Activity of Pirlimycin (U57930E) Against Strains of the 
Bacteroides fragilis Group

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Received 18 June 1982/Accepted 2 September 1982

The activities of pirlimycin (U57930E), lincomycin, clindamycin, erythromycin, josamycin, oleandomycin, and spiramycin were compared against strains of the Bacteroides fragilis group. Pirlimycin was the most active: the 90% minimal inhibitory concentration was 1 μg/ml, and the activity range was 0.125 to 4 μg/ml. This drug was fourfold more active than any of the other drugs, including clindamycin. The minimal bactericidal concentration (range, 0.5 to 16 μg/ml) shows that pirlimycin behaves as a bacteriostatic antibiotic.

The lincosamides constitute an important group of antimicrobial agents in the treatment of infections caused by anaerobes. Lincomycin was the first of these antibiotics found to have activity against anaerobic bacteria, although at present it is not particularly active against bacteria of the Bacteroides fragilis group. The introduction of clindamycin represented a noteworthy advance in the treatment of anaerobic infections, including those caused by B. fragilis (2).

The frequency of anaerobic infections has been increasingly recognized in recent years, and strains have evolved which are now more resistant to clindamycin and lincomycin. The present work examines the activity of pirlimycin (U57930E), a compound derived from clindamycin, against bacteria of the B. fragilis group. Results show that its in vitro activity is greater than that of the other antibiotics assayed.

The susceptibility of 64 strains of the B. fragilis group was studied. Of these strains, 4 belonged to the species Bacteroides distasonis, 37 to B. fragilis, 2 to Bacteroides ovatus, 15 to Bacteroides thetaiotaomicron, and 6 to Bacteroides vulgatus. All 64 strains were characterized by the biochemical methods of Holdeman et al. (3). All produced β-lactamases, as shown by the chromogenic cephalosporin test (4).

The antibiotics tested were clindamycin, lincomycin, and pirlimycin (The Upjohn Co.), erythromycin (Eli Lilly & Co.), josamycin (Liaide), spiramycin (Rhone Poulenc), and oleandomycin (Pfizer Inc.).

The minimal inhibitory concentration (MIC) was determined by using twofold serial dilutions of the antimicrobial agents being incorporated into solid medium without blood, as described by Wilkins and Chalgren (7). The inoculum, a 24-h culture in brain heart infusion broth with yeast extract and cysteine, was adjusted to one-half of a no. 1 McFarland nephelometer standard and then was applied to the surface of the plate with a Steer replicator. Incubation was by the GasPak method (BBL Microbiology Systems). The MIC was recorded as the minimum amount of chemotherapeutic agent which did not allow visible growth after 48 h of incubation at 37°C (6).

The techniques to determine the MIC for broth and the minimal bactericidal concentration (MBC) of pirlimycin were those described by Sutter and Washington (6) and Anhalt et al. (1), respectively.

The media used (broth and agar) were those of Wilkins and Chalgren (7). To determine the MIC and MBC, the inoculum was 10° colony forming units, and the subculture was made with a sample of 0.1 ml by the method of Anhalt et al. (1).

The activities of pirlimycin and the other antibiotics are shown in Table 1. The activity ranges of clindamycin, josamycin, and pirlimycin were similar, and they were more effective than

<p>| TABLE 1. Susceptibility of 64 strains of the B. fragilis group to seven antibiotics |
|----------------------------------|--------|--------|--------|</p>
<table>
<thead>
<tr>
<th><strong>Antimicrobial agent</strong></th>
<th><strong>MIC (μg/ml)</strong></th>
<th><strong>%</strong></th>
<th><strong>Range</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin</td>
<td>1</td>
<td>4</td>
<td>≤0.125–8</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>4</td>
<td>32</td>
<td>2–≥64</td>
</tr>
<tr>
<td>Josamycin</td>
<td>1</td>
<td>4</td>
<td>≤0.125–8</td>
</tr>
<tr>
<td>Lincomycin</td>
<td>8</td>
<td>16</td>
<td>2–32</td>
</tr>
<tr>
<td>Oleandomycin</td>
<td>8</td>
<td>25</td>
<td>1–≥64</td>
</tr>
<tr>
<td>Spiramycin</td>
<td>12.5</td>
<td>&gt;64</td>
<td>0.5–≥64</td>
</tr>
<tr>
<td>Pirlimycin</td>
<td>0.25</td>
<td>1</td>
<td>≤0.125–4</td>
</tr>
</tbody>
</table>
than the other agents assayed. Activity ranges were \( \leq 0.125 \) to 4 \( \mu g/ml \) for pirlimycin and 2 to \( \geq 64 \mu g/ml \) for erythromycin.

The 50% MIC (MIC\(_{50}\)) for pirlimycin (0.25 \( \mu g/ml \)) was fourfold lower than those of clindamycin and josamycin. These differences were identical for the MIC\(_{90}\) of the drugs (1 \( \mu g/ml \) for pirlimycin, 4 \( \mu g/ml \) for clindamycin and josamycin).

Table 2 shows the MBC of pirlimycin assayed in liquid medium. It can be seen that the results of the determination of activity in solid medium and in liquid medium are practically identical.

For pirlimycin, the activity range for the MBC was 0.5 to 16 \( \mu g/ml \), the MBC\(_{50}\) being eightfold higher than the MIC\(_{50}\). However, the MBC\(_{90}\) was only twice the MIC\(_{90}\), showing that pirlimycin behaves as a bacteriostatic antibiotic in particularly susceptible strains; this property is not as evident in less susceptible strains.

The \( B. \ fragilis \) group is the most common group of anaerobic bacteria in clinical practice with humans, and it is also the most resistant to antimicrobial agents (2). Further knowledge of new drugs active against these organisms is therefore of great interest.

From the results obtained, it is apparent that pirlimycin is the most active of the antibiotics assayed against the \( B. \ fragilis \) group. Even though it behaves as a bacteriostatic agent, its activity range does offer some promise for antimicrobial therapy. It can be concluded that unless clinical trials prove otherwise, this drug may be included with clindamycin, josamycin, and other antibiotics of this group in the treatment of \( Bacteroides \) infections.

### LITERATURE CITED


