Susceptibility of common Clostridium difficile PCR ribotype to delafloxacin and seven comparator antimicrobials

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Introduction

Clostridium difficile infection (CDI) is a significant cause of nosocomial diarrhea and remains a major burden on healthcare resources. CDI is linked to depletion of gut microbiota by antimicrobial action, allowing the organism to proliferate and cause symptomatic disease. Most antimicrobials have been associated with CDI, particularly PCR ribotype RT001 (NAP1/BI) 1,2,3. Delafloxacin is an investigational fluorquinolone currently being assessed for the treatment of acute bacterial skin infections and remains a major burden on healthcare resources.

Methods

Delafloxacin was the most active fluorquinolone agent tested in this study, with the lowest MICs for the panel of isolates tested. Resistance among Prevalent C. difficile isolates tested (Table 2). There was no evidence of metronidazole resistance, but genetic mean metronidazole MICs for RT027 isolates were 10-fold higher than for non-RT027 isolates, reflecting previous results. However, moxifloxacin resistance (>8 mg/L) is not uncommon and may be associated with existing QRDR mutations. Previous studies of fluoroquinolone resistance in C. difficile have described a number of mutations in gyrA and gyrB. In particular, a gyrA substitution Thr82 to ile in Gya has been implicated in fluoroquinolone resistance in RT027. Although we did not undertake molecular characterization of the isolates showing reduced susceptibility, it seems likely that existing mutations in QRDR that confer resistance to other fluoroquinolones may confer reduced susceptibility to delafloxacin.

Results

MIC results for metronidazole, vancomycin, meropenem, tigecycline and rifampicin were selected for testing in this study.

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Discussion

Delafloxacin was the most active fluoroquinolone agent tested in this study, with the lowest MICs for the panel of isolates tested. Resistance among Prevalent C. difficile isolates tested (Table 2). There was no evidence of metronidazole resistance, but genetic mean metronidazole MICs for RT027 isolates were 10-fold higher than for non-RT027 isolates, reflecting previous results. However, moxifloxacin resistance (>8 mg/L) is not uncommon and may be associated with existing QRDR mutations. Previous studies of fluoroquinolone resistance in C. difficile have described a number of mutations in gyrA and gyrB. In particular, a gyrA substitution Thr82 to ile in Gya has been implicated in fluoroquinolone resistance in RT027. Although we did not undertake molecular characterization of the isolates showing reduced susceptibility, it seems likely that existing mutations in QRDR that confer resistance to other fluoroquinolones may confer reduced susceptibility to delafloxacin.

Nevertheless, delafloxacin was more active than moxifloxacin and levofloxacin against the panel of isolates selected for testing in this study. Delafloxacin susceptibility was the same as those reported by Buchler et al, although genetic mean MICs were 2-fold higher for RT027 isolates than for non-RT027 isolates (3.25 mg/L vs. 1.51 mg/L).

C. difficile isolates tended to be sensitive to metronidazole but not susceptible. There are several models that may account for this, including the use of certain antibiotic combinations in the gut, which may confer reduced susceptibility to delafloxacin.

Finally, the MIC results for metronidazole, vancomycin, meropenem, tigecycline and rifampicin were selected for testing in this study. These isolates were considered to be indistinguishable.