A comparison of piperacillin/tazobactam and cefepime for the treatment of AmpC-inducible Enterobacteriaceae infections

Michelle Barron*, Meghan Jeffres2, Clayton Foster1, Mary Bessesen3, Randy Fugit3, Bruce Mccollister1

1University of Colorado School of Medicine, Aurora, United States
2University of Colorado Skaggs School of Pharmacy, Department of Clinical Pharmacy, Aurora, United States
3Veterans Affairs Eastern Colorado Health Care System, Denver, United States

Background: There is a lack of data assessing the efficacy of different beta-lactam antibiotics for treatment of Enterobacter spp., Serratia marcescens, Citrobacter freundii, Providencia spp., and Morganella morganii (ESCPM) infections. These pathogens encode for AmpC beta-lactamases on their chromosomes. AmpC expression is generally inducible, although derepressed mutants with constitutive high-level AmpC expression can emerge. Data suggests these pathogens can be successfully treated with carbapenems and cefepime (CEF), as both antibiotics are stable against inducible or constitutive AmpC expression. Although Piperacillin/tazobactam (PT) is not stable against AmpC, it is not a strong AmpC inducer, suggesting a potential therapeutic role for PT against ESCAM pathogens with inducible AmpC expression. The purpose of this study is to compare outcomes between patients with ESCPM infections treated with CEF or PT.

Material/methods: This retrospective chart review compares clinical outcomes for patients with ESCPM infections stratified by empiric beta-lactam (CEF or PT). Patients included had respiratory or blood cultures positive for ESCPM pathogens susceptible to empiric beta-lactam and were admitted to University of Colorado Hospital or Veterans Affairs Eastern Colorado Health Care System between January 1, 2012 and January 1, 2015. The primary outcome was 30-day mortality. Secondary outcomes included emerging resistance to empiric beta-lactam within 30 days and 30-day readmission. Primary and secondary outcomes were analyzed using Fisher's exact test, 2-sided. Logistic regression was utilized to adjust for confounding variables. Statistical significance is defined as a p-value less than 0.05. This study was approved by Colorado Multiple Institutional Review Board.

Results: 152 patients were included in the analysis (PT n=101, CEF n=51). The most common site of infection was respiratory (PT 72.5%, CEF 78.1%). Severity of illness measures were not significantly different between the two groups at the start of antibiotics: intensive care unit (ICU) admission (PT 76.2%, CEF 66.7%), receipt of mechanical ventilation (PT 52.5%, CEF 56.9%), receipt of vasopressor agents (PT 30.7%, CEF 23.5%). Immunosuppression differed between groups (PT 18.9%, CEF 39.2%, p=0.010). Receipt of chemotherapy was the predominant cause of immunosuppression (PT 6.9%, CEF 23.5%, p=0.008). The primary outcome of 30-day mortality was not different between PT 21.8% and CEF 27.5%. Logistic regression identified chemotherapy, ICU admission, receipt of mechanical ventilation, receipt of vasopressor agents, and McCabe score of 3 as predictors of 30-day mortality. Neither empiric treatment with PT or CEF were predictors of 30-day mortality using univariate or multivariate logistic regression. Secondary outcomes of emerging resistance (PT 8.0%, CEF 7.8%) and 30-day readmission (PT 9.9%, CEF 15.7%) were similar between groups.
Conclusions: In addition to the ampC stable antibiotics of carbapenems and CEF, PT appears to be an additional treatment option for AmpC-inducible ESCPM infections.