

Clinical issues of infections due to multidrug-resistant Enterobacteriaceae

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After controlling for usual confounders, multidrug-resistant (MDR) bacteria are associated with worse outcomes. This may be due to any of these reasons or their combinations: increased virulence (which is rarely proved), delayed appropriate therapy (because the probability of prescribing inappropriate empirical antimicrobial therapy is increased), and diminished efficacy or increased toxicity of available second-line drugs. In the case of Enterobacteriaceae, invasive infections caused by ESBL-producers have been shown to be associated with increased mortality; we may assume that the effect is similar for isolates producing other mechanisms of resistance. Infections caused by MDR-E occur more frequently in predisposed patients, as those with underlying diseases, admitted to healthcare centres or undergone invasive procedures, and who had recently received antimicrobial treatment, but may also happen increasingly in healthy patients with community-acquired infections. Thus, in front of patients with serious infections, clinicians frequently need to decide between the empirical use of very broad spectrum antimicrobials (and even second-line drugs) to cover MDR-E, or to reserve them in order to avoid further spread of resistance. Several clues may help in this decision making-process. First, pre-test probability may be estimated in base of local prevalence of antibiotic resistance. Second, evaluation of the individual risk factors for MDR-E may help to identify patients with lower or higher risk for infections caused by these organisms (post-test probability). And third, a careful assessment of the severity of acute disease and systemic inflammatory response syndrome would help to identify patients in which appropriate empirical therapy is an absolute priority. In the absence of randomised clinical trials, decisions for empirical therapy, de-escalation strategies, and use of alternative agents in different situations need to be based on a deep knowledge on the available microbiologic data, PK/PD models, and clinical studies. It follows that management of acute infections in the 21st century demands a certain degree of super-specialisation for performing an adequate and timely clinical work-up, correctly identifying the potential source of infection and severity, and the specific determinants that modify the potential risks, aetiologies and antimicrobial susceptibility, so that the decisions about antimicrobial therapy can be optimised.