Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Aminopenicillins for Enterococcal Cystitis: Teaching an Old Dog New Tricks

Enterococcus species are common pathogens for urinary tract infections (UTIs), especially among hospitalized patients.[1] *Enterococcus* infections can be difficult to manage due to intrinsic resistance to multiple antibiotics.[1] Aminopenicillins (i.e. amoxicillin and ampicillin) can achieve high enough concentrations in the urine to potentially overcome resistance. Is it possible to leverage the high urinary concentrations of aminopenicillins to teach an old dog new tricks in the treatment of Enterococcal UTIs?

Aminopenicillin Breakpoints for *Enterococcus* spp. and Urinary Concentrations

Per Clinical and Laboratory Standards Institute (CLSI), *Enterococcus* spp. with an ampicillin minimum inhibitory concentration (MIC) of 16 mcg/mL or higher are resistant to aminopenicillins. This breakpoint is set based on achievable **systemic** concentrations with typical dosing regimens of aminopenicillins.[1]

Aminopenicillins concentrate well in the urine and reach levels that far exceed the MIC range of ampicillin-resistant *Enterococci.* Ampicillin MICs in resistant strains typically range from 64-512 mcg/mL.[1] Contrast that with urinary concentration of 1500-3300 mcg/mL from a single 1 g parenteral dose of ampicillin. Even a **single** 500 mg dose of oral amoxicillin produces urinary concentration of 115-1850 mcg/mL.[1]

Aminopenicillins to Treat *Enterococcus* Cystitis Irrespective of Susceptibilities

Some hospitals no longer routinely test and report antibiotic susceptibilities on Enterococcal isolates in urine culture, but instead display a comment encouraging use of aminopenicillins for treatment of Enterococcal cystitis.[1, 2] In one institution where VRE is mostly ampicillin resistant, clinical cure for VRE UTIs were similar between patients treated with aminopenicillins (82.2%) vs non-aminopenicillins (81.6%), p=0.9.[2] At another site, high clinical cure rate (88%) were seen among patients who received ampicillin for ampicillin-resistant VRE urinary tract infections.[3]

Key Takeaway: Aminopenicillins (ampicillin/amoxicillin) achieve urinary concentrations high enough to overcome resistance and are still a treatment option for Enterococcal **cystitis** irrespective of antibiotic susceptibility testing. Increasing utilization of aminopenicillins for Enterococcal cystitis helps to preserve alternative agents that are broader spectrum, more expensive, or more difficult to administer such as linezolid and daptomycin.

References:

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2. de Oca JEM, Veve MP, Zervos MJ, Kenney RM. Aminopenicillins vs non-aminopenicillins for treatment of enterococcal lower urinary tract infections. *Int J Antimicrob Agents*. 2023;61(6):106800. doi:10.1016/j.ijantimicag.2023.106800.
3. Shah KJ, Cherabuddi K, Shultz J, Borgert S, Ramphal R, Klinker KP. Ampicillin for the treatment of complicated urinary tract infections caused by vancomycin-resistant Enterococcus spp (VRE): a single-center university hospital experience. Int J Antimicrob Agents. 2018 Jan;51(1):57-61. doi: 10.1016/j.ijantimicag.2017.06.008. Epub 2017 Jun 27. PMID: 28666756.