Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Why Prolong a Beta-Lactam Infusion?

Traditionally, most intravenous β-lactam antibiotics have been administered via 30 or 60-minute intermittent infusions or push.[1] However, β-lactams achieve maximal efficacy when the time the free drug concentration is above the minimum inhibitory concentration (MIC) is optimized. This pharmacodynamic target is often abbreviated as $fT_{>MIC}$. If high peak concentrations of β-lactams are not needed for maximal killing, are shorter infusions times the best approach?[2]

How does slowing the infusion help?

Beta-lactams achieve optimal killing when the $fT_{>MIC}$ is 50%-70% of the dosing interval. This goal may not be reached with traditional infusion times when the bacterial MICs are elevated or in patients with rapid clearance. Figure 1 illustrates how prolonging the β-lactam infusion time by either administering as an extended infusion (i.e., 3-to-4-hour infusions) or continuous infusion can improve the $fT_{>MIC}$ by blunting the peak.[1] By increasing the time above the MIC, prolonged infusions aim to increase bacterial killing, reduce resistance, and improve clinical outcomes including mortality.[1,2,4]

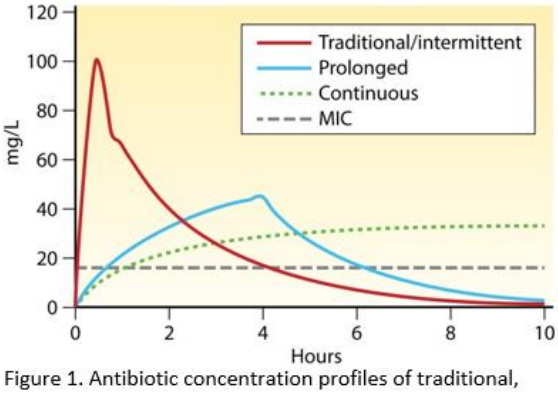

Figure 1. Antibiotic concentration profiles of traditional, prolonged, and continuous infusions[3]

Who should receive prolonged infusions?

Clinical data supporting the use of prolonged infusions is conflicting. Low bacterial MICs, slow clearance, or low severity of illness dilutes the clinical impact of prolonged infusions. Critical illness can lead to pharmacokinetic changes such as augmented renal clearance, higher bacterial inoculum, and greater antimicrobial resistance. Therefore, critically ill patients are more suitable candidates for prolonged infusion.[1,2] The international consensus recommendations for the use of prolonged-infusion β-lactam antibiotics suggests prolonged infusion β-lactams over standard infusion in severely ill adults.[1] Beta-lactams frequently administered as prolonged infusions include antipseudomonals such as piperacillin/tazobactam, cefepime, and meropenem.[1]

Are prolonged infusions easier to administer?

For hospitalized patients, continuous infusions of beta-lactams can present practical challenges due to line dedication. Prolonged infusions can provide needed interruptions to administer other intravenous medications. However, continuous infusions can be an optimal strategy for outpatient antimicrobial therapy as long as the is drug stable.[7]

Key Takeaway: Prolonged infusion β-lactams can increase the chance of achieving optimal antimicrobial killing by increasing the time above the MIC. Not all patients will benefit from prolonged infusions of β-lactams, so use is generally reserved for critically ill patients, infections due to organisms with high MICs, or to facilitate OPAT therapy.

References:

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