

Synergistic Effect of Ceftazidime-Avibactam with Aztreonam on Carbapenemase-Positive *Klebsiella pneumoniae* MBL+, NDM+ [Letter]

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Dear editor

Combining aztreonam with ceftazidime/avibactam presents a viable therapeutic approach for treating metallo-beta-lactamase (MBL)-infections. While no randomized, well-controlled trials have assessed the safety and efficacy of this combination, observational studies suggest that it is clinically useful in treating serious infections caused by MBL-organisms.¹ We deeply studied and discussed the very informative and clinically useful research entitled “Synergistic Effect of Ceftazidime-Avibactam with Aztreonam on Carbapenemase-Positive *Klebsiella pneumoniae* MBL+, NDM+” conducted by Mateusz Szymański et al.² We acknowledge that the research and findings of the author are highly valuable and clinically beneficial.

The authors have retrospectively studied and analysed the efficacy of two different antibiotic regimens for treating the infections caused by *Klebsiella pneumoniae* strains producing carbapenemases (MBL) and compared the clinical outcomes in two patient groups. We are very keen to investigate the clinical outcomes in patients infected with MBL carbapenemase-positive *Klebsiella pneumoniae* coproducing other enzymes such as extended-spectrum beta-lactamases (ESBLs), KPCs or class C enzymes and treated with ceftazidime-avibactam with aztreonam combination therapy as our next research focus, following our recent laboratory based study.³ Invasive infections caused by MBL-gram negative bacteria are linked to high mortality rates (over 30%), particularly among critically ill patients in hospital settings.⁴

The present study included 26 intensive care unit (ICU) patients with various nosocomial invasive infections caused by *Klebsiella pneumoniae* producing class B carbapenemases – MBL, specifically of the NDM type. The authors have concluded that the best treatment outcomes were achieved in the group where a combination antibiotic therapy of ceftazidime-avibactam with aztreonam was utilized.

In this study, the synergy between the two said antibiotics was determined using E strip/disc method and the presence of “reverse D” after incubation of the culture plates.

We would like to add a few comments regarding the synergy testing methods and their actual clinical application. As reported in earlier studies, the broth disk elution shows good correlation with the broth micro-dilution method which is a gold standard method for testing synergy and the E strip/disc method aligns well with the broth disc elution method.^{1,3,5} However, considering the geographical differences in the susceptibility profile of the microorganisms, it is advisable to perform and compare results from at least two different laboratory tests to assess the synergy of the combination for isolates before finalizing the therapy, if resources permit.

Furthermore, in our opinion, there are chances that synergy may still exist in vivo even if in vitro synergy test shows negative results and vice versa considering the different milieu in vivo and different pharmacokinetic and pharmacodynamic parameters inside the host body.

The introduction of this combination has enabled the treatment of severe MBL-gram negative infections with β -lactams, thereby addressing the challenges associated with polymyxins, such as inadequate lung penetration and renal toxicity.⁶

Once again, we sincerely thank the authors for their valuable and timely research, which we hope will pave the way for more extensive future studies on a related topic.

Disclosure

The authors report no conflicts of interest in this communication.

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