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Appropriateness of empiric extended-infusion piperacillin/tazobactam in the Intensive Care Unit

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Background

- Intensive care unit (ICU) patients are at an increased risk of infections, especially with nosocomial pathogens.[1]
- Admission to the ICU is a risk factor for the presence of antimicrobial resistance.
- It has been shown that inappropriate empiric antimicrobial therapy for multi-drug resistant infections leads to increased burden of disease and mortality.[3]
- Monte Carlo simulations indicate that a 4-hour infusion of piperacillin/tazobactam (PTZ) 3.375g administered every 8 hours produces greater time over the minimum inhibitory concentration (T>MIC) than a 30-minute infusion of PTZ 3.375g administered every 4 hours for pathogens with MICs <= 16/4 mcg/mL.[4]
- At our institution, we implemented an extended-infusion PTZ protocol that administers 3.375 grams over 4-hours, given every 8-hours, for empiric coverage of gram-negative infections.
- Institutional antibiogram data has shown an increase in non-urine P*seudomonas aeruginosa* isolates with MICs > 16/4 mcg/mL.
- This has led to a concern at the University of New Mexico Hospital that extended infusion PTZ may not be appropriate for empiric treatment of ICU patients[2,5]

Objective

The objective of the study is to collect and evaluate MIC data for ICU isolates to determine if extended-infusion PTZ is appropriate for empiric treatment in ICU patients.

Outcomes

Primary Outcome:

Primary outcome: To determine the percentage of gram-negative ICU isolates with PTZ MICs > 16/4 in which our current extended-infusion PTZ protocol is inappropriate

Secondary outcomes:

- Determine which gram-negative pathogens are associated with elevated MICs
- Describe patient specific risk factors that may be associated with elevated MICs in gram-negative pathogens
- Determine the most appropriate empiric gram-negative therapy in ICU patients

Methods

- Study setting: University of New Mexico Hospital (UNMH)
- Study design: Retrospective, single-center cohort chart review
- Sample size: 231 patients
- Evaluation period: 01/01/2017 – 12/31/2017

Inclusion	Exclusion
▪ Adult patients > 18 years of age ▪ Admitted to the ICU ▪ Confirmed gram-negative isolate within 48 hours prior to ICU admission	▪ Patients with a gram-negative isolate from a urinary source ▪ Patients with cystic fibrosis ▪ Cultures obtained greater than 48 hours prior to ICU admission

Results

Multiple Logistic Regression Analysis	P value (OR; 95%CI)
Heart Failure	0.51 (1.44; 0.495-4.16)
Chronic Kidney Disease	0.89 (1.11; 0.23-5.4)
Dialysis	**0.03 (5.53; 1.18-26.02)**
Previous ICU admission*	0.67 (0.77; 0.23-2.55)
History of MDRO/PSA	0.87 (1.11; 0.33-3.73)
IV antibiotics*	**<0.001 (4.64; 2.02-10.62)**
Prior hospitalization* (lasting over 4 days)	0.89 (0.93; 0.30-2.82)
Wounds/trauma	**0.02 (2.34; 1.15-4.72)**
Organism identified+	No significance

*Within the past 90 days

+includes all gram-negative organisms identified

Results

Figure 1. Organisms identified

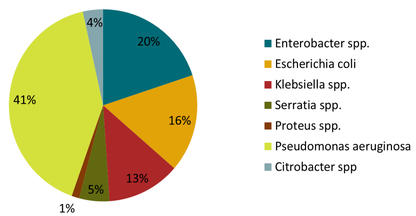


Figure 2. Piperacillin/tazobactam MICs
N = 231

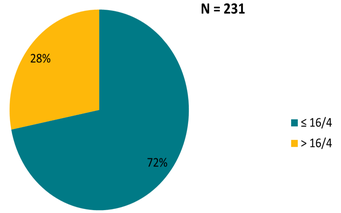
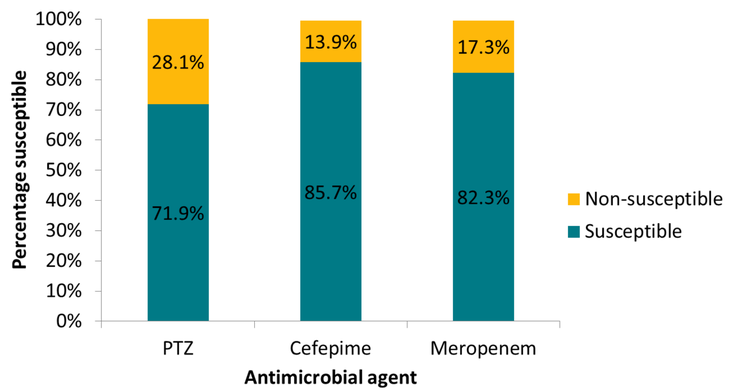


Figure 3. Percentage of isolate susceptibility by agent



Conclusions

- Extended-infusion piperacillin/tazobactam may not be the most appropriate agent for ICU patients especially for patients with previous IV antibiotics, trauma or dialysis.
- No specific organism was associated with a consistently elevated in MICs
- Alternative agents, such as cefepime, may be more appropriate for empiric coverage of gram-negative multi-drug resistant organisms.

References

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