Are Prolonged/Continuous Infusions of β-lactams for All?

TO THE EDITOR—We read with great interest the study by Dulhunty et al [1] and the meta-analysis by Falagas et al [2]. Prolonged/continuous (P/C) infusions of β-lactams will soon become, if they are not already, the standard of care. The potential benefits of this approach will be best realized in patients with high APACHE scores, high apparent volume of distribution, normal or high glomerular filtration rate, or infections with high organism burden, and for organisms with high minimum inhibitory concentrations (MICs). However, we believe that certain points need more study and clarification.

It may be important to consider the penetration and maintenance of antibiotic levels at the sites of extravascular infection, especially the “pharmacologically protected” sites. Meningitis, bone, and joint infections may be limitations to this strategy. Besides, antibiotic levels and time above MIC (T > MIC) in the urine may have an inverse relationship with those in plasma. In the meta-analysis by Falagas et al [2], it may be noted that urinary tract infection has been mentioned in only 2 studies and meningitis and bone and joint infections in none.

During P/C infusions of β-lactams, plasma levels gradually rise until a steady state is reached after 4–5 half-lives. Therefore, a loading dose be may be needed before the P/C infusions to ensure a rapid onset of antimicrobial action.

With P/C infusions, we expect plasma levels not to exceed mutant prevention concentration and to be below MIC only for a short period. Therefore, the levels may remain within the mutant selection-window for a longer duration. This would produce an adverse effect on mutant selection by this approach. Notably, 2 resistant strains were isolated during P/C infusions of piperacillin-tazobactam in one of the studies included by Falagas et al. Although the P/C infusion approach would give good results for the infection under treatment, colonizing flora elsewhere in the body would still be exposed to resistance-selecting concentrations. This will therefore not be an effective strategy, as may perhaps be imagined, to curb the development of collateral damage.

Despite these reservations, to watch the development of the concept of optimizing pharmacodynamics/pharmacokinetics from experimental work to clinical application has been exciting [3]. Science usually progresses by a series of small but firm steps rather than by one giant stride. We do hope that this innovative approach will enhance the ability to treat infections.

Note

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References


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