The Role of Aerolized Colistin in the Treatment of Hospital-Acquired Pneumonia: Experience of Multicenter From Turkey

To the Editor:

We read with great interest, in a recent issue of *Critical Care Medicine*, the meta-analysis and systematic review by Valachis et al (1), which evaluated the efficacy and safety of aerosolized colistin as adjunctive therapy to parenteral antimicrobials or as monotherapy in the treatment of ventilator-associated pneumonia.

We would like to share our experience on patients who were treated with parenteral colistin or combination of parenteral colistin and aerosolized colistin for hospital-acquired pneumonia (HAP) associated with multidrug-resistant (MDR) *Pseudomonas aeruginosa* or *Acinetobacter baumannii* at seven tertiary-care centers in Turkey. In this retrospective study, 279 cases (105 women; median age, 71 years; median Acute Physiology and Chronic Health Evaluation [APACHE II] score, 22) were included. Parenteral colistin was used in 210 patients, whereas 69 patients received combination of parenteral and aerosolized colistin. There were no significant differences between the two groups in terms of age, gender, APACHE II score, the presence of HAP-related septic shock, and bacteremia. Colistin was administered at daily median doses of 300 and 225 mg colistin base activity in parenteral and combination groups, respectively. Besides, 82.8% of the study population received additional IV antibiotics, the rates of which were similar in the two groups (82.9% vs 82.6%; $p = 1.0$). The clinical response rates were found as 47.6% in the parenteral group and 66.7% in the combination group ($p = 0.008$). The eradication rates were 41.0% and 59.4%, respectively ($p < 0.001$), but no follow-up microbiologic data were available in 25.3% of the patients. Nephrotoxicity developed at similar rates in two groups (61.9% vs 63.8%; $p = 0.89$). There were no significant differences in terms of overall mortality rate (60.8% vs 65.2%; $p = 0.57$).

Thus, in our population of HAP associated with MDR *P. aeruginosa* or *A. baumannii*, a combination of inhaled and parenteral colistin was associated with better rates of clinical and bacteriologic response, and overall mortality and nephrotoxicity rates were similar. Our study results in patients with HAP are similar to proven conclusion by this meta-analysis.

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The authors reply:

We thank Korkmaz Ekren et al (1) for their comments on our study and for providing their data on the role of aerosolized colistin in treating nosocomial pneumonia caused by multidrug-resistant *Pseudomonas aeruginosa* or *Acinetobacter baumannii.*

Their study results are consistent with the results of our meta-analysis (2), showing that the addition of aerosolized to parenteral colistin when compared wih parenteral colistin only is associated with improved outcomes, including clinical response and microbiologic eradication rate, whereas overall mortality and nephrotoxicity were occurring in similar rates in both groups.

However, the main question about the role of aerosolized colistin on this treatment setting remains unanswered: Will these promising results be confirmed in well-designed randomized or prospective observational studies? The level of evidence in our results was low because of biases of the eligible studies. The present study by Ekren et al is prone to the same type of biases as the ones included in our meta-analysis: retrospective nature, differences in colistin doses, inadequate data on other antimicrobials used apart from colistin, and relative small sample size.

We need to move forward and use the current knowledge to design and conduct studies that will examine the role of aerosolized colistin by overcoming these biases. The recently proposed complementary information deriving from the combination of well-designed randomized studies and population-based observational studies (3) seems to be the best strategy to provide high level of evidence for or against the use aerosolized colistin in this treatment setting.

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