Bugging the Bugs: Novel Approaches in the Strategic Management of Resistant Staphylococcus aureus Infections

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Antibiotic resistance across multiple organisms represents an alarmingly increasing trend [1]. In 2004, nearly 2 million people in the United States were estimated to have acquired infections while hospitalized, of whom an estimated 90,000 died [2]. More than 70% of the bacteria that caused these infections were resistant to ≥1 of the drugs commonly used for their treatment. Not surprisingly, the total cost of antimicrobial resistance to US society is significant, approaching $5 billion annually, a figure that captures the increased costs associated with treating drug-resistant nosocomial infections [3]. The Infectious Diseases Society of America cites the need for new antibiotics to combat the new resistant bacterial “superbug” infections [3]. Therefore, new antibiotics that offer better coverage, lower resistance potential, and improved adverse-effect profiles provide hope for treating resistant infections and for keeping the incidence of resistance in check.

In the United States, ∼60% of staphylococcal infections in inpatients are now caused by (generally multidrug-resistant) methicillin-resistant Staphylococcus aureus (MRSA), and the percentages continue to rise [4]. Interestingly, along with the trend of increasing numbers of health care-associated MRSA (HA-MRSA) infections, community-associated MRSA (CA-MRSA) infections are also on the increase, and CA-MRSA is typically more susceptible to a wider range of antibiotics than is HA-MRSA [5]. Until recently, pathogens causing nosocomial infections have been described as being different from those associated with community-acquired infections. Infections acquired in an outpatient setting are frequently considered to be due to CA-MRSA and are treated as such, but MRSA strains isolated from health care–associated settings were distinct from true CA-MRSA and had different susceptibility to antibiotics [6]. More recently, there has been increased intermingling of these organism populations, such that their epidemiological profiles are no longer distinct, and MRSA strains with molecular characteristics of CA-MRSA have emerged in hospitals and caused serious nosocomial infections [7]. To optimize patient outcomes, it is important that the antibiotic therapy employed is right the first time, and this highlights the importance of appropriate selection of empirical therapy.

Appropriate initial antibiotic therapy must be active against the pathogens causing the underlying infection in order to optimize clinical outcomes and to decrease the incidence of developing resistant strains. A de-escalation approach starting with broad-spectrum antibiotics that offer sufficient coverage of the suspected infection is recommended. De-escalation involves decreasing the number and/or spectrum of antibiotics on the basis of the culture and drug susceptibility test results, shortening the duration of therapy in patients showing clinical improvement, and discontinuing antibiotic therapy once a noninfectious etiology has been identified [8]. Patients with risk factors for health care–associated infections (e.g., recent hospitalization, admission from a nursing home, prior antimicrobial administration, and immunosuppression) should initially be empirically treated for infection due to antibiotic-resistant pathogens [9]. This will increase the likelihood that appropriate initial therapy is administered. De-escalation can follow on the basis of the identified organisms and their antimicrobial susceptibilities.

Formal protocols and guidelines can help to stabilize antibiotic susceptibility patterns. In its campaign to minimize antimicrobial resistance in health care settings, the Centers for Disease Control and Prevention has put forth a 12-step guideline highlighting prevention measures, appropriate use of antimicrobials, targeting of the pathogen, use of local susceptibility data, minimization of vancomycin use, and health care hygiene [10]. In spite of the availability of formal guidelines and educational materials directed toward the appropriate use of antibiotics, initial in-
appropriate antibiotic treatment of MRSA infection is common. In a recent publication by Schramm et al. [11], ~1 in 3 MRSA-infected patients was found to have initially received inappropriate antibiotic treatment, which doubled the risk of mortality. In a related article, Shorr et al. [12] emphasized the need to update clinicians about the changing approach to antimicrobial therapy, specifically in hospital-acquired resistant infections, such as MRSA infection.

This supplement to Clinical Infectious Diseases brings together a multidisciplinary group of infectious diseases specialists and thought leaders in pulmonology, critical care medicine, clinical microbiology, and clinical pharmacy to provide a critical evaluation and analysis of current practices in the treatment and management of MRSA infection. The articles in this supplement highlight several key issues in the management of challenging nosocomial infections, including (1) clinical microbiological aspects of MRSA and vancomycin nonsusceptibility; (2) improvements in detection methods; (3) the relative virulence of CA-MRSA and HA-MRSA; (4) the epidemiological profile and consequences of resistant Staphylococcus aureus infections; (5) risk factors for MRSA infections; (6) adequate utilization of antibiograms; (7) principles of antibiotic therapy for challenging nosocomial infections, taking into account the microbiological and clinical data; (8) the importance of early and appropriate empirical antibiotic therapy in maximizing optimal outcomes and minimizing development of resistance, (9) the limitations of vancomycin in the treatment of MRSA infections, (10) the relationship of pharmacokinetics and pharmacodynamics in therapeutic success with antibiotic treatment, and (11) novel antibiotics with promising efficacy and excellent adverse-effect profiles for empirical therapy for MRSA infections. The objective of this supplement and educational activity is to improve clinician identification and management of infections due to resistant staphylococci, thereby optimizing clinical outcomes.

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References


