

Emerging Piperacillin/tazobactam Resistance in *E. coli* and *Klebsiella sp.*

Subject category: Resistance mechanisms

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Background: Piperacillin / tazobactam (P/T) plays an important role in the empirical therapy of numerous infections. While *Enterobacteriaceae* resistance to P/T remains relatively low in our institution we have identified an increasing number of *E.coli* and *Klebsiella sp.* isolates with intermediate susceptibility or resistance to P/T (P/T-R). We report the increasing prevalence of P/T-R among *E.coli* and *Klebsiella spp* over an 11 year period, usage of antimicrobials during this time period, and our attempts to document the mechanism of resistance in these isolates.

Methods: Antimicrobial susceptibility testing results using Kirby Bauer disk diffusion method for *E.coli* and *Klebsiella sp.* from all clinical sites were reviewed from January 2006 through December 2016. Duplicates were excluded. Antimicrobial use was expressed as the number of hospital days on antimicrobials per 1000 hospital days. Whole genome sequencing was performed on a subset of isolates identified as P/T-R in order to identify a mechanism of resistance.

Results: From 2006 through 2016 we identified 126,422 *E.coli* and *Klebsiella spp* isolates; 978 were P/T-R (0.78%). Of these 336 were extended spectrum beta lactamase (ESBL) producers. Of the 642 non ESBL- P/T-R, 179 (27.8%) retained susceptibility to all cephalosporins tested. Figure 1 shows the distribution of P/T-R isolates over the period of study and the trend in total antibiotic and specifically P/T use in hospitalized patients. Whole genome sequencing of 4 isolates (*K. pneumoniae* from blood; n=3 and *E. coli* from urine; n=1) showed the presence of Class A beta-lactamase genes; SHV (n=3) and TEM (n=1). All isolates showed presence genes for outer membrane porins and protein efflux pumps, however, there were no detectable mutations that could explain the phenotypic susceptibility profile seen in these isolates.

Conclusion: We describe a novel resistance pattern to P/T in *E. coli* and *Klebsiella spp.* which appears to be slowly increasing over time. This is concurrent with increasing P/T use and overall antimicrobial use during the same time period. While a porin mutation has been described in similar strains, we have not been able to demonstrate this mechanism of resistance to date. Clinicians should be aware of this emerging resistance pattern when prescribing empiric antimicrobials.

