Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Beta-lactamases: Focus on ESBL

What is an ESBL?

ESBLs are enzymes found in gram-negative bacteria that inactive penicillins, most cephalosporins, and aztreonam. However, carbapenems are stable to inactivation by ESBLs. ESBLs can be inhibited *in vitro* by beta-lactamase inhibitors such as tazobactam (found in piperacillin-tazobactam), clavulanate (found in amoxicillin-clavulanate), and avibactam (found in ceftazidime-avibactam). While co-resistance may occur through expression of additional resistance mechanisms, non-beta-lactam antibiotics (e.g. fluoroquinolones, TMP-SMX, nitrofurantoin, aminoglycosides, fosfomycin) are unaffected by ESBLs.[1]

How are ESBLs identified?

ESBLs can be identified phenotypically (e.g. broth microdilution) and genotypically (e.g. polymerase chain reaction [PCR]). Ceftriaxone resistance may serve as a surrogate marker for ESBL production, however this may overcall ESBL presence[2, 3]

Treatment of ESBL Infections

Many clinicians were taught that carbapenems are the drug of choice for the treatment of infectious caused by ESBL producing organisms. However, with increased prevalence of ESBLs, carbapenem sparing regimens are needed since carbapenem-resistant organisms are among the most concerning resistance pathogens.[4]

The Infectious Diseases Society of America provides recommendations for the management of infections due to ESBLs according to source of infection and are summarized in the table below[1]:

Uncomplicated Cystitis	Pyelonephritis/Complicated UTIs	Infections Outside of the Urinary Tract
Preferred • Nitrofurantoin • Trimethoprim-sulfamethoxazole (TMP-SMX) **Alternate** • Single-dose aminoglycoside • Oral fosfomycin • Piperacillin-tazobactam* • Cefepime*	**Preferred** • Ertapenem • Meropenem • Ciprofloxacin • Levofloxacin • TMP-SMX **Alternate** • Aminoglycoside	**Preferred** • Meropenem • Ertapenem **Step down after clinical improvement** • Fluoroquinolones • TMP-SMX

** If initiated as empiric therapy and patient is experiencing clinical improvement*

Key Takeaway: Carbapenems are recommended for severe infections caused by ESBL producing organisms, but emerging carbapenem resistance from carbapenem use is a concern. Non-carbapenem therapy should be utilized whenever possible.

References:

1. Tamma, Pranita D et al. "Infectious Diseases Society of America Guidance on the Treatment of Extended-Spectrum β-lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and Pseudomonas aeruginosa with Difficult-to-Treat Resistance (DTR-P. aeruginosa)." Clinical infectious diseases : an official publication of the Infectious Diseases Society of America vol. 72,7 (2021): e169-e183. doi:10.1093/cid/ciaa1478
2. Tamma PD, Humphries RM. PRO: Testing for ESBL production is necessary for ceftriaxone-non-susceptible Enterobacterales: perfect should not be the enemy of progress. *JAC Antimicrob Resist*. 2021;3(2):dlab019. Published 2021 May 7. doi:10.1093/jacamr/dlab019
3. Palacios-Baena ZR, Giannella M, Manissero D, et al. Risk factors for carbapenem-resistant Gram-negative bacterial infections: a systematic review. *Clin Microbiol Infect*. 2021;27(2):228-235. doi:10.1016/j.cmi.2020.10.016
4. CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019