SUSCEPTIBILITY OF STAPHYLOCOCAL BIOFILMS TO MULTIPLE COMBINATION OF ANTIMICROBIALS

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Background. Staphylococcus epidermidis and Staphylococcus aureus are the most common pathogens associated with infections of surgical implants and other prosthetic devices. These organisms have been shown to form in vivo biofilms on implanted devices. Standardized susceptibility testing fails to predict in vivo resistance of Staphylococcus spp.-related infections to antimicrobials. Antimicrobial therapy is guided by the results obtained from conventional antimicrobial testing of planktonic (free-growing) bacteria. However, this may not necessarily reflect the susceptibilities of these same bacteria when they are grown as biofilms. Biofilm associated bacteria are 100 to 1,000 times less susceptible to antibiotics than are planktonic bacteria, and agents active against planktonic bacteria, but not against biofilms, fail to cure patients with infected prostheses.

The objective of this study was to compare susceptibilities of planktonic and biofilm-grown bacteria to single antibiotics and to combinations of antibiotics in order to identify antibiotic combinations that were effective against staphylococci retrieved from nosocomial infections. It was hypothesized that biofilm-grown bacteria would demonstrate greater resistance to single and combination antibiotics compared to the same bacteria grown under planktonic conditions.

Bacterial strains. In this work Staphylococci isolates associated with hospital infections were obtained from the clinical microbiology laboratories of Kharkov city (usually, from the bacterial museum of I. Mechnikov memorial Inst.Microbiol.Immunol.). Preference was given to isolates recovered from the local site of infection or the device itself. Blood culture isolates from patients with clinically defined line sepsis were also used. Staphylococci were identified by colonial morphology, Gram stain, and coagulase testing. Methicillin-resistant S. aureus (MRSA) was further confirmed by coagulase testing and growth on oxacillin salt agar screen plate. In total, 10 isolates of S. epidermidis, 4 isolates of methicillin-sensitive S. aureus (MSSA), and 6 isolates of methicillin-resistant S. aureus (MRSA) were obtained and studied.

Antibiotics. Antibiotics tested were azithromycin (Pfizer, Zetamax), cefazolin (Arterium), ciprofloxacin (Arterium), fusidic acid (Arterium), gentamicin (KMP), linezolid (Pfizer), teicoplanin (Aventis Pharma), rifampin (KMP), and vancomycin (Sigma). Interpretation criteria for susceptibility testing were based on NCCLS, now CLSI guidelines.

Results. We assessed agents and combinations of antimicrobials against isolates of S. epidermidis and S. aureus retrieved from medical devices and instruments. Isolates were grown planktonically and as biofilms. Biofilm cultures of the organisms were found to be much more resistant to inhibitory and bactericidal effects of single and combination antibiotics than planktonic cultures ($P < 0.001$). Rifampin was the most common constituent of antibiotic combinations active against staphylococcal biofilms. Other frequently effective antimicrobials were vancomycin and fusidic acid.

Conclusion. Susceptibility testing involving biofilm-associated bacteria suggests new options for combination antibiotic therapy.