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Synergistic effects of combinations of antibiotics on coagulase negative staphylococcal (CoNS) biofilms

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Background. Previous studies examining synergistic effects of antibiotics against CoNS biofilms often relied on drug concentrations higher than the peak serum (PS) concentration, as determined by MIC assays, therefore having little clinical applicability. Other studies investigated synergistic effects of a wide range of antibiotics, however many are not routinely used in a clinical setting. Dicloxacillin is the major antibiotic used in Portugal to treat staphylococci infections, and we evaluated the synergistic effect of antibiotics with different mechanisms of action combined with dicloxacillin and other cell wall synthesis inhibitors.

Methods. We used combinations of 5 antibiotic agents (cefazolin, vancomycin, dicloxacillin, tetracycline and rifampicin) at the PS concentration of each agent, and evaluated the killing rate over a 24 h period using biofilms made by 10 CoNS clinical isolates. Results from all of the assays were compared using ANOVA.

Results. Among all of the combinations tested there was an increase in the killing rate of the antibiotics when compared to the killing rates when only one antibiotic was used. However, only the combination of dicloxacillin with rifampicin resulted in a true synergistic effect for most CoNS strains. When tetracycline was used in combination with any other antibiotic, a decrease in the killing rate was obtained.

Conclusions. Our results indicate that dicloxacillin could be useful against CoNS biofilms when combined with a small amount of rifampicin (10 µg/ml). Antibiotics highly effective against planktonic cells, like vancomycin, were minimally effective against cells in biofilms, even after adding more antibiotics with distinct mechanisms of action. Also, except for dicloxacillin, adding more antibiotics to the biofilm did not result in an increase in killing efficiency, and there were even antagonistic in some instances. Screening for synergistic effects of different combinations of antibiotics might be a useful tool to determine a therapeutic approach to infections involving CoNS biofilms.