12-Dec-2023

Dr. Andrzej S Tarnawski

Editor-in-Chief & Co-Editor World Journal of Gastroenterology

Dear Editor:

Thank you for inviting us to submit a revised draft of our manuscript entitled "Effectiveness of antibiotic prophylaxis for acute esophageal variceal bleeding in patients with band ligation: A large observational study." We also appreciate the time and effort you and each of the reviewers have dedicated to providing insightful feedback regarding changes to strengthen the paper. Thus, it is with great pleasure that we resubmit our response letter for further consideration. We have incorporated changes that reflect the detailed suggestions you have graciously provided. We also hope that our edits and the responses we provide below satisfactorily address all the issues and concerns you and the reviewers have noted. To facilitate your review of our revisions, the following is a point-by-point response to the questions and comments delivered in your letter dated 07-Dec-2023.

# Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: An important and interesting topic that has been taken for granted for years. I was wondering whether information regarding the presence of ascites was available in your patients to include it in the subgroup analysis.

# Response:

We appreciate your positive assessment of our manuscript's scientific and language quality and the recognition of the importance and interest of our study's topic. We have revised Table 3 to include the number of patients with ascites.

### Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: While the message is clear that antibiotic prophylaxis is not indicated as an across-the-board measure for all patients undergoing EVL, the authors should clarify the following:

1. Do all currently valid guidelines recommend antibiotic prophylaxis for bleed control? If not, do they make a distinction between EVL and EIS, presence or absence of ascites, and ranking as per Child or MELD status? This is important as it then justifies the need for such a study in all patients undergoing EVL

2. How many patients in the authors' cohort had ascites / pre-existing SBP?

3. Is there any way to know why the endoscopists chose to administer antibiotics in individual patients?

### **Response:**

We appreciate your valuable feedback and acknowledgment of the clarity of our message regarding antibiotic prophylaxis in patients undergoing EVL. We have addressed your specific comments as follows:

# 1. Antibiotic Prophylaxis in Guidelines:

Current Western guidelines generally recommend the prophylactic administration of antibiotics for all patients. Considering the growing issue of multidrug resistance, the inappropriate use of antibiotics is a significant concern. This concern underpins the necessity of our study. Our study solely involved patients treated with EVL; no patients in this study underwent EIS. We have adjusted for disease severity as a confounder based on the patients' Child-Pugh scores using inverse probability of treatment weighting and propensity score matching. Data regarding presence of ascites, as part of the Child-Pugh classification, has now been included in Table 3.

# 2. Presence of Ascites / Pre-existing SBP in Cohort:

Data regarding the presence or absence of ascites has been added to Table 3. Unfortunately, we were unable to obtain data regarding the history of SBP in this cohort. We apologize for not being able to provide this information.

# 3. Reasons for Antibiotic Administration:

The exact reasons for antibiotic administration were not fully ascertainable. However, in this study, patients with a temperature above  $38^{\circ}$  at admission and those from whom blood cultures were obtained were excluded. This approach likely ensured that patients who received antibiotics due to infection, as opposed to prophylaxis, were appropriately excluded from the study.

We believe these revisions and clarifications will enhance the understanding and impact of our study. We appreciate your guidance in making these improvements.

Additionally, to further improve the clarity and quality of our manuscript, we have enlisted the services of a professional English language editing company. These edits have been incorporated throughout the document, with changes highlighted in yellow for ease of review. Sincerely,

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#### Journal editor-in-chief

Thank you for insightful comments and suggestions regarding our manuscript. We are grateful for the opportunity to enhance our work based on feedback.

1. Discussion Section Revision Considering Multidrug-Resistant Organisms: We have carefully revised the discussion section to incorporate considerations regarding multidrug-resistant organisms (MDROs). This revision not only acknowledges the growing concern about antibiotic resistance in the context of prophylactic antibiotic use, as highlighted in recent literature, but also includes references to several key studies, including those specifically pointed out by the reviewers. By integrating these citations, we aim to provide a comprehensive view of the current understanding of MDROs and their implications in clinical settings. We believe this addition significantly enriches the manuscript by situating our findings within the broader challenges of antibiotic stewardship in clinical practice.

2. Addition of a Table Detailing Antibiotic Usage: In response to your suggestion, we have created a new table (Table 4) that outlines the specific antibiotics used in the prophylaxis group and the number of patients who received each type. This table provides a clearer picture of the patterns of antibiotic use in our study and aligns with the aim to offer more detailed information on prophylactic antibiotic practices.

3. Limitations in Addressing the Emergence of MDROs in Current Study: While we acknowledge the importance of discussing the implications of MDRO emergence in patients receiving prophylactic antibiotics, our current study's scope primarily focuses on the effectiveness of such prophylaxis in esophageal variceal bleeding treated with EVL. Therefore, we have chosen to limit our discussion to the scope of our findings and have not delved into the specific management of patients who develop MDROs. We believe this approach maintains the clarity and focus of our research objectives. We hope these revisions adequately address the concerns raised and enhance the overall quality and relevance of our manuscript. Sincerely, Corresponding author Chikamasa Ichita