

Selection between aztreonam and cephalosporins for treatment of infections with pseudomonads needs more caution

Bhoj R Singh

Division of Epidemiology, ICAR-
Indian Veterinary Research Institute,
Izatnagar, India

Dear editor

In the recently published study¹ to evaluate the use of aztreonam as an active empiric therapy against subsequent culture of *Pseudomonas aeruginosa*, empiric therapy failure using aztreonam is reported more common than on using β -lactam antibiotics in patients suffering *P. aeruginosa* infection. Though the study is interesting and revealing important findings regarding antibiotic use for treatment of *P. aeruginosa* infection, it should be accepted with caution as suggested by the authors¹ repeatedly due to limited number of cases. In our observations on *P. aeruginosa* (95) and other pseudomonads (40) isolates from veterinary clinical cases we found that instead of generalizing the lesser efficacy of aztreonam in-depth studies are required. Although insignificant, aztreonam inhibited more numbers of extended spectrum β -lactamase (ESBL) producing (57) *P. aeruginosa* strains (56.1%) than most of the β -lactams including cefotaxime, ceftriaxone and piperacillin (53.3%). However, on non-ESBL producing (37) strains aztreonam inhibited 42.1% isolates, much less than cefepime (68%), ceftriaxone (50%) and piperacillin + tazobactam (61.1%). Therefore, it is suggested to use the two classes of antibiotics (aztreonam and β -lactams) judiciously based on antibiotic stewardship principle¹ instead of following some general rule for infections with pseudomonads.

In the analysis, antibiotic sensitivity patterns, available in clinical epidemiology laboratory of the Institute, of the 82 ESBL producers pseudomonads including *P. aeruginosa* (57), *P. alcaligenes* (1), *P. fluorescens* (7), *P. paucimobilis* (8), *P. pseudoalcaligenes* (5), *P. stutzeri* (3), *P. testosteronii* (1) and 53 ESBL negative pseudomonads including *P. aeruginosa* (38), *P. alcaligenes* (1), *P. diminuta* (1), *P. fluorescens* (6), *P. paucimobilis* (2), *P. pseudoalcaligenes* (3), *P. stutzeri* (1), *P. vesicularis* (1) were included. All the isolates were associated with one or other clinical condition in animals and were tested for antibiotic sensitivity pattern using standard disc diffusion assay.²

The analysis of the data (Table 1) for sensitivity of *P. aeruginosa* included in the study for aztreonam, carbapenems (meropenem, imipenem, ertapenem), cefepime, cefotaxime, ceftriaxone, colistin, gentamicin, piperacillin + Tazobactam, tetracycline and tigecycline revealed ESBL negative *P. aeruginosa* (PA) isolates were more often (though statistically insignificant, $P > 0.05$) resistant (57.9%) to aztreonam than the ESBL positive isolates (43.9%). However, significantly more number of the ESBL negative *P. aeruginosa* isolates resisted gentamicin ($P < 0.001$) than ESBL positive

Correspondence: Bhoj R Singh
Division of Epidemiology, ICAR-Indian
Veterinary Research Institute, Izatnagar
243122, India
Email brs1762@gmail.com

Table I Antibiotic sensitivity pattern of *Pseudomonas aeruginosa* and other pseudomonads isolated from clinical infections in animals

Antibiotics tested	<i>P. aeruginosa</i> (N=95)		Other pseudomonads (N=40)		Total (N=135)	
	ESBL-ve (38)	ESBL+ve (57)	ESBL-ve (15)	ESBL+ve (25)	ESBL-ve (53)	ESBL+ve (82)
Aztreonam	42.1	56.1	46.7	64.0	43.4	58.5
Carbapenems	57.9	66.7	50.0	33.3	64.2	67.1
Cefepime	68.0	90.0	40.0	60.0	62.9	72.4
Cefotaxime	31.6	42.1	66.7	64.0	34.0	47.6
Ceftriaxone	50.0	49.1	66.7	84.0	54.7	53.7
Colistin	89.5	93.0	80.0	68.0	83.0	90.2
Gentamicin	68.4	94.7	93.3	88.0	75.5	92.7
Piperacillin + Tazobactam	61.1	53.3	64.3	78.9	62.0	60.9
Tetracycline	18.4	21.1	46.7	60.0	26.4	32.9
Tigecycline	28.9	42.1	80.0	72.0	43.4	51.2

Abbreviations: ESBL-ve, extended spectrum β -lactamase negative; ESBL+ve, extended spectrum β -lactamase positive.

isolates. The ESBL negative *P. aeruginosa* isolates were significantly more commonly resistant to aztreonam than to cefepime ($P=0.04$), colistin ($P<0.001$) and gentamicin ($P=0.02$) but less often than to tetracycline ($P=0.025$). The ESBL positive *P. aeruginosa* isolates were significantly ($P<0.001$) more often resistant to aztreonam than to colistin and gentamicin but less than to tetracycline. The ESBL and non-ESBL pseudomonads other than *P. aeruginosa* (NPA) had not differed significantly ($P>0.05$) in their sensitivity to any of the antibiotics, however, aztreonam inhibited 64% ESBL producers and only 46.7% of ESBL negative isolates. Though for most of the antibiotics, including aztreonam and cephalosporins, sensitivity of *P. aeruginosa* and NPA had not differed significantly ($P>0.05$), NPAs were significantly more often resistant to cefepime ($P<0.001$), colistin ($P=0.02$), but less often ($P<0.001$) to tetracycline and tigecycline.

The analysis on antibiotic sensitivity patterns of *P. aeruginosa* and NPA isolates from veterinary clinical cases indicated need of antibiotic sensitivity assay for judicious use of antibiotics in therapy ie, need to reinforce antimicrobial stewardship principles.¹

Disclosure

The author reports no conflicts of interest in this communication.

References

1. Hogan M, Bridgeman MB, Min GH, Dixit D, Bridgeman PJ, Narayanan N. Effectiveness of empiric aztreonam compared to other beta-lactams for treatment of *Pseudomonas aeruginosa* infections. *Infect Drug Resist*. 2018;11:1975–1981.
2. CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 24th informational supplement M100-S24 and M11-A8. Wayne, PA, USA: Clinical and Laboratory Standards Institute; 2014.

Authors' reply

Response to Letter to the Editor regarding publication, Effectiveness of empiric aztreonam compared to other beta-lactams for treatment of *Pseudomonas aeruginosa* infections

Michael Hogan¹

Mary Barna Bridgeman¹

Gee Hee Min¹

Deepali Dixit¹

Patrick J Bridgeman¹

Navaneeth Narayanan^{1,2}

¹Department of Pharmacy Practice and Administration, Ernest Mario School of Pharmacy, Rutgers University, Piscataway, NJ, USA;

²Division of Infectious Diseases, Department of Medicine, Rutgers, Robert Wood Johnson Medical School, New Brunswick, NJ, USA

Correspondence: Mary Barna Bridgeman

Department of Pharmacy Practice and Administration, Ernest Mario School of Pharmacy, Rutgers University, 160 Frelinghuysen Road, Piscataway, NJ 08854, USA

Tel +1 848 445 6815

Email Mary.bridgeman@pharmacy.rutgers.edu

Dear editor

We appreciate the author of this letter reading our article with such great interest. We believe, however, in this response that there is limited application to the context and overall content of our clinical study of human patients. First, the data cited in this response are from veterinary clinical cases. Though general principles of understanding of antibiotic sensitivity testing and resistance mechanisms apply regardless of species, there are major differences that impede reasonable comparisons between the assertions in this letter and findings of our original study. This includes the choice of antibiotics used, at least for sensitivity testing for *Pseudomonas* in animals, as cited by Singh. Antibiotics such as cefotaxime, ceftriaxone, tetracycline, and tigecycline are never clinically utilized or tested for susceptibility against *Pseudomonas aeruginosa* (*P. aeruginosa*) in the treatment of human infections. It is universally taught to clinicians that these antibiotics lack clinically relevant activity against *P. aeruginosa* and

therefore should not be used as empiric therapy if there is potential for infection with *P. aeruginosa*; similarly, these agents are not tested to assess as an option for definitive therapy based on a lack of clinical efficacy.^{1,2} Second, Singh cited data by stratifying *P. aeruginosa* by extended-spectrum beta-lactamase (ESBL) production and compared aztreonam susceptibility to ceftriaxone, cefotaxime, and piperacillin. At least in the US, genotypic testing for ESBL production in *P. aeruginosa* is not routinely performed in the clinical setting and as mentioned previously, many of the antibiotics mentioned (eg, cefotaxime and ceftriaxone) would never be tested against *P. aeruginosa* regardless of suspicion of ESBL production. The differential susceptibility by ESBL production, therefore, has limited application. Additionally, in the US where our study takes place, plasmid-mediated ESBL production by *P. aeruginosa* is not common while AmpC beta-lactamase production is the primary beta-lactamase resistance mechanism found in *P. aeruginosa*.³ Third, and finally the primary objective and underlying context of our study is not readily considered. We sought to assess the utility of aztreonam as an empiric agent (prior to any culture and susceptibility results) against *P. aeruginosa* in human clinical cases as compared to other antipseudomonal beta-lactams (eg, cefepime, piperacillin/tazobactam and not agents such as ceftriaxone). The final point by Singh notes the need for antibiotic sensitivity testing for judicious use of antibiotics, which we believe is true for most clinical cases of infection in general but overlooks the message of empiric therapy selection, which is what our study aimed to evaluate.

Disclosure

The authors report no conflicts of interest in this communication.

References

1. Gilbert DN, Chambers HF, Eliopoulos GM, Saag MS, Pavia AT, editors. *Sanford Guide to Antimicrobial Therapy 2018*. 48th ed. Sperryville, VA: Antimicrobial Therapy, Inc.; 2018.
2. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 28th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.
3. Nguyen L, Garcia J, Gruenberg K, MacDougall C. Multidrug-resistant pseudomonas infections: hard to treat, but hope on the horizon? *Curr Infect Dis Rep*. 2018;20(8):23.

Dove Medical Press encourages responsible, free and frank academic debate. The content of the Infection and Drug Resistance 'letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the Infection and Drug Resistance editors. While all reasonable steps have been taken to confirm the content of each letter, Dove Medical Press accepts no liability in respect of the content of any letter, nor is it responsible for the content and accuracy of any letter to the editor.

Infection and Drug Resistance

Dovepress

Publish your work in this journal

Infection and Drug Resistance is an international, peer-reviewed open-access journal that focuses on the optimal treatment of infection (bacterial, fungal and viral) and the development and institution of preventive strategies to minimize the development and spread of resistance. The journal is specifically concerned with the epidemiology of antibiotic

resistance and the mechanisms of resistance development and diffusion in both hospitals and the community. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/infection-and-drug-resistance-journal>