Author's response to reviews

Title: Nososcomial candidaemia in cancer patients: are all patients the same?

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Version: 3  Date: 11 January 2006

Author's response to reviews: see over

To the Editor
BMC Infectious Diseases

Re: New version of the manuscript

Dear Sir,

Thank you for considering our manuscript for publication in the BMC Infectious Diseases. In addition, we would like to thank the reviewers for their comments on our paper.

We did all the modifications requested by the three reviewers. These are described below. Our study originally focused on nosocomial infections, but we now included patients with community-acquired candidaemia as well, as suggested by one of the reviewers. The methodology, results, and discussion sessions were improved. New comparisons are presented, and multivariate analysis is provided.

Please, contact us if any additional modification is required.

With best regards,

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Author's response to reviews

**Title:** Nosocomial candidaemia in cancer patients: patients are not all the same

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**Version:** 2 **Date:** 11 January 2006
First reviewer: Gerald Bodey, M.D., F.A.C.P.

Reviewer's report:
General

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Major Compulsory Revisions
1. This report is presented in a sketchy fashion. Differences between solid tumors and hemat. Ca should be discussed in results in some detail, not just shown in table.
   
   Our results were described in more details on pages 6-9.
2. A multi-variate analysis of predisposing factors should be included.
   
   A multivariate analysis was included.
3. Were there major differences in predisposing factors between types of S. T. malignancies with large numbers of patients?
   
   No. However, there were only few patients in each subgroup.
4. No denominators are provided.
   
   Unfortunately, no denominator was available to calculate the incidence of candidaemia in the different population of patients studied. This limitation was commented in the discussion (page 11, lines 9-10).
5. Of course, there will be more infections in S.T. patients if the hospital has only small numbers of hemat ca. patients.
   
   We agree. This was briefly presented in the discussion (page 11, lines 5-9).
6. Hopefully, the authors learned more from their study than what was presented in the abstract conclusion.
   
   We hope that this new version of the article could be more interesting for readers. As neutropenia was not an important risk factor for patients with solid tumours, we were interested to document if patients with solid tumours had any particular risk factor for candidaemia in addition to the risk factors presented in other critically ill non-cancer patients. In order to do that, we compared two
groups: (1) non-neutropenic adult patients with solid tumours and candidaemia, and (2) all other adult patients with candidaemia seen in our medical centre during the same period, with diagnoses other than cancer. This comparison is presented in page 9. Our main results were that patients with solid tumours might have gastrointestinal surgery as an important and independent risk factor for acquiring candidaemia. Confounding variables could not be totally controlled in the multivariate analysis due to the limited number of patients included in the study. The hypothesis here generated could be useful for further research. In addition, the study confirmed the higher proportion of *Candida albicans* infections in surgical patients.

7. Why were no factors considered after onset of infection with their impact on response?

   We modified the article to focus on risk factors for candidaemia. Antifungal therapy and the outcome were only described.

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Minor Essential Revisions

1. In results gram positive organisms or species, not strains.

   That alteration was performed on page 7, line 9. Thank you very much for your comments.
Second reviewer: Marcio Nucci

Reviewer’s report:

General

This is a retrospective analysis of characteristics of candidemia in patients with solid tumors and hematologic malignancies. As stated by the authors, this distinction is important and has not been well addressed. The paper is well written and provides useful information.

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Major Compulsory Revisions

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Minor Essential Revisions

1. Why did the authors include only nosocomially acquired candidemia? How many "community-acquired" candidemias were diagnosed during the study period? Cancer patients (especially those with hematologic malignancies) who have a catheter and are admitted and readmitted to receive courses of chemotherapy are at increased risk to develop candidemia. Even if candidemia is diagnosed at admission, these episodes should not be considered "community-acquired".

   As requested, we modified our study to include patients with outpatient-acquired candidaeemia. Therefore, the total number of patients increased to 83 patients.

2. The last paragraph of Results seems to have been truncated. The authors should expand the description of the differences between the two groups, including those that were significant.

   Our results were described in more details on pages 6-9.

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Discretionary Revisions

1. As stated by the authors in the last paragraph of the discussion, further studies are needed to better characterize the risks and epidemiology of candidemia in
patients with solid tumor. Some variables that could be explored include complications of surgery (duration of surgery) and site of the tumor.

We added some additional details concerning the number of surgical procedures per patient on page 8 (lines 10-12). As neutropenia was not an important risk factor for patients with solid tumours, we were interested to document if these patients had any particular risk factor for candidaemia in addition to the risk factors presented in other critically ill non-cancer patients. In order to do that, we compared two groups: (1) non-neutropenic adult patients with solid tumours and candidaemia, and (2) all other adult patients with candidaemia seen in our medical centre during the same period, with diagnoses other than cancer. This comparison is presented in page 9.

2. The comment that non-albicans species predominate in oncology patients because of the use of fluconazole is simplistic. For example, C. tropicalis has been associated with cancer (especially neutropenia and mucositis) long before the introduction of fluconazol in clinical practice; C. parapsilosis has emerged in cancer patients possibly as a result of the widespread use of catheters. The authors should comment on these other factors.

We modified this topic in the discussion (pages 12 and 13). As the number of patients in the study increased after the inclusion of individuals with outpatient-acquired candidaemia, species other than Candida albicans were significantly more common in haematological patients, in comparison with patients with solid tumours.

3. Please comment why multivariate analysis was not performed.

This new version of the paper includes multivariate analysis. Thank you very much for your comments.
Third reviewer: Monica Slavin

Reviewer’s report:

General

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Major Compulsory Revisions

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Minor Essential Revisions
1. Spelling errors eg However (abstract), temporally, ethics (patients and methods).

   These were modified. Thank you.

2. As the numbers are small it would be preferable to include actual numbers of cases in text and table as well as percentages.

   We included number all over the text. We preferred to keep the table only with percentages just to make it easier for the reader. The total number of patients in each group is presented at the bottom of the table.

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Discretionary Revisions (which the author can choose to ignore)