

Outcomes demonstrate why empirical antimicrobial therapy should be appropriate

Professor Wang-Huei Sheng, reviewing Bassetti M, *et al. Int J Antimicrob Agents* 2020; **56**: 106184, published online 9 October 2020.

Systematic review confirms the positive impact of appropriate versus inappropriate initial antibiotic therapy on multiple outcomes for patients with severe bacterial infections

The adverse consequences of using inappropriate compared with appropriate antimicrobial therapy have generally been observed in studies of specific outcomes conducted in selected subgroups of seriously ill patients. A study in Taiwan, for example, found that appropriate therapy given in the emergency room significantly reduced the 28-day mortality of patients with bacteraemia compared with inappropriate therapy or no therapy, and the difference was more marked in those who were critically ill (1).

In a recent systematic review and analysis, Bassetti and colleagues assessed the impact of appropriate versus inappropriate initial antimicrobial therapy for hospitalised patients with a range of community- and hospital-acquired severe bacterial infections (2). Data from 114 studies reporting comparisons of initial therapy were analysed and pooled for outcomes including mortality, hospital length of stay (LOS) and treatment failure. The definition of appropriate antibiotic therapy varied between studies, but usually included therapy to which the pathogen was susceptible and could also specify appropriate dosing or concordance with guidelines. Overall and at the majority of time points, mortality rates were significantly lower with appropriate therapy than with inappropriate therapy (odds ratio [OR] 0.44, 95% confidence interval [CI] 0.38 to 0.50). Rates of treatment failure were significantly reduced in patients receiving appropriate therapy compared with inappropriate therapy (OR 0.33, 95% CI 0.16 to 0.66), including in patients with urinary tract infection or acute pyelonephritis, bacteraemia or sepsis. Appropriate therapy was also associated with shorter duration of antibiotic treatment, higher rates of clinical cure and shorter LOS compared with inappropriate therapy.

Comment

Numerous investigations and analyses have identified the association between inappropriate empirical antibiotic therapy for severe infections and poor patient outcomes. The strength of the report by Bassetti *et al.* (2) is the evaluation of findings on multiple outcomes, including mortality rate, treatment failure or success, rate of clinical cure, hospital LOS and hospital costs, across a range of severe infections. The report notes the importance of effective broad-spectrum empirical antibiotic therapy, which should consider clinical management guidelines, local resistance epidemiology and patient risk factors, and be followed by subsequent de-escalation to targeted treatment as soon as possible. In a separate systematic review and analysis, the same authors found an approximately 20% higher risk of in-hospital mortality or discharge to hospice among patients who experienced delayed treatment with appropriate antibiotics compared with those who did not, regardless of the antibiotic susceptibility of the causative pathogen (3). Thus, for patients with severe bacterial infections, who are often critically ill, early initiation of effective broad-spectrum empirical therapy is paramount. De-escalation to targeted treatment can follow upon characterisation of the causative pathogen, which may take 2–3 days. In many settings, this highlights the continued need for rapid diagnostics and will remain a challenge until real-time molecular tests and point-of-care diagnostics become more widely accessible.

References

1. Lee CC, *et al.* Impact of inappropriate empirical antibiotic therapy on outcome of bacteremic adults visiting the ED. *Am J Emerg Med* 2012; **30**: 1447–56.
2. Bassetti M, *et al.* Systematic review of the impact of appropriate versus inappropriate initial antibiotic therapy on outcomes of patients with severe bacterial infections. *Int J Antimicrob Agents* 2020;**56**:106184.
3. Zasowski EJ, *et al.* A systematic review of the effect of delayed appropriate antibiotic treatment on the outcomes of patients with severe bacterial infections. *Chest* 2020;**158**:929–38.