The Activity of Five Cephalosporins Against Bacteroides fragilis

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ABSTRACT

Forty-two isolates of Bacteroides fragilis were tested against five new cephalosporin antibiotics by two quantitative methods, microdilution and agar dilution. Results indicated satisfactory methodological agreement. Mean minimum inhibitory concentrations (MIC) of thienamycin, moxalactam, and ceftizoxime were significantly lower than with the other antibiotics tested.

Introduction

There is extensive literature on the microbiological and pharmacological response to the newly developed and tested cephalosporin antibiotics.1,2,3,4,5,6 Because of the claimed “broad-spectrum” nature of these antibiotics, as well as scattered reports of efficacy for anaerobic bacteria, 42 strains of Bacteroides fragilis were tested for susceptibility to cefoperazone,* n-formimidoyl thienamycin,† ceftizoxime,‡ moxalactam,§ and cefotaxime.¶

Methods

Isolates of Bacteroides fragilis were obtained from patients at the John Dempsey Hospital, University of Connecticut Health Center. The isolates were identified by standard procedures.5 The antibiotics used were a gift.11 Forty-two isolates of B. fragilis were maintained at −20°C in a buffered glycerol solution until testing. The minimal inhibitory concentration (MIC) to each of the five cephalosporins was determined using two methods: microdilution (MD)6 and agar dilution (AD).§ Wilkens-Chalgren media9 was used for both broth and agar tests. All antibiotics were tested in serial two-fold concentrations from 0.06 mcg per ml to 64 mcg per ml. Microtiter plates and antibiotic containing agar plates were incubated in Gas-Pak jars at 35°C for 24 hrs prior to reading. The following isolates were used as quality control strains: B. fragilis ATCC 252285, B. thetaiotaomicron

* Pfizer T1551.
† Merck—MK-0787.
‡ Smith, Kline, and French—FK-749.
§ Lilly—LY 127935.
¶ Hoechst-Roussel—HR-756.

From Richard Quintiliani, M.D., Hartford Hospital, Hartford, CT.
Results

In table I are shown the geometric mean MIC's and MIC range of the antibiotics tested. In most instances, there was good methodological agreement. Only with cefotaxime was there a > 1 dilution interval between MD and AD MIC's. Mean MIC's of thienamycin and moxalactam were significantly lower than with the other antibiotics. In table II it is shown that thienamycin was the only antibiotic to which the 42 isolates of *B. fragilis* were uniformly susceptible. Although no specific MIC breakpoints for these antibiotics have been published, cephalosporins, in general, have been classified as susceptible if the MIC was ≤ 8 mcg per ml and resistant if the MIC was ≥ 16 mcg per ml. Using these breakpoints, thienamycin, moxalactam, and ceftizoxime were the only antibiotics effective against >75 percent of the strains tested. Only 14 percent of isolates were inhibited by cefoperazone at 8.0 mcg per ml. There were 78.5 percent of strains susceptible to ceftizoxime and 45.5 percent of strains susceptible to cefotaxime at this same breakpoint. The MIC, as a measure of antibiotic efficacy, is a function of achievable antibiotic concentration. Average peak achievable blood levels for these cephalosporin antibiotics range from 90 to 150 mcg per ml after a 1.0 g intravenous infusion dosage.

The unique advantages of these newly introduced cephalosporins include their broad range of microbial activity including *Pseudomonas*, their relative lack of toxicity, and their resistance to the various beta lactamases produced by Gram negative bacteria. Sato et al, however, reported that purified *B. fragilis* beta lactamase hydrolyzed cephalosporins including cefotaxime and ceftizoxime but the 7α methoxylated cephalosporins, including moxalactam, were not affected.

Others have reported that thienamycin and ceftizoxime showed good activity against *B. fragilis*. It is concluded by us that of the five drugs tested, thienamycin and moxalactam showed the highest "in vitro" activity, followed closely by ceftizoxime.

### TABLE I

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Geom. Mean MIC (24 hrs)</th>
<th>AD (48 hrs)</th>
<th>MD</th>
<th>Range AD</th>
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<tbody>
<tr>
<td>Cefoperazone</td>
<td>20.9</td>
<td>24.6</td>
<td>4.0</td>
<td>&gt;64</td>
</tr>
<tr>
<td>Thienamycin</td>
<td>0.06</td>
<td>0.06</td>
<td>&lt;0.06</td>
<td>&gt;0.125</td>
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<td>0.35</td>
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<td>Moxalactam</td>
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<td>1.12</td>
<td>0.125-32</td>
<td>&lt;0.125-16</td>
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<tr>
<td>Cefotaxime</td>
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<td>4.1</td>
<td>1.5</td>
<td>&gt;64</td>
</tr>
</tbody>
</table>

MIC = Minimum inhibitory concentration
MD = Microdilution
AD = Agar dilution

### TABLE II

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>&lt;0.06</th>
<th>0.06</th>
<th>0.125</th>
<th>0.25</th>
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<th>4.0</th>
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<td>81.0</td>
<td>88.1</td>
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*Microdilution method - 24 hour incubation
The MD method for the determination of MIC's to these cephalosporins compares favorably with AD and can be used routinely in those laboratory settings where the numbers of isolates to be tested does not justify the use of AD.

References


