Author's response to reviews

Title: Evolving epidemiology and antimicrobial resistance in spontaneous bacterial peritonitis: a two-year observational study

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Version: 3
Date: 11 April 2014

Author's response to reviews: see over
April 8th, 2014

Dear Sir,

We are pleased to send to you the revised version of our article entitled “EVOLVING EPIDEMIOLOGY AND ANTIMICROBIAL RESISTANCE IN SPONTANEOUS BACTERIAL PERITONITIS: a two-year observational study”, for publication in the *BMC Infectious Diseases*, if you now find it suitable.

This article deals with the epidemiology of causative bacteria in bactercisites and spontaneous bacterial peritonitis, with the associated therapeutic consequences. We thank the reviewers of the initial version for their positive tone and comments. The article has been modified taking into account these comments, and a point by point response to the concerns has been added at the bottom of this letter. The modifications are indicated in bold and italics in the manuscript. This article is still submitted as an original article. It has been written in accordance with the instructions for authors of the *BMC Infectious Diseases*. All the authors have seen and approved the manuscript, which has not been published and is not under consideration for publication elsewhere. I hope that it will now meet with your approval.

Sincerely yours,

Lionel PIROTH

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Point by point response to the reviewers’ concerns

Reviewer: Gavin Barlow

Major compulsory:
1. I do appreciate the authors concerns expressed, but I think readers will want to know crude mortality statistics in those receiving initial appropriate antibiotic therapy versus inappropriate stratified by SBP and bacteriascites; you clearly have these data - please add - thanks.

The results of the complementary analyses on the relationship between mortality and other factors, in particular appropriate antibiotic therapy, have been added. Though SBP was significantly associated with a higher death rate, inappropriate antibiotic therapy was not in multivariate analysis. The method of analysis has been also described in the statistical analysis section.

Minor compulsory:
1. In the Patients and Methods section under Study Design, please define how many "multiple classes of antibiotics" was; what was the minimum?

This is the accepted definition of BMR. In our study, it was considered when the resistance concerned at least three usually-active drugs from different classes). This was added to the text.

2. How did you account for patients admitted with SBP, but who had a delayed aspirate beyond 48h of admission; these patients will have been wrongly defined as health care associated or did this not happen!? What was the cut-off for “recent hospitalisation”?

These episodes were considered nosocomial, even though we agree that they may have been misdiagnosed genuine community infections. Nevertheless, we found that the risk of error was lower by strictly applying the 48-hour rule, considering both the sometimes limited clinical details at baseline and the often unspecific initial clinical presentation of SBP. Recent hospitalisation was under 3 months.

We added this information in the text.

3. Please provide clear definitions for nosocomial and health care related infections; i.e. what the differences were?

We tried to clarify the differences by modifying the paragraph, which is now: The infection was deemed nosocomial when the ascitic fluid paracentesis was performed after 48 hours of hospitalization. The infection was deemed related to health care when it was nosocomial and/or when it occurred in patients with previous repeated and/or recent hospitalization (<3 months) for medical care. Thus, though a nosocomial infection is always health-care related, a health-care related infection may be not nosocomial.
4. In the Results section, I'm a bit confused by line "...increased the expected coverage of most beta-lactams by 10 to 15%". That does not make sense given the figures in the table; could you explain/review?

We agree that it was an approximation in an attempt to very simply summarize the results rather than a true difference between the different single and combined therapies. We thus removed the “10 to 15%” from the text.

Reviewer: Jun Yong Park

Reviewer’s report:
I would like to thank the authors for the opportunity to review their manuscript. I think this is an important paper and provides a very good addition to recently changing epidemiological and microbiological data.

We thank the reviewer, who is an expert in this field, for spending time to review our manuscript, and for his very positive comments.

If added, I would like the authors to analyze and describe the effect of Multi(drug) resistant SBP a little more.

The impact of MDR and SBP on mortality has been analysed and the results have been added in the text.