β-lactam Activity Tested in Combination with β-lactamase Inhibitor Candidates against Enterobacteriaceae Producing Class A, B, and D Carbapenemases

RE MENDES, PR RHOMBERG, HK BECKER, RN JONES
JMI Laboratories, North Liberty, iowa, USA

ABSTRACT

Background: Carbapenemases enzymes have challenged antimicrobial therapy worldwide. This is illustrated in the outcome of the β-lactam activity tested with and without a β-lactam inhibitor. Several combinations of β-lactam-carbapenem agents have shown promising activity against these production. These combinations of β-lactam-carbapenem are proven effective for treating infections caused by these organisms. However, the use of β-lactam-carbapenem combinations limits the potential use of β-lactam inhibitors due to bacterial resistance.

METHODS: 27 molecularly characterized isolates were selected for carbapenemase analysis to determine the β-lactamase combinations. These were used for further susceptibility testing against a panel of extended-spectrum β-lactamase producers. These data warrant further development of this extended-spectrum β-lactamase inhibitor candidates for carbapenemases.

RESULTS: Overall, only 11.1% of 7.4% of tested isolates were susceptible to aztreonam (MIC₅₀ <0.5, <1) when tested with and without β-lactam inhibitors. The β-lactam-carbapenem combinations tested were: Ceftazidime (MIC₅₀, 128 µg/mL), Ceftazidime-FPI-1465 (MIC₅₀, 0.12 µg/mL), Ceftazidime-FPI-1465 demonstrated highest activity against these isolates. These data warrant further development of this extended-spectrum β-lactamase inhibitor candidates for carbapenemases.

CONCLUSIONS: These in vitro MIC results illustrate the potential antimicrobial activity against these isolates. These data warrant further development of β-lactam inhibitors for carbapenemases for treatment of multidrug-resistant Gram-negative bacteria.

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REFERENCES