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EDITORIAL

Trends in antimicrobial resistance

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The problem of increasing resistance to antimicrobial agents is of concern to the medical community and to public health. Just 60 years after the commercial release of penicillin, increasing rate of antimicrobial resistance among bacteria have reduced the usefulness of an array of antimicrobial agents (1). Most troublesome is the trend of increasing resistance to newer antibiotics, including those previously regarded as "drug of last resort". Antibiotic-resistant strains of Staphylococcus aureus, Enterococcus faecium, Streptococcus pneumoniae, Klebsiella pneumoniae, Enterobacter species, pseudomonas aeruginosa, Acinetobacter species, and even Escherichia coli are significant causes of infection in both hospitals and the community (1).

In Iran, an effective strategy to eliminate the effect of multidrug resistance has been initiated and focused on education of physicians and patients to consume antimicrobial agents appropriately. Other activities are; use of effective infection control practice to prevent being transmitted from an infected individual, surveillance of antimicrobial resistance, and antimicrobial use. Data from Shiraz showed that the threat of increasing resistance to antimicrobial agents is a great health concern in Iran (2). A recent shift in the epidemiological profile of methicillin-resistant Staphylococcus aureus (MRSA) has resulted not only in health care associated infection, but also, now, it is a community-associated infection.

Reports of multidrug resistance in Pseudomonas aeruginosa is increasing while carbapenem-resistant Klebsiella strains are emerging. Acinetobacter species cause a significant health care-associated illness in intensive case setting in Iran, but a growing proportion is resistant to third generation cephalosporins and carbapenem. Most carbapenem derivatives are expensive and poorly available all around the country. The presence of these resistant organisms could limit the number of available effective antimicrobial agents.

A multifaceted approach to the reduction of antimicrobial resistance in hospitals emphasizes infection-control measures, but it often includes guidelines on antimicrobial use (e.g. promotion of the use of narrower-spectrum agents, shorter courses of therapy, and reduction of empirical therapy) and formulary restrictions on the use of certain broad-spectrum agents. Conversely, recent evidence suggests that prompt use of potent broad-spectrum agents may reduce morbidity, mortality, and health care-associated costs of infection. For instance, in a prospective cohort study of 492 infected patients who required admission to an intensive care unit, Ibrahim et al. found that inappropriate initial antimicrobial therapy was an independent determinant of in-hospital mortality among patients with blood-stream infections (adjusted OR=6.86, $p<0.001$) (3).

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The selection of antimicrobial agents is a fact of daily life for clinicians, hospital epidemiologists, microbiologists, pharmacologists, and others. Optimizing the outcome for an individual patient by administering empirical broad-spectrum antibiotic therapy appears to conflict with the goal of minimizing the emergence of resistance.

Gram-positive organisms

During the past 3 decades, MRSA has created significant epidemiological, infection-control, and therapeutic management challenges. According to data from National Nosocomial Infection Surveillance (NNIS) System of the CDC, the prevalence of MRSA in ICUs almost doubled (from 36% to 62%) between 1992 and 2002 (4). Although in the 1980s, there was a definite stepwise increase in the rate of methicillin resistance among S. aureus, according to the hospital size (5), this is no longer the case, with similar rates now observed in small community hospitals and large medical centers (4).

The increasing prevalence of MRSA in hospitals has led to the increase use of vancomycin for treatment (6). Although vancomycin remains the active agent against the majority of MRSA strains, infections caused by vancomycin-nonsusceptible S. auereus have been reported (7-9).

Although rates of resistance appear to be stable in ICUs, VRE (vancomycin-resistant entrococci) may be emerging as a cause of occasional infection in new patient population, such as patients receiving hemodialysis and patients in pediatric hematology/oncology departments (10,11).

Multidrug-resistant gram-negative bacteria

Most attention to the emergence of antimicrobial-resistant bacteria in hospitals has been focused on gram-positive organisms for which new antimicrobial agents Results: available for treatment. In contrast, less attention has been focused on emerging multidrug-resistant gram-negative organisms, for which there is a current need for new antimicrobials for treatment (12). For instance, data collected between 1994 and 2002at one tertiary care center in the United States not only showed the emergence of multidrug resistant Pseudomonas aeruginosa (prevalence, 1-16%) but also showed the emergence of multidrug-resistant Klebsiella species (prevalence, 0.5-17%) (13). The most common resistance pattern was coresistance to quinolones, third-generation cephalosporins, and aminoglycosides. Related trends in resistance among P. aeruginosa have been observed in the national NNIS database. Among P. aeruginosa isolates recovered from ICU patients in 2003, the overall rate of resistance to crbapenems was 20% and that of resistance to third-generation cephalosporins and quinolones was about 30%. Acetinobacter baumannii has emerged worldwide as an important pathogen in hospitalized patients, causing high mortality rates. the organism can cause many infections, including pneumonia, bacteremia, meningitis, urinary tract infection, and skin and soft tissue infections (14).National data from NNIS indicate that the prevalence of Acetinobacter organisms among gram-negative pathogens causing pneumonia in ICU has increased from 4.2% in 1986 to 7% in 2003, with resistance to imipenem (increase in prevalence, from 0% to 42%) and ceftazidime (increase in prevalence, from 18% to 68%) increasing substantially during the same period.

In conclusion, an effective strategy to limit the effect of multidrug resistance must be multifaceted and must include education of physicians and patients about appropriate antimicrobial use, use of effective infection-control practices to prevent transmission from infected to uninfected patients, surveillance of antimicrobial resistance and antimicrobial use, improved use of immunization, and development of alternative therapies that may, in some cases, circumvent the need for antimicrobial therapy.

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