



Symposium 3.3

Antibiotic Therapy of Staphylococcal Infections in the Era of Resistance

Visanu Thamlikitkul MD

Department of Medicine, Faculty of Medicine
Siriraj Hospital, Bangkok, Thailand

Antimicrobial resistance among staphylococci has been increasing during the past several decades. Vancomycin, an antibiotic in glycopeptides, has always been considered the treatment of choice for methicillin-resistant *Staphylococcus aureus* (MRSA) infections. However, vancomycin is facing several challenges in therapy of staphylococcal infections. *S. aureus* isolates with reduced susceptibility or full resistance to vancomycin are emerging. Treatment of *S. aureus* infections with vancomycin is at times associated with clinical failure, prolonged duration of bacteremia, higher relapse rates of infections, and worse clinical outcomes. The alternative antimicrobial agents for infections caused by resistant staphylococci include arbekacin, quinupristin/dalfopristin, linezolid, daptomycin and tigecycline.

Arbekacin is an aminoglycoside antibiotic that has a dose-dependent bactericidal action.

It is active against most isolates of MRSA. Arbekacin alone or arbekacin combined with other antibiotics (fosfomicin, imipenem, minocycline) is moderately effective in therapy of MRSA infections in Japan. Arbekacin is administered by intravenous infusion of 200 mg per day divided into 2 doses. The side effect of arbekacin is nephrotoxicity.

Quinupristin-dalfopristin is a combination of streptogramins. This combination is synergistic and bactericidal. Quinupristin-dalfopristin is active against a wide variety of multidrug-resistant gram-positive organisms, including MRSA. Quinupristin-dalfopristin is effective in therapy of complicated gram-positive skin and skin structure infections comparable to cefazolin, oxacillin, and vancomycin; and in the treatment of catheter-related bacteremia caused by *S. aureus* or coagulase-negative staphylococci. The recommended dosage for complicated skin and skin structure infections is 7.5 mg per kg given intravenously every 12 hours. The most common adverse effects are pain and inflammation at the infusion site.

Linezolid is the first agent in oxazolidinone compounds. Oxazolidinones are totally synthetic compounds. Linezolid has excellent in vitro activity against gram positive organisms including MRSA. The bioavailability of linezolid is 100% when given orally. Linezolid is approved for the treatment of pneumonia and complicated skin and soft tissue infections caused by *S. aureus*. Linezolid has also been demonstrated to be effective in infective endocarditis and bone and joint infections. Linezolid at a dosage of 600 mg every 12 hours is recommended for treatment of serious infections in adults. Thrombocytopenia and myelosuppression are major side effects of linezolid therapy. These side effects are time- and dose-dependent, and reversible.

Daptomycin is a cyclic lipopeptide drug. It has a unique but not fully understood mechanism of action. It is active against some gram positive bacteria including MRSA. Daptomycin is effective in skin and soft tissue infections caused by *S. aureus* comparable to vancomycin and semisynthetic penicillins. A clinical study of treatment of right-sided endocarditis/bacteremia due to *S. aureus*, using a once daily dose of daptomycin for 14-28 days, is being conducted. The recommended dose of daptomycin is 4mg/kg IV once daily. The commonly reported side effects are elevation of CPK and myopathy.

Tigecycline is a semisynthetic glycycline. Tigecycline is bacteriostatic. Tigecycline is a broad-spectrum antimicrobial agent. It is highly active against most gram positive organisms including MRSA, gram negative bacteria (excluding *P. aeruginosa*, *Proteus* spp.) and anaerobes. Tigecycline is currently approved for the treatment of patients with complicated skin and skin-structure infections and complicated intra-abdominal infections. Tigecycline was also effective in community-acquired pneumonia. A study on therapy of MRSA infections by tigecycline was reported to be satisfactory. Tigecycline is administered via intravenous infusions for 30 to 60 minutes. The initial dose is 100 mg followed by 50 mg every 12 hours. The most common side effects of tigecycline are nausea and vomiting. Both are mild or moderate and usually occur during the first few days of therapy.

Many strains of community-associated *S. aureus* (CA-MRSA) are susceptible to co-trimoxazole, fusidic acid, fluoroquinolones, clindamycin. Therefore, the infections caused by such isolates could be treated with aforementioned oral antibiotics.

Other new antimicrobial agents, such as ceftobiprole and dalbavancin, for therapy of staphylococcal infections are being developed.