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Correspondence

Reply: The Efficacy of Penicillins with β-lactamase Inhibitor or Cefmetazole against Pneumonia in which ESBL-Producing Bacteria were Isolated from Sputum

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▸ See the letter "The Efficacy of Penicillins with β-lactamase Inhibitor or Cefmetazole against Pneumonia in which ESBL-Producing Bacteria were Isolated from Sputum" in volume 53 on page 562.

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No conflicts of interest.

Dear Editor:

We read with interest the recent paper by Goto et al.[1], which discussed the efficacy of penicillins with β-lactamase inhibitor or cefmetazole against pneumonia in which extended spectrum β-lactamase (ESBL)-producing bacteria were isolated from sputum. Carbapenems are considered the drugs of choice for treating such infections. However, increased empirical use of carbapenems in response to an increased prevalence of ESBL-producing isolates may be accompanied by the rapid emergence of carbapenem resistance in other pathogens [2]. Therefore, therapeutic options other than carbapenems would be attractive. Several observational studies have suggested that beta-lactam/beta-lactamase inhibitors (BL/BLIs) may be clinically effective for treating infections caused by ESBL producers [2-5]. A more prudent use of carbapenems as the initial empirical antibiotic may be reasonable in suspected Gram-negative bacteremia.

In the noninferiority randomized clinical trial that included 391 patients with *Escherichia coli* or *Klebsiella pneumoniae* bloodstream infection and ceftriaxone resistance, the 30-day mortality rate for patients treated with piperacillin-tazobactam (TZP) compared with meropenem was 12.3% *vs.* 3.7%, respectively [6]. Unfortunately, the difference did not meet the noninferiority margin of 5% [6]. These findings do not support TZP compared with meropenem for these infections. With these data, the Infectious Diseases Society of America (IDSA) has published the clinical practice guideline on the treatment of ESBL-producing *Enterobacterales*. In this guideline, a carbapenem is preferred for the treatment of pyelonephritis, complicated urinary tract infections, and infections outside of the urinary tract caused by ESBL producers [7]. TZP is not recommended for the treatment of infections caused by ESBL producers, even if susceptibility to TZP is demonstrated [7].

Several questions may be still unanswered, including whether TZP with extended infusion would be more effective, and whether BL/BLIs are noninferior to carbapenems for empirical treatment of serious infections or for treatment of nonbacteremic ESBL-producing bacterial

infection [8]. The data on previous studies should not be extrapolated to newer BL/BLIs. Studies of short-duration antibiotic treatment and noncarbapenem options for empirical and step-down therapy are needed to identify safe and effective regimens that limit carbapenem exposure [8]. During the last decade, new antimicrobial agents have been developed against multidrug resistant Gram-negative pathogens [9]. Treatment of ESBL-producing pathogens is no longer limited to carbapenems as new BL/BLIs combinations such as ceftolozane/tazobactam and ceftazidime/avibactam have been available [9]. However, these new antimicrobial agents are not yet available in many countries including Korea. Therefore, there is still an ongoing quest for carbapenem-sparing regimens for treatment of ESBL-producing organisms [8-10].

The findings reported by Goto et al. challenge us to revisit a fundamental therapeutic approach against pneumonia caused by ESBL producers [1]. Clinicians in Korea and elsewhere may be able to use these data to consider the alternative options for the treatment of serious infections caused by ESBL producer, but this will not be easy. The current crisis in antibiotic development and public health threat by antimicrobial resistance impose a reappraisal of therapeutic strategies that have been successful in the past. Given the poor outcome of serious infections caused by ESBL producers and a lack of therapeutic options other than carbapenems, further studies are needed to define optimal alternative antimicrobial therapy for infections caused by ESBL-producing pathogens. Indeed, we look forward to the further clinical advancement of therapeutic strategy and to new developments of potent anti-ESBL antimicrobials.

REFERENCES

1. Goto A, Komiya K, Hiramatsu K, Kadota J. The efficacy of penicillins with β lactamase inhibitor or cefmetazole against pneumonia in which ESBL producing bacteria were isolated from sputum. Infect Chemother 2021;53:562-4.
CROSSREF
2. Kang CI, Park SY, Chung DR, Peck KR, Song JH. Piperacillin-tazobactam as an initial empirical therapy of bacteremia caused by extended-spectrum β-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae*. J Infect 2012;64:533-4.
PUBMED | CROSSREF
3. Rodríguez-Baño J, Navarro MD, Retamar P, Picón E, Pascual Á; Extended-Spectrum Beta-Lactamases–Red Española de Investigación en Patología Infecciosa/Grupo de Estudio de Infección Hospitalaria Group. β-Lactam/β-lactam inhibitor combinations for the treatment of bacteremia due to extended-spectrum β-lactamase-producing Escherichia coli: a post hoc analysis of prospective cohorts. Clin Infect Dis 2012;54:167-74.
PUBMED | CROSSREF
4. Tamma PD, Rodriguez-Bano J. The Use of Noncarbapenem β-lactams for the treatment of extended-spectrum β-lactamase infections. Clin Infect Dis 2017;64:972-80.
PUBMED | CROSSREF
5. Son SK, Lee NR, Ko JH, Choi JK, Moon SY, Joo EJ, Peck KR, Park DA. Clinical effectiveness of carbapenems versus alternative antibiotics for treating ESBL-producing *Enterobacteriaceae* bacteraemia: a systematic review and meta-analysis. J Antimicrob Chemother 2018;73:2631-42.
PUBMED | CROSSREF
6. Harris PNA, Tambyah PA, Lye DC, Mo Y, Lee TH, Yilmaz M, Alenazi TH, Arabi Y, Falcone M, Bassetti M, Righi E, Rogers BA, Kanj S, Bhally H, Iredell J, Mendelson M, Boyles TH, Looke D, Miyakis S, Walls G, Al Khamis M, Zikri A, Crowe A, Ingram P, Daneman N, Griffin P, Athan E, Lorenc P, Baker P, Roberts L, Beatson SA, Peleg AY, Harris-Brown T, Paterson DL; MERINO Trial Investigators and the Australasian Society for Infectious Disease Clinical Research Network (ASID-CRN). Effect of piperacillin-tazobactam vs meropenem on 30-day mortality for patients with *E coli* or *Klebsiella pneumoniae* bloodstream infection and ceftriaxone resistance: a randomized clinical trial. JAMA 2018;320:984-94.
PUBMED | CROSSREF

7. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America guidance on the treatment of extended-spectrum β-lactamase producing Enterobacterales (ESBL-E), carbapenem-resistant enterobacterales (CRE), and *Pseudomonas aeruginosa* with difficult-to-treat resistance (DTR-P. aeruginosa). Clin Infect Dis 2021;72:1109-16.
PUBMED | CROSSREF
8. Hayden MK, Won SY. Carbapenem-sparing therapy for extended-spectrum β-lactamase-producing *E coli* and *Klebsiella pneumoniae* bloodstream infection: the search continues. JAMA 2018;320:979-81.
PUBMED | CROSSREF
9. Paterson DL, Isler B, Stewart A. New treatment options for multiresistant gram negatives. Curr Opin Infect Dis 2020;33:214-23.
PUBMED | CROSSREF
10. Aslan AT, Akova M. Extended spectrum β-lactamase producing enterobacteriaceae: carbapenem sparing options. Expert Rev Anti Infect Ther 2019;17:969-81.
PUBMED | CROSSREF