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LETTER TO THE EDITOR

Treatment of nosocomial infections in intensive care unit with colistin and polymyxin B

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To the editor,

We read with interest the article entitled "Colistin and polymyxin B for treatment of nosocomial infections in intensive care unit patients: pharmacoeconomic analysis" by Quintanilha et al. [1]. The study provides valuable data regarding nephrotoxicity, as a known complication of polymyxins (polymyxin B and colistin).

The authors described patients in the neurosurgical, cardiovascular, or transplantation intensive care units (ICUs) who received colistin or polymyxin B for the treatment of documented nosocomial infections. Their results revealed that neither the incidence of nephrotoxicity nor the 30-day mortality rate differed significantly between the patients who received either colistin or polymyxin B. Additionally, they found that colistin was superior to polymyxin B in terms of pharmacoeconomic aspects.

The mean rate of nephrotoxicity with polymyxins was reported to be as high as 32% based on the Acute Kidney Injury Network (AKIN) criteria [2]. Despite their prevalent nephrotoxicity, the high rate of emergence of multidrug-resistant Gram-negative bacteria has made polymyxins an option for the last resort with increasing utilization.

The study findings are remarkable and due to the importance of the treatment of multidrug-resistant infections with these agents, we would like to mention a few points regarding the article.

In their retrospective study, Quintanilha et al. included adult patients who received polymyxins for at least 72 hours and excluded patients who did not have an antimicrobial susceptibility test or those who had received the medications for empiric treatment. However, other influential factors which are necessary to be considered as the exclusion criteria were not noted by the researchers. For example, it was previously shown that patients with an underlying chronic kidney disease were significantly more susceptible to the renal side effects of colistin [3] and polymyxin B [4]. However, patients with renal impairment were not excluded from the study and the results of the baseline renal function test of the patients were not presented in the article. Such data is very valuable to enable the readers to compare the patients in the two groups. The main concern arising here is that if the baseline renal function of the patients in the two groups differed significantly, the incidence of nephrotoxicity in the groups could have probably been affected.

In terms of nephrotoxicity, one of the important issues is the severity of this complication. In the study, renal impairment was defined based on the AKIN criteria. However, the incidence of each stage of acute kidney injury (AKI) was not discussed. It seems to be useful to know if the non-significant difference in the incidence of nephrotoxicity between the colistin and polymyxin B groups is replicated in all the AKI stages or not.

In the study, the resolution of nephrotoxicity was also documented which is of substantial importance. However, a clear definition was not provided for it. Various definitions have been used for renal recovery in different studies including dialysis independence or decrease in serum creatinine (SrCr) to 20% above the baseline level, and it is useful to know the definition used in this study by the researchers.

It seems that one of the major drawbacks of the study by Quintanilha et al. [1] is related to the assessment of causality of the nephrotoxicity due to polymyxins. Based on the included ICUs, it seems that patients who received transplantation were eligible to enter the study. The importance of inclusion of such patients relies on their susceptibly to nephrotoxicity due to receiving immunosuppressive agents. In these patients, the distinction between the two factors as the cause of nephrotoxicity is critical and needs

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further elaboration. Additionally, despite their importance and effects, it seems that due to the limitations of the study, the use of concomitant nephrotoxic medications was not addressed in the results.

Moreover, it is informative to know if some of the patients had received kidney transplantation, how the researchers distinguished the increase in the SrCr due to probable organ rejection from that of polymyxins nephrotoxicity. This is the case for some other conditions that can result in declined renal function or end organ damage.

Regarding polymyxin-induced nephrotoxicity, several administration-related factors are also worth to be considered. First of all, this side effect is correlated with the medication dosage and higher doses increase the risk of nephrotoxicity [2]. Second, the frequency of the medication administration was proposed as an effective factor, and there are some reports of higher risk of nephrotoxicity with once daily dosing of polymyxin B compared to the divided doses [5]. The average daily dose administered to the patients was mentioned in the article. However, it was not clear whether the percentage of patients receiving the high dose of the medication was comparable between the groups or not. The last issue is the route of polymyxin administration. The study recruitment criteria did not limit the route of polymyxin administration and this issue was not pointed out in the text. This factor is important as previous findings demonstrated that the nephrotoxicity of aerosolized colistin is considerably less than the IV administration [3]. Since the administration route has been proposed to affect the incidence of nephrotoxicity, further data can probably elucidate the findings.

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Conflicts of interest The authors declare that they have no conflict of interest.

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