Peer Review File

Article information: https://dx.doi.org/10.21037/jtd-23-336

Review Comments-reviewer A

Comment 1: This article reviews the effectiveness of colistin sulfate against carbapenem-resistant organisms (CRO) through a retrospective data analysis.
I have two main comments for authors:
- The dose used for about 76% of the patients was 1 MU/day of colistin sulfate. Could the authors relate this value to mg of colistin base activity (CBA)? What would be the expected steady-state concentration of colistin?
Reply: Polymyxins are polypeptide antibiotics, and mainly include polymyxin B (PMB), colistin sulfate, and colistimethate sodium (CMS). Consensus guidelines recommend that the dosages of these three drugs should be used according to their respective product labels and should not be confused. The steady-state concentration of polymyxins should not exceed 2mg/L.

- Previous studies have shown that colistin, unlike CMS, is essentially eliminated by the non-renal route [1]. However, Garonzik et al [2] argued that the hypothesis of an eventual decrease in colistin clearance in case of renal dysfunction could not be ruled out. Therefore, it would be interesting to evaluate creatinine clearance parameters of the patients and verify whether renal function could influence the treatment.
1. Li J, Milne RW, Nation RL, Turnidge JD, Smeaton TC, Coulthard K (2003) Use of high-performance liquid chromatography to study the pharmacokinetics of colistin sulfate in rats following intravenous administration. Antimicrobial agents and chemotherapy 47 (5):1766-1770
2. Garonzik S, Li J, Thamlikitkul V, Paterson D, Shoham S, Jacob J, Silveira F, Forrest A, Nation R (2011) Population pharmacokinetics of colistin methanesulfonate and formed colistin in critically ill patients from a multicenter study provide dosing suggestions for various categories of patients. Antimicrobial agents and chemotherapy 55 (7):3284-3294
Reply: Firstly, thank you very much for your suggestion. Due to limited resources, we were unable to measure the weight of ICU patients, which resulted in an inaccurate calculation of their creatinine clearance. This is a limitation of our study. We will strive to address this issue in the future.

Comment 2：Minor comment: Figure 1 is illegible.
Reply: We have uploaded a new editable version of Figure 1.

Review Comments-reviewer B

First of all, my major concern regarding this study is that a retrospective single-arm cohort study cannot answer the clinical question of efficacy and safety. The authors can only describe the rate of clinical improvement and adverse events in patients receiving the colistin sulfate and the administration of the colistin sulfate was associated with lower mortality, but the authors cannot say colistin sulfate is effective and safe, because this is not a RCT and many confounders can influence the treatment outcomes. Please consider to revise the whole paper all throughout. Second, the abstract needs some revisions. The background did not clearly indicate the clinical significance of this research focus, the methods did not describe the inclusion of subjects, the assessment of baseline clinical factors including the administration of colistin sulfate, follow up procedures, and outcome assessment on efficacy, safety, and mortality, the results did not describe the clinical characteristics of the study sample, and the HR and P values for the identified factors associated with mortality, and the conclusion needs more detailed comments for the clinical implications of the use of colistin sulfate and measures to reduce mortality. Third, the introduction of the main text needs to explain why "clinical data on colistin sulfate are still lacking" and which data are lacking. Since colistin sulfate has been used in real-word clinical practice to treat CRO infections, it is not convincing that the efficacy and safety data of colistin sulfate are still lacking. The authors need to further review related literature and clinical guidelines. Fourth, the methodology of the main text needs to describe the sample size estimation procedures, and explain why the authors still focused on the factors associated with 8-day mortality since this is not related to the research focus of this study, the efficacy ad safety of colistin sulfate. In statistics, please describe the details of multiple Cox regression analysis and ensure $P<0.05$ is two-sided. Finally, please consider to cite the below related paper: Jin J, Zhu J, Zhu Z, Kim WY, O'Rourke J, Lin Z, Chen M. Clinical efficacy and nephrotoxicity of intravenous colistin sulfate in the treatment of carbapenem-resistant gram-negative bacterial infections: a retrospective cohort study. Ann Transl Med 2022;10(20):1137. doi: 10.21037/atm-22-4959.

Comment 1：

Reply 1： We have modified our text as advised. We describe the rate of clinical improvement and adverse events in patients receiving the colistin sulfate in the whole text.

Changes in the text: Page 2/Line 8-11、Page 3/Line 9-10、Page 4/Line 22-26、Page 12/Line 25-29

Comment 2：

Reply 2： We have modified our text as advised. The methods added the data source and primary、secondary endpoints. Take into account the number of words,the results only added the HR and P values. The conclusion added monitoring the nephrotoxicity.

Changes in the text: Page 2/Line 12-18、Page 2/Line 31-33、Page 2/Line 34-Page 3/Line 2.

Comment 3：

Reply 3： Beacuse the colistin sulfate is available late, clinical data of efficacy and safety on colistin sulfate are still limiting. Most of the articles we found were about polymyxin B and colistimethate sodium.

Changes in the text: Page 4/Line 21-23