抗微生物製劑之分類、使用及抗藥性

Classification, application, and drug resistance of antimicrobial agents

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Antimicrobial agents have been greatly important cornerstones of clinical medicine since the second half of the 20th century and have saved a great number of people from life-threatening bacterial infections. However, the bacteria world is in a state of constant evolution and change. In combination of dwindling antibiotic development and progressive antimicrobial resistance cause the difficulty of management of infectious diseases. On 30 April 2014, WHO announced that antimicrobial resistance is a global problem with serious threat to public health. The factors of increasing antibiotic resistance are quite complicated. The common causes include increased severity of illness, more severely immunocompromised patients, newer devices and procedures, resistance in the community, ineffective infection control and compliance, and increased prophylactic, empiric antibiotic use. The impact of antimicrobial resistance may increase the length of hospital stay, mortality and healthcare costs.

The current major antimicrobial resistance regarding gram-positive bacteria includes MRSA (methicillin-resistant *Staphylococcus aureus*), VRE (vancomycin resistance Enterococcus) and *S. aureus* and Penicillin-and cefotaxime-resistant pneumococci. The risk factors for colonization or infection with MRSA in hospitals include prior antibiotic exposure, admission to an intensive care unit (ICU), surgery and exposure to an MRSA-colonized patient. According to the TNIS (Taiwan Nosocomial Infections Surveillance System) reports, the prevalence rate of MRSA in healthcare-associated infections of medical center ICUs had decreased from 83.4% in 2005 to 72.5% in 2014. However, there are increasing reports of community-acquired MRSA infections in Taiwan, especially among soft tissue infections which make the treatment more complicated. Furthermore, we also notice the clinical MRSA isolates had become less susceptible to vancomycin in recent years. The clinician should be careful about the MIC of isolated MRSA. When the MIC of MRSA was over 1 µg/mL, the successful rate of vancomycin treatment for MRSA bacteremia would largely decrease from 55.6 % to 9.5% (MIC ≤0.5 vs. MIC ≥1) according a literature report. The drug choices of MRSA for glycopeptide failure cases may include daptomycin, linezolid and tigecycline. VRE is also an important worldwide resistance issue and most of the isolated species was *Enterococcus faecium.* Because of Enterococcus being an important pathogen of healthcare-associated infections makes

the situation worse. The prevalence rate of VRE in healthcare-associated infections of medical center ICUs, Taiwan, had reached 31.2 % in 2014 according to TNIS report. The current major antimicrobial resistance regarding gram-negative bacteria include extended-spectrum β-lactamases (ESBL), fluoroquinolone resistance, and carbapenem resistance: *Pseudomonas aeruginosa*, *Acinetobacter spp.* and Enterobacteriaceae. ESBL is due to a ß-lactamase that hydrolyses broad-spectrum cephalosporins (include 3rd cephalosporins). Most of isolated pathogens of ESBL were *Enterobacteriaceae spp.*, especially *Escherichia coli* and *Klebsiella Pneumoniae*. ESBL was majorly a plasmid mediated resistance and makes the 3rd cephalosporins ineffective to the treatment of the isolated pathogens. According to SMART study, ESBLs is quite prevalent in Asia/Pacific areas compared to other continents. The main drug of choice for ESBLs was carbapenems. Another important issue of gram negative resistance was carbapenem resistance among *Pseudomonas aeruginosa*, *Acinetobacter spp.* and Enterobacteriaceae. Since carbapenems are the last stronghold of defense against gram negative pathogens, the increase in carbapenem resistance will be a major threat in the future. Carbapenem resistance Enterobacteriaceae (CRE) is an important emerging issue in Taiwan. The prevalence rate of carbapenem resistance *K. pneumoniae* (CRKP) in healthcare-associated infections of medical center ICUs, Taiwan, had increased from 1.8% in 2005 to 13.6% in 2014. The prevalence rate of Carbapenem resistance *Acinetobacter baumannii* (CRAB) in healthcare-associated infections of medical center ICUs, Taiwan, had also increased from 25.9% in 2005 to 64.9% in 2014. Since most clinical isolated CRAB was resistant to most available antimicrobial agents, the treatment for serious CRAB infection is very challenging to the clinicians. In conclusion, physicians should be aware of the current epidemiological status of resistance and understand the appropriate use of antimicrobial agents in clinical practice.