Ceftobiprole Activity Tested Against North American Enterobacteriaceae, Pseudomonas aeruginosa, and Acinetobacter spp. in 2005-2007

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Abstract

Background: Ceftobiprole, an investigational parenteral cephalosporin active against Enterobacteriaceae, has been evaluated for its activity in clinical isolates of Gram-negative pathogens. Importantly, ceftobiprole also displays activity against most Enterobacteriaceae unique spectrum, broad safety profile, and predominant bactericidal activities. Results: Among all tested Enterobacteriaceae, ceftobiprole was similar in potency to ceftazidime and cefepime against Proteus mirabilis, E. coli, and Klebsiella spp. (MIC50 values, 2, >16, and 16 µg/ml, respectively) and greater than ceftazidime against Acinetobacter spp. (MIC50, 0.5 µg/ml) and extended-spectrum cephalosporins. These characteristics warrant continued evaluation of ceftobiprole as an empiric therapy for CSID and pneumonia, especially in those medical centers where MRSA and other extended-spectrum cephalosporins may be prevalent pathogens.

Introduction

Emergence of resistance among commonly occurring bacterial pathogens has driven the need for new and effective antimicrobial agents, including recently marketed agents such as ceftobiprole, meropenem, aztreonam, and tigecycline, and thienamycin for Gram-positive pathogens.

Ceftobiprole (formerly BAL8141), an expanded-spectrum cephalosporin with potent activity against community-occurring Gram-negative pathogens including resistant strains, has been evaluated for its activity in clinical isolates of Gram-negative pathogens. Importantly, ceftobiprole also displays activity against most Enterobacteriaceae (MIC50 values, 2, >16, and 16 µg/ml, respectively), and extended-spectrum cephalosporins. These characteristics warrant continued evaluation of ceftobiprole as an empiric therapy for CSID and pneumonia, especially in those medical centers where MRSA and other extended-spectrum cephalosporins may be prevalent pathogens.

Materials and Methods

Bacterial Isolates

Ceftobiprole was similar in potency to ceftazidime and cefepime against Proteus mirabilis, E. coli, and Klebsiella spp. (MIC50, 2, >16, and 16 µg/ml, respectively) and greater than ceftazidime against Acinetobacter spp. (MIC50, ≤0.5 µg/ml) and extended-spectrum cephalosporins. These characteristics warrant continued evaluation of ceftobiprole as an empiric therapy for CSID and pneumonia, especially in those medical centers where MRSA and other extended-spectrum cephalosporins may be prevalent pathogens.

Ceftobiprole was similar in potency to ceftazidime and cefepime (MIC 50 ≤8 µg/ml) was similar (ceftobiprole, 57-83; ceftazidime, 75-81; cefepime, 56-71) against most Enterobacteriaceae (Table 1). Ceftobiprole was more active than either ceftazidime or cefepime against Proteus mirabilis, Enterobacter, and Klebsiella spp. (152 isolates, 12.9% at 4 µg/ml vs. 7.5% at 8 µg/ml, and 3.7% at 16 µg/ml vs. 1.4% at 16 µg/ml, respectively). These characteristics warrant continued evaluation of ceftobiprole as an empiric therapy for CSID and pneumonia, especially in those medical centers where MRSA and other extended-spectrum cephalosporins may be prevalent pathogens.

Results

Among all tested Enterobacteriaceae, ceftobiprole was similar in potency to ceftazidime (MIC50, 16 µg/ml) and cefepime against Proteus mirabilis, E. coli, and Klebsiella spp. (Table 1). Coverage against E. coli was nearly identical for the three agents (Table 1). Ceftazidime was 4-fold more potent than cefepime against the other Enterobacteriaceae (Table 1).

Breakpoints have not been approved for ceftobiprole, although this agent is known to have pharmacokinetic and pharmacodynamic features similar to those of other advanced-generation cephalosporins.

Conclusions

Ceftobiprole is a new inhibitor of β-lactamases and aminoglycosides with potent activity against most Enterobacteriaceae, and a broad spectrum, broad safety profile, and predominant bactericidal activities.

Acknowledgment

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Selected References