Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Ceftriaxone Guided IV to PO

The Clinical and Laboratory Standards Institute (CLSI) recommends cefazolin, a first generation cephalosporin, as a surrogate for oral cephalosporins in uncomplicated urinary tract infections caused by *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis*.[1] However the CLSI notes that cefazolin may overcall resistance to 2nd and 3rd generation oral cephalosporins such as cefuroxime, cefpodoxime, and cefdinir.[1] In practice, susceptibility testing for specific oral cephalosporins is not often performed. Clinicians may be tempted to use ceftriaxone as a surrogate to predict oral 2nd and 3rd generation cephalosporin activity. Is this safe?

How well does ceftriaxone predict oral 2nd and 3rd generation cephalosporin susceptibility?
In a study of 312 ceftriaxone-susceptible Enterobacterales isolates from clinical blood cultures, susceptibilities to cefuroxime, cefdinir, cefpodoxime, and cefixime were 89%, 86%, 90%, and 94%, respectively.

When inducible AmpC organisms were excluded and only ceftriaxone-susceptible *E. coli*, *K. pneumoniae*, *K. oxytoca* and *P. mirabilis* were examined, 95%, 96%, 92%, and 98% of isolates were susceptible to cefuroxime, cefdinir, cefpodoxime, and cefixime, respectively.[2]

Another study of 88 *E. coli*, *K. pneumoniae*, *K. oxytoca*, *P. vulgaris* and *P. mirabilis* isolates assessed the use of ceftriaxone as a surrogate for cefpodoxime. The categorical agreement rate between ceftriaxone and cefpodoxime was high at 97%.[3]

Key Takeaway: Ceftriaxone susceptibility does not guarantee susceptibility to oral 2nd and 3rd generation cephalosporins, but high agreement (> 90%) has been seen with *E. coli*, *K. pneumoniae*, *K. oxytoca* and *P. mirabilis* isolates. Consult your microbiology lab for oral cephalosporin susceptibility availabilities.

References:

1. Clinical and Laboratory Standards Institute. M100: performance standards for antimicrobial susceptibility testing. 35 ed. 2025
2. Claeys KC, Simner PJ, Tekle T, et al. How accurate is ceftriaxone at predicting susceptibility of enterobacterales isolates to oral higher-generation cephalosporins? *Antimicrob Agents Chemother*. 2025;69(2):e0138724. doi:10.1128/aac.01387-24
3. Lambert KV, Demkowicz R, Murray A, Howard C, Slain D. Ceftriaxone Versus Cefazolin Susceptibility as a Surrogate Marker for Cefpodoxime Susceptibility in Enterobacterales. *Open Forum Infect Dis*. 2024;11(7):ofae377. Published 2024 Jul 3. doi:10.1093/ofid/ofae377

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