Trends in Antimicrobial Resistance among Clinical Isolates of the *Bacteroides fragilis* Group from 1992 to 1997 in Montreal, Canada

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The objective of the present study was to analyze the susceptibility profiles of 911 clinical strains of the *Bacteroides fragilis* group isolated from 1992 to 1997 in our institution in order to monitor susceptibility changes over time. Whereas the rates of resistance to metronidazole, imipenem, piperacillin-tazobactam, ticarcillin-clavulanic acid, penicillin, piperacillin, and cefoxitin remained essentially unchanged, there was a significant increase in the rates of resistance to clindamycin, which rose from 8.2% in 1992 to 19.7% in 1997 (*P* < 0.0004).

Species of the *Bacteroides fragilis* group are the most clinically important anaerobic pathogens given the fact that they are most frequently isolated from suppurative anaerobic infections and that they have the widest range of antimicrobial resistance (5, 10, 13). During the past two decades, the rates of resistance to commonly used antimicrobial agents among these species have been shown to increase in North America and in Europe (6, 11). As routine susceptibility testing of anaerobes is of utmost importance (5).

itoring of resistance patterns in institutions and regions is of utmost importance (5).

The objective of the study reported herein was to determine the susceptibility profiles of clinical strains of the *B. fragilis* group isolated from 1992 to 1997 in our institution and to monitor susceptibility changes over time. All nonduplicate strains of the *B. fragilis* group recovered from 1992 to 1997 at the Centre Hospitalier de l’Université de Montréal, Campus Saint-Luc, were included in the analysis. Identification of the organisms was established by means of a standard methodology (12). Susceptibility testing was performed by the National Committee for Clinical Laboratory Standards (NCCLS) agar dilution method with Wilkins-Chalgren agar (8). The antibiotics tested and their concentration ranges were as follows: cefoxitin, 0.06 to 128 μg/ml; clindamycin, 0.5 to 128 μg/ml; imipenem, 0.007 μg/ml to 16 mg/ml; metronidazole, 0.5 to 16 μg/ml; penicillin, 0.015 to 64 μg/ml; piperacillin, 2 to 128 μg/ml; piperacillin-tazobactam, 0.125/4 to 128/4 μg/ml; and ticarcillin-clavulanate, 0.125/2 to 128/2 μg/ml. The resistance breakpoints were as follows: cefoxitin, 64 μg/ml; clindamycin, 8 μg/ml; imipenem, 16 μg/ml; metronidazole, 32 μg/ml; penicillin, 2 μg/ml; piperacillin, 128 μg/ml; piperacillin-tazobactam, 128/4 μg/ml; and ticarcillin-clavulanate, 128/2 μg/ml. These breakpoints incorporate as “susceptible” organisms that are either “intermediate” or “susceptible” (designations in the recently published NCCLS approved standards [9]). Piperacillin-tazobactam and ticarcillin-clavulanate susceptibility testing was introduced in 1995. All data were stored, retrieved, and analyzed with Lotus 1-2-3 software (Lotus Development, Cambridge, Mass.). Statistical analysis was performed with Epi INFO, version 6.0, software (Centers for Disease Control and Prevention, Atlanta, Ga.).

Susceptibility results were available for 911 strains isolated from the following sites: blood (9.4%), abdomen (63.1%), female genital tract (3%), muscle and bone (3.3%), and miscellaneous foci of infection (21.2%). The distribution of species within the 911 strains of the *B. fragilis* group was as follows: *B. fragilis*, 31.2%; *B. thetaiotaomicron*, 19.4%; *B. ovatus*, 14.7%; *B. vulgatus*, 13.9%; *B. distasonis*, 7.7%; *B. uniformis*, 6.5%; *B. eggerthii*, 0.3%; *B. cacae*, 4.1%; *B. stercoris*, 2.0%. The species of two strains (0.2%) could not be determined and the strains were reported as indole-positive *B. fragilis*. Analysis of the species distribution over time revealed no statistically significant change.

The organisms were uniformly susceptible to metronidazole, and only one isolate of *B. fragilis* was found to be resistant to imipenem. Rates of resistance to piperacillin-tazobactam (0.5%) and ticarcillin-clavulanate (3.4%) were minimal among the 443 strains tested, and no significant change was noted over the period from 1995 to 1997. The rates of resistance to piperacillin, piperacillin, and cefoxitin remained unchanged (Table 1). The most noticeable change was observed with clindamycin: rates of resistance to clindamycin increased from 8.2 to 19.7% (chi-square analysis for linear trend = 12.537; *P* = 0.0004).

The rates of resistance to clindamycin among the different

**TABLE 1. Resistance rates of *B. fragilis* group isolates by year**

<table>
<thead>
<tr>
<th>Year</th>
<th>No. (%) of isolates resistant per yr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Penicillin</td>
</tr>
<tr>
<td>1992</td>
<td>158</td>
</tr>
<tr>
<td>1993</td>
<td>186</td>
</tr>
<tr>
<td>1994</td>
<td>124</td>
</tr>
<tr>
<td>1995</td>
<td>148</td>
</tr>
<tr>
<td>1996</td>
<td>153</td>
</tr>
<tr>
<td>1997</td>
<td>142</td>
</tr>
<tr>
<td>Total</td>
<td>911</td>
</tr>
</tbody>
</table>

* Only 2 of 443 (0.5%) strains from 1995 to 1997 were resistant to piperacillin-tazobactam.
species of the *B. fragilis* group are listed in Table 2. Controlling for the potentially confounding effect of the distribution of the *B. fragilis* group species for each time period, resistance to clindamycin increased significantly from 1992 to 1997 (chi-square analysis for linear trend = 11.89; *P* = 0.00054). Compared to the rate in 1992, the odds ratios were 0.95 for 1993, 1.64 for 1994, 1.00 for 1995, 2.03 for 1996, and 2.56 for 1997, indicating that the significant increase in resistance occurred during the last 2 years of the study period. *B. thetaiotaomicron* is the only species for which a significant increase in resistance was demonstrated (chi-square analysis for linear trend = 7.603; *P* = 0.00583). The change in the susceptibility of *B. fragilis* did not reach statistical significance (chi-square analysis for linear trend = 2.851; *P* = 0.09130). No trend was apparent for *B. distasonis*, *B. ovatus*, or *B. vulgatus*, but the small number of strains limited the power to detect a trend in resistance changes over time. In our hospital, the results for the *B. fragilis* group susceptibility survey over time confirm the excellent in vitro activities of metronidazole, imipenem, piperacillin-tazobactam, and ticarcillin-clavulanate. The rates of resistance to piperacillin (20%) and to cefoxitin (18%) remained unchanged and were not different from those found in a Canadian multicenter survey conducted in 1990 with 348 *B. fragilis* group strains (3): 19 and 26% of these strains were resistant to piperacillin and cefoxitin, respectively. These resistance rates are higher than those found in other studies (5, 11) and can possibly be explained by differences in species distributions. The *B. fragilis* group strains isolated in 1997 were significantly more resistant to clindamycin than those isolated in 1992. In two previous Canadian surveys (2, 3), the rates of resistance to clindamycin among *B. fragilis* group strains increased from 0.6% in 1984 to 8.9% in 1990. There has therefore been a significant increase in the rate of clindamycin resistance during the last 13 years in Canada. Studies in several other countries have shown similar trends in levels of resistance to clindamycin. In eight medical centers in the United States, 3,177 isolates were tested from 1990 to 1994 (11). The percentage of *B. fragilis* isolates resistant to clindamycin rose from 8 to 14%. For non-*B. fragilis Bacteroides* species, the resistance rate fluctuated over time, from 16 to 22%. In Spain, the rate of resistance to clindamycin rose from 2% in 1982 to 20% in 1984 and then fell back to 7% in 1987 after interventions to reduce the use of clindamycin in hospitals and in the community (6). In Argentina, the rate of resistance to clindamycin varied from 0 to 17% over a 13-year period (1975 to 1987), with the highest resistance rate found in 1982 (1). In Korea, in 1994, the rates of resistance to clindamycin for the *B. fragilis*, *B. thetaiotaomicron*, and other *Bacteroides* spp. were 38, 45.5, and 60%, respectively (7). The investigators believed that their results were a consequence of the frequent use of macrolides and lincosamides.

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**REFERENCES**


