Treatment of *Pseudomonas aeruginosa* ventilator-associated pneumonia

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Case Presentation

A 36-year-old male was admitted to the medical ICU for a chronic obstructive pulmonary disease (COPD) exacerbation four days ago where he was intubated for respiratory support. The patient has failed daily spontaneous breathing trials and remains on ventilatory support. The patient currently has a blood pressure of 138/84 mmHg, temperature of 39.2°C, heart rate of 104 bpm, and respiratory rate set at 18 bpm. A complete metabolic panel indicated levels within normal limits and the patient's creatinine clearance is calculated to be 67 mL/min. A daily complete blood count has been collected over the last four days, with values within normal limits except for the white blood cell count that has trended as follows up to the present (x10^9/L): 8, 9, 15, 21.

Following suspicion of infection, a culture from a bronchealvolar lavage grew *Pseudomonas aeruginosa* with the following susceptibilities:

Antimicrobial agent	MIC (mcg/mL)	Interpretation
Ceftazidime	2	S
Cefepime	4	I
Piperacillin-tazobactam	1	S
Imipenem	2	S
Meropenem	2	S
Tobramycin	2	S
Ciprofloxacin	8	R

During interdisciplinary rounds, the following five options are discussed. Which of the following options is most appropriate for this patient and indication?

A. Cefepime 2g q8h and piperacillin-tazobactam 4.5g q8h for 15 days.
B. Piperacillin-tazobactam 4.5g q8h for 15 days.
C. Cefepime 2g q8h for 8 days.
D. Tobramycin 5mg/kg q24h for 8 days.
E. Cefepime 2g q8h and vancomycin 1500mg q12h for 8 days.

Discussion

Pneumonia is the second most common nosocomial infection, with 86% of nosocomial pneumonia associated with mechanical ventilation, termed ventilator-associated pneumonia (VAP). Choice of agent for the treatment of VAP is guided by the 2016 clinical practice guidelines by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society, with duration of treatment explored through several clinical trials. [1]

The patient is currently not exhibiting signs of septic shock secondary to VAP. However, the patient is febrile with a trending leukocytosis and a positive bronchial culture for *Pseudomonas aeruginosa*. Absent of septic

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shock or otherwise high risk of death, when the results of antibiotic susceptibility testing are known the 2016 IDSA guidelines for pneumonia recommend monotherapy with an antibiotic to which the isolate is susceptible.[1] A landmark trial indicated that, compared to a 15-day treatment course, 8 days of antibiotic therapy for VAP in adults demonstrated no difference in mortality, recurrent infections, ICU length of stay, and 60-day mortality.[2] However, a subsequent trial, iDIAPASON, conducted to explore a sub-analysis of patients with *Pseudomonas aeruginosa*-related VAP found a higher rate of recurrence and suggested that a shortened antibiotic duration of 8 days was not noninferior to a duration of 15 days due to increased disease recurrence.[3] Therefore, **answer choice B is correct**, monotherapy of piperacillin-tazobactam 4.5g q8h for 15 days is the most appropriate choice based on recent evidence due to a lack of need for combination therapy and a potential inferiority of a shortened antibiotic duration in patients with VAP caused by *Pseudomonas aeruginosa*. However, iDIAPASON did not meet power to find a statistically significant difference between the 8-day and 15-day group. Further research is needed to confirm optimal duration of antimicrobials for *Pseudomonas aeruginosa* VAP based on patient-specific factors such as clinical response and severity of disease which have not previously been assessed in clinical trials.

Evaluation of alternative options proposed for acute management

Aminoglycoside monotherapy is associated with a higher risk of death and is strongly recommended against in the IDSA guidelines.[1] Additionally, the breakpoint for tobramycin in *Pseudomonas aeruginosa* is 2 compared to the isolated 2, which is less favorable when comparing it to piperacillin-tazobactam's 16 compared to the isolated 1.[4]

Combination therapy in patients who are not exhibiting signs of septic shock and are not at high risk of death is not recommended; second, vancomycin does not cover *Pseudomonas aeruginosa* and the patient currently does not have a positive blood or bronchial culture for microorganisms that may be covered by vancomycin, such as methicillin-resistant *Staphylococcus aureus*.[1]

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References

1. Kalil, A, Metersky, M, Klompas, M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016;63(5):e61-e111.

2. Chastre, J, Wolff, M, Fagon, JY, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults. JAMA. 2003;290(19):2588- 2598.

3. Bouglé A, Tuffet S, Federici L, et al. Comparison of 8 versus 15 days of antibiotic therapy for Pseudomonas aeruginosa ventilator-associated pneumonia in adults: a randomized, controlled, open-label trial. Intensive Care Med. 2022;48(7):841-849.

4. Breakpoint tables for interpretation of MICs and zone diameters; version 12.0. EUCAST. April 21, 2022. Accessed http://www.eucast.org