Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Know your Antibiotic: Ceftriaxone for MSSA Infections

The ceftriaxone package insert reports activity against various gram-negative and gram-positive organisms including methicillin susceptible *Staphylococcus aureus* (MSSA). Ceftriaxone is commonly dosed once daily for most infections.[1] However, there are efficacy concerns with ceftriaxone for MSSA infections and ceftriaxone has broad gram-negative activity and is a high risk antibiotic for *C. difficile* infection. Does the convenience of ceftriaxone once daily dosing overcome the efficacy concerns?

Does ceftriaxone pharmacokinetic-pharmacodynamic (PK-PD) data support its use for MSSA?

Yes, but **dosing matters.** In a PK-PD simulation study of different cefazolin and ceftriaxone dosing regimens, only ceftriaxone 2 g Q12H was able to achieve reliable bacterial killing against most MSSA isolates. Ceftriaxone 1-2 g Q24H **FAILED** at even being able to achieve bacteriostasis. Comparatively, just cefazolin 2 g every 12 hours predicted extensive killing of MSSA.[2]

What about clinical data on ceftriaxone for MSSA?

Observational data reports mixed outcomes and no prospective clinical trials exist.

✗ A multicenter, retrospective cohort study found increased mortality or recurrence with ceftriaxone (84% receiving 2 g daily) compared with an anti-staphylococcal penicillin (ASP) or cefazolin in the treatment of MSSA bacteremia, despite lower rates of complicated bacteremia in the ceftriaxone group.[3] Another study found higher mortality associated with other beta-lactams including ceftriaxone compared with oxacillin in definitive treatment of MSSA bacteremia.[4] Lastly, a retrospective study in VA patients found increased 90-day treatment failure with ceftriaxone compared with cefazolin.[5]

✓ A retrospective study of patients receiving ceftriaxone 2 g Q24H or cefazolin 2 g Q8H (renally adjusted when needed) post discharge for MSSA bacteremia found no difference in treatment failures. However patients in the ceftriaxone arm were more likely to have MSSA bacteremia secondary to a bone & joint source, while those in the cefazolin arm were more likely to have a line source, pulmonary source, endocarditis, and primary bacteremia.[6] In a meta-analysis of seven studies, no difference in 90-day mortality, recurrence, or readmission was found between patients that received ceftriaxone and cefazolin or ASP for the definitive treatment of MSSA bacteremia.[7]

Key Takeaway: Currently available data suggest potential inferiority of ceftriaxone for severe MSSA infections compared with cefazolin or anti-staphylococcal penicillins, particularly when dosed once daily. Select patients may achieve clinical success with ceftriaxone, but which patients are good candidates remains unknown. Ultimately, ceftriaxone is higher risk for C. *difficile* infection and has broad gram-negative spectrum. Alternatives to ceftriaxone for the treatment of MSSA infections should be used whenever possible.

References:

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Created 11.9.23