Author's response to reviews

Title: Stenotrophomonas maltophilia bloodstream infection in patients with hematologic malignancies: a retrospective study and in vitro activities of antimicrobial combinations

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Version: 3 Date: 27 January 2015

Author's response to reviews: see over
Dear Dr. Philippa Harris:

We would like to thank you and the reviewers of the *BMC Infectious Diseases* for taking the time to review our article. We have made some corrections and clarifications in the manuscript after going over the reviewers’ comments. The changes are summarized below:

**MS: 6753762871501673 Stenotrophomonas maltophilia bloodstream infection in patients with hematologic malignancies: a retrospective study and *in vitro* activities of antimicrobial combinations**

**Responses to reviewer’s comments**

**Reviewer: Geetika Sood**

**Comment 1:** (L180) How was attributable mortality defined?  
Reply: The previously described definition of attributable mortality have revised with additional pertinent reference in detail as follows: “mortality was considered attributable to the *S. maltophilia* if the patient died within 7 days of the onset of BSI and with no other identifiable cause” (P9-10, L152-153)  
*Mortality was considered attributable to the *S. maltophilia* BSI in any of the following cases: (1) blood cultures positive for *S. maltophilia* at the time of death; (2) death before the resolution of signs and symptoms related to *S. maltophilia* BSI; (3) death within 7 days of the onset of *S. maltophilia* BSI and with no other identifiable cause.” (P9-10, L152-156)

**Comment 2:** (L204-212) More detail on why only 50% of isolates were tested for synergy and the results in table 4 should be described a little more in this section.  
Reply: We selected 15 of 27 *S. maltophilia* clinical isolates based upon the MIC values (P12, L204-205). Initially, we performed both broth microdilution test and time-kill analysis for all available 27 clinical isolates, and found that several isolates showed identical or similar (within 2 fold) MICs to each antimicrobial agent used for synergy test (trimethoprim/sulfamethoxazole [SXT], ticarcillin/clavulanic acid, levofloxacin, and moxifloxacin). In addition, the results from time-kill analysis of all 27 isolates revealed that the clinical isolates having similar MIC profile showed consistent synergy test results. Therefore, we selected the 15 of *S. maltophilia* isolates to identify synergy effect by checkerboard assay using 96-well microplate. We believe that this data may represent the synergy results of clinical isolates.

As the reviewer suggested, we have described the reason why we selected the part of isolates (P12, L204-206) and the synergy results in more detail (P12, L210-212) in the result section.

**Comment 3:** (L250-251) The paper does not address biofilm issues, only in vitro susceptibility testing.
Reply: As the reviewer pointed out, we agree that the biofilm issue is a separate subject of research, which need to study further. Therefore, we have revised the sentence in the discussion section (P14, L250-253).

Comment 4: (L257) Further studies will also be needed to determine if this in vitro synergy has any important clinical impact.
Reply: As the reviewer pointed out, we have revised the manuscript as follows: ‘Further studies with larger number of patients will be needed to assess whether the combination therapy has clinical impact in improving outcomes of *S. maltophilia* BSI in hematologic patients.’ (P14, L257-259)

Comment 5: (L268-270) It is a big jump to say that the primary treatment of *S. maltophilia* should be TMP sulfa based on such limited testing and based simply on in vitro testing. There is no evidence presented here to support that conclusion.
Reply: We thought that the decreased susceptibility of levofloxacin (44.4%) in this study could be one of the evidence to support SXT for primary empirical treatment of *S. maltophilia* bloodstream infection especially in hematologic patients. Recent guidelines suggest the primary use of SXT for *S. maltophilia* BSI in hematologic patients as we have added in the introduction section (P5, L68-71). We have added another recent review article as a reference (ref [9]). However, as the reviewer pointed out, we agree that the sentence could misleading that levofloxacin cannot be used in hematologic patients. Therefore, we have checked the sentences in the discussion section (P14, L237-241) that presents levofloxacin can be used as ‘targeted therapy after confirming susceptibility results’.

Comment 6: (L74-75) Is there references to demonstrate this or is it speculation?
Reply: As the reviewer commented, we have added a pertinent reference (ref [11], [13]). In addition, we made some corrections to clarify the meaning (P5, L68-71)

Reviewer: Bradley Ford

Comment 1: (L201) "Evidence of the outbreak" is better phrased as "evidence of clonality" or similar. Written English is otherwise excellent and minor errors will be removed in editing.
Reply: As the reviewer pointed out, we have revised the phrase into “without evidence of the clonality”. (P12, L198-199)

We hope the revised manuscript will better meet the requirements of your journal for publication. We thank the editor and the reviewers of the *BMC Infectious Diseases* once again for the constrictive review of our paper.

Sincerely yours,

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