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Editorial

Colistin, Hot Potato for the Therapy of Carbapenem-resistant *Acinetobacter baumannii infections*

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▸ See the article "Early Intravenous Colistin Therapy as a Favorable Prognostic Factor for 28-day Mortality in Patients with CRAB Bacteremia: a Multicenter Propensity Score-Matching Analysis" in volume 34, number 39, e256.

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Carbapenem-resistant multidrug-resistant Gram-negative pathogens which usually accompany concurrent resistance to most other classes of antibiotics are global issues to be solved urgently. *Acinetobacter baumannii* is already a major pathogen in intensive care units and its carbapenem resistance is around 90% in Korea.[1] New agents recently approved for drug-resistant Gram-negative bacilli are not effective against carbapenem-resistant *A. baumannii* (CRAB). Mortality rates for the most common CRAB infections may approach 60%.[2]

Empirical administration of antibiotics is a standard start to cope with undetermined infections and the empirical regimen needs to have enough spectrum to cover possible major pathogens, effectiveness to change the clinical course before the start of definite therapy which is usually 3–4 days long, and low toxicity profiles which does not cause clinicians to hesitate its eager selection. The presence of reliable predictors for a specific pathogen may decrease the uncertainty of the clinicians. Colistin is a drug of first choice for CRAB infections. However, there are many uncertainties for colistin. Although it has potent in vitro activity against *A. baumannii* strains, the uncertainties are a lack of clinically relevant susceptibility breakpoints, narrow therapeutic spectrum, and serious side effects like nephrotoxicity and neurotoxicity. Increasing resistance is also worrisome and several combination regimens versus colistin monotherapy have been tried. All these problems lead to the reluctance for the clinicians to select colistin as an initial empirical agent. Better clinical evidence for effectiveness may guide the clinical decision for empirical use better.

In this issue, Kim et al. [3] tried to answer the last question. In a previous study,[4] the authors reported that the 28-day mortality in patients with CRAB bacteremia without appropriate antibiotic treatment was 69.8%. Of patients with 28-day mortality, 88.9% (127/143) died within 5 days. Among the survivors more than 5 days, the 28-day mortality was 20.5% (16/78). In line with the previous study the authors in the current study compared two groups with and without early empirical administration of intravenous colistin for 28-day mortality in similar study subjects with CRAB bacteremia. Early colistin therapy was defined as intravenous colistin administration for > 48 hours within five days after the blood culture collection. To adjust the nonrandomization bias they used propensity score-matching analysis. Early colistin therapy was associated with lower 28-day mortality (adjusted odds

ratio, 0.31; 95% confidence interval, 0.11–0.88). However, critical weakness of this study is that two comparative groups did not have similar appropriate antibiotic treatment or homogenous treatment background in definite treatment phase (after five days of the initial blood cultures). This incomplete comparative design makes the conclusion incomplete.

As the prevalence of CRAB infections is expected to be persistent and increasing in Korea or globally under severe pressure of limited antibiotic armaments,[5] this kind of multicenter cooperative study is valuable. The complexity of the variables to be considered and the quality of conclusion may be improved through prospective multicenter cooperation. Systemic support from infectious diseases societies in Korea or relevant researchers regarding the priority of research agenda will be helpful. Nation Health Insurance Service as a final consumer also needs to provide appropriate resources considering the disease burden of antibiotic resistance in Korea. The clinical studies should be performed in concert with multifaceted infection prevention activities to maximize the effect.

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