Lack of Synergy With Six Blood Isolates of MRSA (Vancomycin MIC of 2) Tested with Combinations of Vancomycin + Gentamicin, Vancomycin + Rifampin and Vancomycin + Cefazolin

Virginia Long, Paul O’Keefe, Paul Schreckenberger, Departments of 1Medicine, 2Pathology, and 3Infectious Disease and Immunology Research Institute, Stritch School of Medicine, Loyola University Chicago

ABSTRACT

Background: Vancomycin (V) is the mainstay for treatment of infections caused by MRSA. Yet failures of therapy with V are common. Current guidelines recommend V alone for treatment of infections caused by MRSA. Yet failures of therapy with V are associated with the presence of resistance factors. Our purpose was to determine whether antibiotic synergy could be achieved with V in combination with various antibiotic agents.

Methods: We used time kill-curves to test antibiotic combinations used in our center against six isolates of MRSA. These six with V MICs of 2 confirmed by Microscan and E test were chosen from 15 blood isolates of MRSA saved over three years. We used V and gentamicin (G), V and rifampin (R), two combinations used to treat MRSA, and V and cefazolin (C), a combination recommended in recent publications. Colonies were counted in duplicate at 0, 24, 48, 72 and 124 hours.

RESULTS

Multiple antibiotics are used in various combinations to treat MRSA, such as aminoglycosides, rifampin, tetracycline, vancomycin and β-lactams. A survey of 400 Infectious Disease Consultants (CDC), revealed that in the case of persistent MRSA bacteremia with vancomycin MIC 2µg/ml, 72% of the IDDs would continue vancomycin but add an additional drug, typically rifampin or gentamicin (1). The in vitro pharmacodynamics of vancomycin and cefazolin against MRSA were studied in 24h time kill experiments. The results show that both significantly reduced the bacterial concentration of MRSA when compared to vancomycin alone after 24h of incubation.

MATERIALS AND METHODS

Bacterial Strains: The six isolates used were chosen from 1500 staphylococcal isolates collected over 3 years by the clinical microbiology laboratory at Lurmc and stored at -80°C. The strains chosen for further study were MRSA blood isolates with MICs of 2 confirmed by both Microscan and E test.

Antibiotics: The antibiotics and concentrations used were vancomycin (10µg/ml), gentamicin (1µg/ml), rifampin (1µg/ml), and cefazolin (1µg/ml). Stock solutions of the antibiotics were obtained from Sigma-Aldrich (St. Louis, MO) and were prepared in sterile water or sterile water containing 0.05% Tween 80 (DMSO) (rifampin). The combinations used were vancomycin + gentamicin + rifampin or vancomycin + cefazolin.

Combination: No antibiotic tube (NA) served as the control for each experiment, and as a growth control for each strain. Drug X was gentamicin, rifampin, or cefazolin and sulfated gentamicin stock, 2x of rifampin stock, and 15x of cefazolin were used to achieve the desired concentrations in each tube. Colony counts were performed from each tube at the following time points: 0.4, 8, 12, 24 hrs.

Our results show that combining gentamicin, rifampin or cefazolin with vancomycin against six strains of MRSA with vancomycin MIC of 2µg/ml, is not synergistic in vitro. Enhanced killing with vancomycin + gentamicin was shown in three strains, and with vancomycin + rifampin in one strain. Kiling with vancomycin + rifampin was worse than both antibiotics alone in four strains, and achieved antagonism in one of those strains. These results, although not demonstrating synergy may support the use of vancomycin + gentamicin, but do not support the use of vancomycin + rifampin or vancomycin + cefazolin for treatment of MRSA infections.

DISCUSSION/CONCLUSION

References


Paul C. Schreckenberger, Ph.D.
2160 S. First Ave. Maywood, Illinois 60153
Email: P скаrecken@lurmc.edu
Phone: 1-708-216-5682