ICU
MANAGEMENT & PRACTICE

Timing of Antibiotic Therapy in the Intensive Care Unit

Severe infections are common among patients in the ICU. According to findings from the Extended Study on Prevalence of Infection in Intensive Care III (EPIC III), 54% of the study patients had at least one suspected or proven infection on the study day, and 24% of these patients had more than one suspected or proven infection.

These infections are generally either bacterial or fungal in origin and require antimicrobial therapy. In the EPIC III study, infection with *Enterococcus* (VRE), *Klebsiella* species, or *Acinetobacter* species were associated with a higher risk of in-hospital death compared to susceptible microorganisms

Antibiotics are the first line of treatment but are often not optimally administered. The WHO considers antimicrobial resistance a major threat to human health. A Wellcome Trust report suggests that nearly 300 million people will die over the next several decades because of antimicrobial resistance. In the U.S, antibiotic-resistant pathogens cause over 2 million infections and 23,000 deaths per year.

One of the most important determinants of survival among patients with severe or life-threatening infections, including sepsis and septic shock is the timing of antibiotics. Any delay in the administration of antibiotic therapy can impact survival. In addition, the timing of an appropriate antibiotic regimen that is active against the offending pathogen also influences survival. Therefore, early empiric antibiotic administration and selection of the antibiotic are critical for survival. The duration of antibiotic infusions can also influence the efficacy of the drugs.

The choice of agents in ICU patients is often based on the site of infection, clinical severity and patient comorbidities. An important element for guiding appropriate empirical therapy is identifying risk factors for infection with multidrug-resistant bacteria (MDRB). Antibiotic therapy that is too broad is associated with poor outcomes. Several factors can help clinicians guide the use of broad-spectrum therapy. Conditions that can influence risk for MDRB infection include recent hospitalisation, prior antibiotic exposure, hospital or healthcare-associated infection, known colonisation with MDRB pathogens and local hospital and ICU epidemiology.

A combination antibiotic regimen can help provide appropriate coverage. However, the beneficial effect of dual antibiotic therapy is debated and is most useful in neutropenic patients and infections due to *Pseudomonas aeruginosa.*

Delayed antibiotic therapy is associated with increased mortality in patients with invasive fungal infections. Guidelines recommend initiation of empirical antifungal therapy but deciding which subgroup of patients requires prompt empirical treatment remains a challenge. Clinicians should make sure to reassess the need for antifungal therapy 72-96 h after starting treatment to permit early discontinuation of therapy when needed.

Antimicrobial de-escalation (ADE) refers to the early modification of empiric antimicrobial therapy to prevent antimicrobial resistance by decreasing the overall exposure to broad-spectrum agents. ADE is proven to be a safe and effective strategy and is feasible to carry out for both bacterial and fungal infections. However, the overall utilisation of de-escalation remains low. Clinicians should try to routinely carry out ADE to better guide antibiotic theory and optimise clinical outcomes.

Source: Critical Care

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