Bactericidal Activities of New Quinolones WCK 771 A, WCK 919, and Its Two Isomers WCK 1152 and WCK 1153 against Vancomycin Resistant Staphylococcus aureus (VRSA)

Bülent Bozdogan & Peter C. Appelbaum
Penn State Milton S. Hershey Medical Center, Penn State College of Medicine, Hershey, Pennsylvania

ABSTRACT

A vancomycin-resistant Staphylococcus aureus was isolated September 2002, Hershey, Pennsylvania.

OBJECTIVE

To determine the quinolone resistance mechanisms in VRSA and to test the MICs and time kill activities of two isomers of WCK 919, WCK 1152 and WCK 1153 against VRSA compared to the parent WCK 919, WCK 771 A ciprofloxacin, levofloxacin, gatifloxacin and moxifloxacin.

METHODS

DNA from VRSA was isolated and used for amplification of gyrA, gyrB, grlA, and grlB from the VRSA strain. Antibiotic susceptibility was determined by a dilution method prescribed NCCLS (11) and time-kill studies were performed as described previously (12). Bacitracin MIC were analyzed by determining viable counts (2 x MIC ≥ 3 log10 cfu/ml)

RESULTS

• Aspartic acid to asparagine at codon 83
• Cysteine to arginine at codon 302

• The vancomycin and teicoplanin MICs of VRSA-Hershey were 32 and 4 µg/ml, respectively (Table 1).

• Available fluorquinolones, moxifloxacin (4 µg/ml), gatifloxacin (9 µg/ml), levofloxacin (32 µg/ml) and ciprofloxacin (>4 µg/ml) were not active against VRSA-Hershey strain (Table 1).

• MICs of gatifloxacin and quinolones against VRSA-Hershey strain

• Bactericidal activities of new quinolones WCK 771 A, WCK 919, and its two isomers WCK 1152 and WCK 1153 against VRSA-Hershey

CONCLUSIONS

• The VRSA strain was resistant to currently available quinolones.

• The experimental quinolones, WCK 771 A and WCK 1153 had MICs ≤ 2 µg/ml against VRSA together with bactericidal activity.

• VRSA mutants S84L in GyrA and E47K in GyrB do not have adverse impact on the potency.

REFERENCES


