

Minimal inhibitory concentrations and minimal bactericidal concentrations of quinupristin/dalfopristin against clinical isolates of *Corynebacterium jeikeium* and *Listeria monocytogenes*

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Thirty clinical isolates of *Listeria monocytogenes* and 30 clinical isolates of *Corynebacterium jeikeium* were tested against quinupristin/dalfopristin by the NCCLS broth macrodilution technique for determination of MICs. MBC testing was also performed on the 60 isolates. Quinupristin/dalfopristin MIC₉₀ values against *L. monocytogenes* and *C. jeikeium* were 1.6 mg/L and 0.2 mg/L, respectively. Quinupristin/dalfopristin was bacteriostatic against these organisms.

Introduction

Quinupristin/dalfopristin is an investigational antimicrobial agent with activity against Gram-positive organisms.^{1–6} This injectable compound belongs to the macrolide–lincosamide–streptogramin family, and is a combination of two semisynthetic derivatives of pristinamycin in a fixed 30:70 ratio. These two compounds act synergically by binding to the bacterial ribosome and inhibiting protein synthesis.⁷ Quinupristin/dalfopristin is usually bactericidal *in vitro*.

The purpose of this study was to evaluate and compare MIC and MBC values obtained with this agent against clinical isolates of *Corynebacterium jeikeium* and *Listeria monocytogenes*.

Materials and methods

Test organisms

Sixty clinical isolates (30 *C. jeikeium*, 30 *L. monocytogenes*) were evaluated. All isolates were maintained in stock by ultrafreezing methods. Isolates were identified in the clinical microbiology laboratory and submitted to the Infectious Disease Research Laboratory for inclusion in the study.

Antimicrobial agent

Quinupristin/dalfopristin was obtained from the manufacturer (Rhône-Poulenc Rorer, Collegeville, PA, USA) as standard reference powder. Once the vial contents had been reconstituted, the solution was used immediately. Unused drug solution was discarded.

Susceptibility testing

Broth macrodilution testing was performed according to NCCLS M7-A3 guidelines.⁸ After preliminary tests, some stock solution concentrations were adjusted to accommodate the more susceptible strains. Organisms were grown in trypticase soy broth, Becton Dickinson, Cockeysville, MD, USA and tested in cation-adjusted Mueller–Hinton broth with NAD and 3% lysed horse blood. Glass tubes were used and MIC tests were incubated at 35°C for 18–20 h in air (no added CO₂). Tubes showing no visible growth were subcultured on to sheep blood agar plates and incubated overnight for the MBC test. Quality control organisms used were *Staphylococcus aureus* ATCC 29213 and *Enterococcus faecalis* ATCC 29212.

Results

The results of the in-vitro susceptibility tests are shown in the Table. Quinupristin/dalfopristin was active against both organisms; *L. monocytogenes* and *C. jeikeium* MIC₉₀ values were 1.6 mg/L and 0.2 mg/L, respectively. MBC₉₀ values were considerably higher than MIC₉₀ values against both organisms.

Discussion

L. monocytogenes and *C. jeikeium* are increasingly being recognized as important pathogens, particularly in the immunocompromised host.^{9,10} Recently, multiresistant strains of these Gram-positive bacilli have emerged.¹¹ Co-trimoxazole or ampicillin plus gentamicin have been

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Table. In-vitro activity of quinupristin/dalfopristin against *L. monocytogenes* and *C. jeikeium*

Organism	MIC (mg/L)			MBC (mg/L)		
	range	MIC ₅₀	MIC ₉₀	range	MBC ₅₀	MBC ₉₀
<i>L. monocytogenes</i>	0.4–1.6	0.8	1.6	0.8–100	6.25	50
<i>C. jeikeium</i>	<0.1–0.4	<0.1	0.2	0.2–2.5	1.6	12.5

recommended for the treatment of listeriosis in immunocompromised transplant patients while the use of vancomycin plus erythromycin has been recommended against *C. jeikeium* in this setting.¹² However, the new macrolides, azalides and streptogramins may have an extended role against these organisms.

MICs obtained in this study with quinupristin/dalfopristin against *L. monocytogenes* are in concordance with those from other studies.^{6,13} In a previous comparative study, quinupristin/dalfopristin was as potent (MIC₉₀ 2 mg/L) as erythromycin, clarithromycin, azithromycin and rokitamycin against this organism.¹³ Quinupristin/dalfopristin was as effective as erythromycin in a mouse model of listeriosis.¹⁴

Despite being bactericidal against other Gram-positive bacteria, quinupristin/dalfopristin has proved bacteriostatic against *L. monocytogenes* and *C. jeikeium* in this and other studies.¹⁴ Further work may be indicated to confirm these results using time–kill studies. This is of concern because bactericidal activity may be necessary in the treatment of the neutropenic patient.

In summary, quinupristin/dalfopristin is active *in vitro* against *L. monocytogenes* and *C. jeikeium* and may be a potential candidate for the treatment of infections caused by these organisms.

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