

January 28, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8186 Review.doc).

Title: Hematologic Diseases: High Risk of Clostridium difficile associated Diarrhea

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1

1. The etiology of hematologic and non-hematologic disease should be shown. How many patients with hematologic diseases were performed hematopoietic stem cell transplantation and how the outcome of the treatments for the primary disease affected the recurrence of C.difficile?

-> We appreciated your comment. We described as you commented in the 'RESULTS – Incidence of CDAD, on page 8 line 14'

2. Did IVIG also reduce recurrence of CDAD in patients with nonhematologic diseases?

-> In patients with nonhematologic disease, IVIG was used only in 11 patients (6.8%). There was no significant difference. Due to small number of IVIG use in patients with nonhematologic disease, we did not described in our manuscript.

3. Was there any difference in the background immune status, e.g., leucopenia, neutropenia, CD4/CD8 count, between patients with hematologic and non-hematologic diseases? Was there any difference of background status of the hematologic disease patients treated with IVIG or without?

-> WBC count, number of neutropenia was added in the Table 1 (page 17 line 8). Due to retrospective design it was hard to find background status of the hematologic disease patients treated with IVGV or without.

4. Due to the retrospective design, some patients may not have tested for C.difficile regardless of diarrhea. If such cases may happen, the authors should state this as a limitation.

-> We described your comment in 'Discussion, on page 11 line 9'

Due to the retrospective design, some patients might have been omitted from C. difficile testing which is a limitation of our study

5. It is confusing to see in Table 3 that cessation of causative antibiotics for CDAD in 43 (29.9%) and continuous use of causative antibiotics for CDAD in 109 (75.7%). It exceeds 100%. Similar discrepancy was shown in Table 4. What was true for the cessation of causative antibiotics?

-> Some patients who discontinued the causative antibiotics for CDAD reused it due to immunocompromised status. We replaced 'continuous use of antibiotics' for 'additional of causative antibiotics' in the Table 3 (page 19) and Table 4 (page 21). Additional use of antibiotics was defined as continuous use of antibiotics for CDAD or re-use of causative antibiotics for CDAD. We divided 'additional use of causative antibiotics' into 'continuous use' and 're-use' in the Table 3 and Table 4. In addition, among HD group, number of patients who were treated by cessation of causative antibiotics for CDAD was 42. We corrected it (43 -> 42).

Minor 1. There are some mistyping e.g., in Table 1, Acvclovir, Acyclovir; Propon pump, proton pump, in Table 3 causeative, causative.

➔ We corrected as you commented in Table 1 (page 17 line 19,20) and Table 3 (page 19).

Reviewer 2

The authors have retrospectively investigated the incidence and clinical outcome of C. difficile associated diarrhea (CDAD) in patients with hematologic disease and compared with those in patients with nonhematologic disease in a large-scale single center. The data are interesting and provide some reference in clinical practice. I have a few comments:

1. Abstract: Two important findings in this article should be added in result of abstract:

Higher recurrence of CDAD in patients with hematologic disease was associated with higher number of antibiotics with longer treatment duration. Mortality due to CDAD did not differ between the two groups.

➔ I appreciated your comment. We added your comment in 'ABSTRACT, on page 3 line 11'

Recurrence of CDAD was more frequent in patients with hematologic disease compared to those with nonhematologic disease (18.8% vs 8.5%, $p < 0.01$), which was associated with higher re-use of causative antibiotics for CDAD. Mortality due to CDAD did not differ between the two groups.

2. MATERIALS AND METHODS: Is there total number of patients with hematologic disease and nonhematologic disease in 2011 ?

-> We described in 'MATERIAL AND METHODS - Study population, on page 6 line 3'.

Between January 2011 and December 2011, 53,334 patients (hematologic disease patients 2,061; nonhematologic disease 51,273) were admitted to Seoul St. Mary's Hospital

3. Results: In table 3 and 4, why the sum of patient number in cessation and continuous use of causative antibiotics group is not equal to the total number of each group?(in table 3 $43+109>144$)

-> Some patients who discontinued the causative antibiotics for CDAD reused it due to immunocompromised status. We replaced 'continuous use of antibiotics' for 'additional of causative antibiotics' in the Table 3 (page 19) and Table 4 (page 21). Additional use of antibiotics was defined as continuous use of antibiotics for CDAD or re-use of causative antibiotics for CDAD. We divided 'additional use of causative antibiotics' into 'continuous use' and 're-use' in the Table 3 and Table 4. In addition, among HD group, number of patients who were treated by cessation of causative antibiotics for CDAD was 42. We corrected it (43 -> 42).

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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