Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Amoxicillin-Clavulanate for ESBL UTIs

Recommended treatments for extended spectrum beta-lactamase (ESBL) infections typically include carbapenems, which are stable to ESBLs, and non-beta-lactam antibiotics (e.g. quinolones, nitrofurantoin, etc.), which are not inactivated by ESBLs. Use of beta-lactam/beta-lactamase inhibitors is controversial, as common beta-lactamase inhibitors (e.g. tazobactam, clavulanate) inhibit ESBLs and susceptibility is often demonstrated, however outcomes data has suggested inferiority in severe infections.[1] A common beta-lactam/beta-lactamase inhibitor is amoxicillin-clavulanate and many urinary tract infections (UTI) are not severe infections. Can amoxicillin-clavulanate be used to treat ESBL UTIs?

What is the available guidance?

The 2024 Infectious Diseases Society of America (IDSA) guidance on antimicrobial resistant gram-negative infections suggest against the use of amoxicillin-clavulanate for cystitis due to ESBL Enterobacterales.[2] They note that robust data informing this question is lacking and that the deterrence is primarily based on a RCT that found 3-days of amoxicillin-clavulanate 500/125 mg BID to be inferior to ciprofloxacin 250 mg BID in clinical cure of cystitis (58% to 77%). Prevalence of ESBL was not reported.[3]

They acknowledge that amoxicillin-clavulanate may still be selected when resistance and toxicities preclude use of alternatives and it is preferred to avoid intravenous antibiotics. They recommend cautioning patients about the risk for recurrent infection in these situations.

What is the evidence?

In one observational study, use of amoxicillin-clavulanate 500/125 mg TID for 5- 7 days achieved clinical cure in 31/37 (84%) outpatients with cystitis due to ESBL Enterobacterales.[4]

In another retrospective cohort that included both inpatients and outpatients with uncomplicated UTI, complicated UTI, and pyelonephritis, 90-day clinical failure rates were similar among patients who received amoxicillin-clavulanate (5/26, 19.2%) and standard of care (10/33, 30.3%). Most patients received amoxicillin 875 mg/125 mg every 12 hours and mean duration of treatment was 7 days with amoxicillin-clavulanate.[5]

Key Takeaway: Amoxicillin-clavulanate may be active in vitro against ESBL Enterobacterales, but limited data exists to inform its role in therapy compared with alternatives for mild infections such as cystitis or uncomplicated UTI. If selecting amoxicillin-clavulanate higher doses and 7-day duration may be needed.

References:

1. Harris PNA, Tambyah PA, Lye DC, et al. Effect of Piperacillin-Tazobactam vs Meropenem on 30-Day Mortality for Patients With *E coli* or *Klebsiella pneumoniae* Bloodstream Infection and Ceftriaxone Resistance: A Randomized Clinical Trial. *JAMA.* 2018;320(10):984–994. doi:10.1001/jama.2018.12163
2. Tamma PD, Heil EL, Justo JA, Mathers AJ, Satlin MJ, Bonomo RA. Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections. *Clin Infect Dis*. Published online August 7, 2024. doi:10.1093/cid/ciae403
3. Hooton TM, Scholes D, Gupta K, Stapleton AE, Roberts PL, Stamm WE. Amoxicillin-clavulanate vs ciprofloxacin for the treatment of uncomplicated cystitis in women: a randomized trial. *JAMA*. 2005;293(8):949-955. doi:10.1001/jama.293.8.949
4. Rodríguez-Baño J, Alcalá JC, Cisneros JM, et al. Community Infections Caused by Extended-Spectrum β-Lactamase–Producing Escherichia coli. *Arch Intern Med*. 2008;168(17):1897–1902. doi:10.1001/archinte.168.17.1897
5. Salam ME, Jeffres M, Molina KC, Miller MA, Huang M, Fish DN. Evaluation of Oral Amoxicillin/Clavulanate for Urinary Tract Infections Caused by Ceftriaxone Non-Susceptible Enterobacterales. *Pharmacy* (Basel). 2024;12(2):60. Published 2024 Apr 1. doi:10.3390/pharmacy12020060

Created 1.19.26