



Clinical use of beta-lactam antibiotics in critically ill patients



Antimicrobials, specifically beta-lactam antibiotics are the most commonly prescribed drugs in the management of critically ill patients. However, pathophysiological factors in these patients can often lead to altered pharmacokinetics and pharmacodynamics of beta-lactams.

While choosing the most appropriate antimicrobial is critical, determining the correct dosage regimen is equally important for successful clinical cure and microbiological eradication. However, with antibiotics, it could take 24 to 72 hours for any signs of resolution of infection thus making it difficult to determine the optimum dosage.

A comprehensive bibliographic search of all articles published from January 2000 to December 2017 that addressed beta-lactam pharmacokinetics or pharmacodynamics was conducted. 214 studies were included in this review.

Antimicrobial activity of drugs is generally assessed by determination of the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of the drug in-vitro. But in-vitro conditions are significantly different from those at the site of infection. Also, these measures do not provide sufficient information on the time course of the antimicrobial effect.

The efficacy of beta-lactam antibiotics is related to $fT > MIC$. Drug concentrations above the MBC do not enhance bacterial killing and the action of the drug is relatively slow. If drug levels fall below the MIC, the residual population can resume growth since beta-lactams have no or only a short post-antibiotic effect. 50% $fT > MIC$ of the dosage interval is required for standard efficacy and 100% $fT > MIC$ of the dosage interval has to be ensured for optimal exposure in immunocompromised patients. Efficacy can be further improved with antibiotic concentrations four to five times greater than MIC.

Several factors may have an impact on the volume of distribution and renal clearance in critically ill patients. The duration of beta-lactam infusion can influence the $fT > MIC$ and an improved pharmacodynamic profile may be obtained by longer exposure with more frequent dosing, extended infusions or continuous infusions.

Extracorporeal support techniques which are also frequently used in critically ill patients can also contribute to this problem. It is recommended that antibiotic dosing should not be reduced since no drug accumulation was found and to maintain continuous or prolonged infusion, especially in patients with infections caused by multidrug-resistant bacteria.

A therapeutic drug monitoring-guided (TDM) approach could prove to be useful in critically ill patients when target concentrations is difficult to achieve. This is true in the case of patients who are obese, immunocompromised, infected by highly resistant bacteria strains, with augmented renal clearance or those undergoing extracorporeal support techniques.

However, more studies are needed to define optimal dosing of new beta-lactams and new beta-lactam/beta-lactamase combinations which are important to treat multi-drug resistant bacterial strains. A beta-lactam TDM approach with daily dose adaptation and personalised dosing can prove to be very useful in critically ill patients.

Source: [Critical Care](#)

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