 (excluding patients with fistula and grafts)?
   
   **Response**: We believe bias and confounding factors could be reduced if we only analyzed 42 patients, all with catheter-related bacteremia.

5. **RESULTS**: Prior use of antibiotics (i.e. 3rd generation cephalosporins) may represent an epidemiological bias and needs to be commented in the discussion.
   
   **Response**: We have added a comment regarding this issue in the discussion session. “Although broad-spectrum antibiotic treatment prior to the onset of bacteremia was also highly prevalent, its contribution to the acquisition of ESBL infection and effect on patient outcome were not analyzed; this might contribute to an epidemiological bias.”

6. **RESULTS**: Data on the use of Flomoxef and carbapenems was not reported on both Tables 1 and 2.
   
   **Response**: We have included more detailed data on the use of flomoxef and carbapenems in Table 1.

7. **RESULTS**: As underlined previously, it is not clear why the study included 57 patients (42 HD, 7 with fistula and 8 with grafts) but the analysis and conclusions were carried out only on 42
HD patients (excluding patients with fistula and grafts)?

Response: We believe bias and confounding factors could be reduced if we only analyzed 42 patients, all with catheter-related bacteremia.

8. RESULTS: Last paragraph: the results of multivariate analysis should be presented all together.

Response: We have made this modification. “Flomoxef use, higher PBS, and catheter-dependent HD > 30 days were independently associated with increased mortality (OR, 3.52; 95% CI, 1.19–58.17; OR, 2.92; 95% CI, 1.36–6.26 and OR, 5.73; 95% CI, 1.21–63.2, respectively).”

9. DISCUSSION: It is too long, it may be shortened.

Response: We have shortened the discussion section.

10. TABLES AND FIGURES: Table 3: may be eliminated (redundant).

Response: We have eliminated Table 3.

Reviewer Two(L. Silvia Munoz-Price)

11. What do you mean by antibiotics started within 5 days of the availability of blood culture results…? Does this mean from obtaining blood cultures or from the day blood cultures were finalized? How many days does your microbiology lab usually take to finalize blood cultures (5 days)?

Response: We mean antibiotics started within 5 days after the day blood cultures were finalized (final results available). The sentence in our manuscript has been modified as follows: “For each included patient, the prescribed flomoxef or a carbapenem was administered for at least 2 days, starting within 5 days after receiving finalized blood culture results…” Routine blood cultures for sepsis diagnosis in our microbiology laboratory require 5 days before they can be finalized as negative. The majority of common infectious organisms such as Escherichia coli and Klebsiella species will grow within the 5-day time frame, and the final result is usually available on days 5 to 7.

12. Page 6, last sentence of first paragraph: “The diagnosis was made by patient’s physician”. What diagnosis are you referring to?

Response: We have eliminated this sentence to avoid confusion.

13. Flomoxef is not used in the USA; thus, consider giving a better introduction to the readers about this antibiotic.
Response: We have provided more details about flomoxef in the revised manuscript.

14. Results, page 9, line 8: “…initially hospitalized due to the onset of an infectious disease”. Do you mean fever?
Response: We mean infectious diseases such as pneumonia, cellulitis, and urinary tract infection.

15. Lastly, the results of this manuscript contradict a previous article published by the same leading author in JAC 2006.
Response: The author in JAC 2006 is Chen-Hsiang Lee (Lee CH), while the author of our manuscript is Chih-Hsiung Lee (Lee CH).