

RESPONSE TO REVIEWERS

Reviewer #1

Up to now, there were two meta-analyses about prophylactic use of antibiotics in ERCP, i.e. in 2009 and 2010, respectively. In particular, the publication in 2010 concluded the same result as the present manuscript. More importantly, the both nearly included the same studies except for only one study (Finkelstein 1996) in the present manuscript. Since 2006, no additional literature has been published about this.

Thus, the submission seems not innovative. Additionally, there was an error in the study name of "Van den Hazel S J 1999", which should be corrected as "Van den Hazel S J 1996".

ANSWERS:

We would like to thank the reviewer for revising our article. Although there are no more recent randomized controlled trials evaluating the prophylactic use of antibiotics, we did include one more study that was not included in the last meta-analysis, thus increasing the level of evidence. Additionally, our meta-analysis may rise the discussion on this important topic which is now oblivious.

1. There was an error in the study name of "Van den Hazel S J 1999", which should be corrected as "Van den Hazel S J 1996".

Thank you for your observation, we have corrected the year of the publication.

Reviewer #2

This is an exciting manuscript examining an important topic, especially for endoscopists facing this question. Approaching this condition is a common problem nowadays. The authors should be commended on their work. There are a few areas where additional information would enhance the manuscript.

Thank you for your comments. We considered all your valuable suggestions and made several corrections to the revised version of the manuscript. We are optimistic that the quality of our manuscript has improved after your review.

1 - The affiliation 1 was incorrect, please adjust it.

We have already adjusted this. Thank you for your observation.

2. In the results subsection of the abstract section, the author used (ERCP). I thought it was a mistake.

Thank you. We made this correction.

3. The citation pattern was wrong. For example, please use [1-3] instead [1], [2], [3].

Thanks for your comment. We made the corrections as suggested.

4. To enhance the readiness, please provide the definition of endpoint namely "septicemia".

Thanks for the recommendation. We made the corrections based on your valuable comment.

5. As author defined "bacteremia" as "positive culture or fever". This means that the patient developed fever with or without positive culture was labeled as the positive event of bacteremia, is it correct?

Thank you for your observation. We have corrected this in the revised version of the manuscript.

"Bacteremia was defined as a positive culture with no evidence of systemic inflammatory response."

6. In the "discussion" section, the author discussed the results of the study are inappropriate. Especially regarding the lack of discussion on the effect of antibiotics on septicemia. Please take the discussion more intensively.

Thanks for your suggestion. We have included more details about this important topic in the Discussion.

Sepsis remains a major cause of morbidity and mortality worldwide ^[34]. Antibacterial therapy is usually recommended as a major treatment for infection ^[35] as it reduces the risk of septic shock and the duration of hospitalization.

However, the prophylactic use of antibiotics is not a consensus in terms of minimizing the risk of infection after some procedures. In ERCP procedures, the factor for the development of clinical sepsis appears to be biliary obstruction. The presumed mechanism by which obstruction leads to sepsis is increased biliary pressure leading to bile-venous reflux producing bacterial colonization ^[36]. The use of prophylactic antibiotics to prevent bacterial colonization in an unobstructed biliary system is not recommended, because bacteria in the bile (bacterobilia) are clinically silent. On the other hand, the use of prophylactic antibiotics appears to be beneficial for patients with biliary obstruction and known or suspected bacterobilia. Antibiotics should be typically continued until the obstruction is relieved. In addition, antibiotic prophylaxis to try to prevent biliary colonization that can lead to systemic sepsis is warranted in special circumstances such as an immunocompromised patient or a patient with PSC ^[37].

7. English editing is recommended.

This manuscript will be fully reviewed by Dr. Sergio A. Sánchez-Luna, a native English speaker and current interventional endoscopist and Assistant Professor of Medicine at the Division of Gastroenterology and Hepatology at The University of Alabama at Birmingham Heersink School of Medicine.