Yonsei Medical Journal
Vol. 39, No. 6, pp. 578-586, 1998

☐ Review Article ☐

Antimicrobial Resistance Patterns of *Bacteroides fragilis* Group Organisms in Korea

Kyungwon Lee, Hee Bong Shin, and Yunsop Chong

Antimicrobial resistance patterns of 913 clinical isolates of Bacteroides fragilis *group organisms were monitored during an 8-year period in Korea. In general the resistance rates of the non-*fragilis B. fragilis *group species were higher than those of* B. fragilis *for all the drugs tested. The rate of resistance to clindamycin remarkably increased and those to some β-lactam drugs such as piperacillin and cefotaxime also increased. No isolates were found to be resistant to imipenem, metronidazole, or chloramphenicol. β-lactam and β-lactamase inhibitor combinations and cefoxitin were more active than the other β-lactams. Therefore, these agents may be considered when empirical selection of antimicrobial agents is required to treat severe anaerobic infections.*

Key Words: *Bacteroides fragilis* group organisms, antimicrobial resistance pattern

Bacteroides fragilis group organisms are important human anaerobic pathogens frequently causing various infections (Finegold and Wexler, 1988; Lee *et al.* 1991). *B. fragilis* is the most common causative agent of anaerobic bacteremia with relative high mortality (Redondo *et al.* 1995; Kim *et al.* 1996). Appropriate antimicrobial therapy is considered necessary to reduce the morbidity and mortality (Finegold, 1991).

Routine susceptibility testing of anaerobic bacteria is not considered necessary because of the predictability of the susceptibility (Finegold, 1988; Baron *et al.* 1990). However, antimicrobial resistance among *B. fragilis* group organisms has been known to vary between species, institutions, and countries (Dubreuil *et al*, 1992; Tanaka-Bandoh *et al*, 1995; Snydman *et al.* 1996). Furthermore, antimicrobial resistance of these organisms to some commonly used antimicrobial agents has been increasingly reported (Betriu *et al.* 1992; Snydman *et al.* 1996). Therefore, at least periodic monitoring of the susceptibility is considered necessary.

Aerobic bacteria isolated in Korea were more often resistant than those isolated in other countries, possibly due to more selective pressure of antimicrobial agents (Chong *et al.* 1993; Chong *et al.* 1996). Therefore, anaerobes in Korea could also be more often resistant.

The purpose of this article is to report the changing antimicrobial susceptibilities of *B. fragilis* group organisms isolated during an 8-year period.

MATERIALS AND METHODS

Anaerobic bacteria were isolated from various clinical materials except those from the respiratory and gastrointestinal tract. Species of the isolates were identified by established methods (Holdeman *et al.* 1977; Summanen *et al.* 1993) and with the ATB 32A system (bioMerieux SA, Marcy l'Etoile, France).

A total of 913 nonduplicate clinical isolates of *Bacteroides fragilis* group organisms isolated during an 8-year period were tested for their susceptibility.

Received December 15, 1998

Department of Clinical Pathology and Research Institute of Bacterial Resistance, Yonsei University College of Medicine, Seoul, Korea

Address reprint request to Dr. K. Lee, Department of Clinical Pathology and Research Institute of Bacterial Resistance, Yonsei University College of Medicine, C.P. O. Box 8044, Seoul, Korea. Tel: 82-2-361-5866, Fax: 82-2-313-0956, E-mail: leekcp@yumc.yonsei.ac.kr

Table 1. *Bacteroides fragilis* group organisms tested for in vitro susceptibility which were isolated from 1989 to 1996

Bacteroides species	No. (%) of strains tested					
	1989–1990	1991	1992–1993	1994	1995–1996	Total
B. fragilis	113	192	185	63	88	641 (70.2)
B. thetaiotaomicron	25	16	22	11	28	102 (11.2)
B. ovatus	17	22	31	4	7	81 (8.9)
B. vulgatus	11	9	14	2	2	38 (4.2)
B. distasonis	6	8	7	4	4	29 (3.2)
Others	0	10*	0	5†	7†	22 (2.4)
Total	172	257	259	89	136	913 (100)

*: *B. uniformis* 3, *B. eggerthii* 7.
†: *B. uniformis*.

The organisms tested were isolated from 1989 to 1993 at Wonju Christian Hospital, Wonju, and from 1989 to 1996 at Severance Hospital, Seoul. The years of isolation and the number of isolates were 172 isolates in 1989 and 1990, 257 isolates in 1991, 259 isolates in 1992 and 1993, 89 isolates in 1994, and 136 isolates in 1995 and 1996 (Table 1).

The strains were kept frozen until used for susceptibility testing. Antimicrobial susceptibility was tested by an agar dilution method (NCCLS, 1993). Antimicrobial powders used were chloramphenicol (Chong Kun Dang, Seoul); sulbactam (Pfizer Korea, Seoul); piperacillin (Yuhan, Seoul); cefotaxime (Han-Dok, Seoul); cefepime (Bristol-Myers Squibb, Prinston, NJ, U.S.A.); cefoxitin (Merck Sharp & Dohme, West Point, PA, U.S.A.); cefotetan (Je Il, Seoul); imipenem (Choong Wae, Seoul); meropenem (Sumitomo, Osaka, Japan); clindamycin (Korea Upjohn, Seoul); metronidazole (Choong Wae, Seoul); ofloxacin (Daiichi, Tokyo, Japan); tosufloxacin (Yuhan Cynamid, Seoul). For the combination of β-lactam and β-lactamase inhibitors, a constant amount of clavulanic acid (2 μg/mL, final concentration) was added to amoxicillin, or 1/2 the amount of sulbactam was added to ampicillin.

An inoculum of 10^5 CFU was applied with a Steers replicator (Craft Machine, Chester, PA, U.S.A.) onto brucella agar supplemented with vitamin K_1 (10 μg/ml) and 5% laked sheep blood from 1989 to 1994 and onto Wilkins-Chalgren agar from 1995 to 1996. Plates were incubated in an anaerobic chamber for 48 hours at 37°C. The MIC was defined as the lowest concentration of an antimicrobial agent permitting no growth, lighter growth, haze, multiple tiny colonies, or one to several normal-sized colonies (one discrete colony from 1989 to 1993) (NCCLS, 1993). *B. fragilis* ATCC 25285 and *B. thetaiotaomicron* ATCC 29741 were used as a control. The breakpoints recommended by the National Committee for Clinical Laboratory Standards (NCCLS, 1995) were applied to interpret the MICs.

RESULTS AND DISCUSSION

Trends of resistance of *B. fragilis* group organisms which were isolated during an 8-year period from 1989 to 1996 are shown in Tables 2-4.

In vitro activity of β-lactam agent

β-lactam agents are very useful in general for the treatment of aerobic infections. However, most *Bacteroides fragilis* group isolates are naturally resistant to many penicillins and cephalosporins because of their production of chromosomal class A β-lactamase with predominantly cephalosporinase activity (Wexler *et al.* 1991; Livermore, 1995). These are inhibited by β-lactamase inhibitors, as are most other class A enzymes.

Table 2. Antimicrobial susceptibility of *Bacteroides fragilis* isolated from 1989 to 1996

Antimicrobial agents	Resistance breakpoint* (μg/mL)	MIC range, MIC_{50}, MIC_{90} (μg/mL) (% of isolates resistant)				
		1989 – 1990 (n = 113)	1991 (n = 192)	1992 – 1993 (n = 185)	1994 (n = 63)	1995 – 1996 (n = 88)
Piperacillin	≥128	0.5 ->256, 4, 128 (12)	1 ->256, 16, >256 (21)	1 ->256, 16, >256 (20)	2 ->256, 8, 256 (25)	0.5 ->256, 8, 256 (25)
Ampicillin/ sulbactam	≥32/16	NT†	NT	0.25-16, 0.5, 4 (2)‡	1-64, 1, 16 (5)	0.5-64, 1, 8 (1)
Cefotaxime	≥64	0.5 ->256, 8, 64 (17)	2 ->256, 64, >256 (57)	2 ->256, 64, >256 (54)	1 ->128, 32, >128 (37)	1 ->128, 16, >128 (33)
Cefepime	≥32	NT	NT	NT	NT	4 ->128, 64, >128 (85)
Cefoxitin	≥64	2-64, 8, 16 (4)	4 -128, 8, 32 (3)	2-128, 8, 32 (4)	4-32, 8, 16 (0)	4 ->128, 8, 32 (1)
Cefotetan	≥64	1-256, 8, 8 (6)	4 ->256, 8, 32 (8)	2-256, 8, 64 (10)	4-128, 4, 16 (5)	2 ->128, 8, 16 (9)
Imipenem	≥16	≤0.06-4, ≤0.06, 0.25 (0)	≤0.06-8, 0.25, 1 (0)	≤0.03-4, 0.25, 1 (0)	0.06-8, 0.12, 0.5 (0)	0.015-4, 0.06, 0.5 (0)
Meropenem	≥16	NT	NT	0.12-8, 2, 2 (0)	0.06-8, 0.12, 1 (0)	NT
Chloramphenicol	≥32	1-4, 2, 4 (0)	2-16, 4, 8 (0)	2-8, 4, 8 (0)	4-8, 8, 8 (0)	2-8, 4, 4 (0)
Clindamycin	≥8	≤0.06 ->256, 0.5, >256 (18)	≤0.06 ->256, 1, >256 (39)	≤0.06 ->256, 1, >256 (31)	0.12 ->256, 2, >256 (38)	0.12 ->128, 1, >128 (43)
Metronidazole	≥32	0.5-8, 2, 4 (0)	0.5-16, 2, 8 (0)	0.25-16, 4, 8 (0)	0.5-8, 4, 4 (0)	0.5-2, 1, 1 (0)
Ofloxacin	≥8	NT	NT	0.5-256, 4, 8 (15)	2-64, 4, 8 (21)	NT
Tosufloxacin	≥8	NT	NT	0.25 ->256, 1, 2 (5)	0.5-32, 1, 4 (3)	NT

*: Based on the criteria of the National Committee for Clinical Laboratory Standards (NCCLS, 1995); aerobic or arbitrary resistant breakpoints were used for cefepime, meropenem, ofloxacin and tosufloxacin.

†: Not tested.

‡: The results were for amoxicillin/clavulanate (resistance breakpoint, ≥16/8 μg/mL) not for ampicillin/sulbactam.

Table 3. Antimicrobial susceptibility of *Bacteroides thetaiotaomicron* isolated from 1989 to 1996

Antimicrobial agents	Resistance breakpoint* (μg/mL)	MIC range, MIC_{50}, MIC_{90} (μg/mL) (% of isolates resistant)				
		1989 – 1990 (n = 25)	1991 (n = 16)	1992 – 1993 (n = 22)	1994 (n = 11)	1995 – 1996 (n = 28)
Piperacillin	≥128	8 ->256, 32, 256 (32)	16 ->256, 32, >256 (25)	16 ->256, 64, >256 (27)	32 ->256, 32, >256 (36)	16 ->256, 32, >256 (36)
Ampicillin/ sulbactam	≥32/16	NT†	NT	0.5-8, 0.5, 4 (0)†	2-32, 2, 8 (9)	1-64, 1, 32 (14)
Cefotaxime	≥64	16 ->256, 64, 256 (68)	32 ->256, 64, >256 (88)	4 ->256, 128, >256 (91)	64 ->128, 128, >128 (100)	16 ->128, 64, >128 (82)
Cefepime	≥32	NT	NT	NT	NT	>128, >128, >128 (100)
Cefoxitin	≥64	4-64, 16, 32 (8)	8-64, 32, 64 (13)	8-128, 32, 128 (23)	16-32, 32, 32 (0)	8 ->128, 32, >128 (14)
Cefotetan	≥64	8-256, 64, 128 (76)	4-256, 64, 256 (94)	32 ->256, 128, >256 (96)	8 ->128, 64, 128 (73)	4 ->128, 64, >128 (79)
Imipenem	≥16	0.12-4, 0.25, 0.5 (0)	0.12-8, 1, 4 (0)	0.25-8, 0.5, 2 (0)	0.06-1, 0.5, 0.5 (0)	0.06-8, 0.12, 4 (0)
Meropenem	≥16	NT	0.25-0.5, 0.25, 0.5 (0)	0.25-4, 0.25, 8 (0)	0.25-4, 0.25, 0.5 (0)	NT
Chloramphenicol	≥32	1-8, 4, 4 (0)	4-8, 8, 8 (0)	4-8, 8, 8 (0)	4-8, 8, 8 (0)	4-8, 4, 4 (0)
Clindamycin	≥8	0.5 ->256, 2, >256 (32)	1 ->256, 4, >256 (50)	2 ->256, >256, >256 (59)	2 ->256, 4, >256 (46)	1 ->128, >128, >128 (75)
Metronidazole	≥32	1-4, 2, 4 (0)	0.5-4, 4, 4 (0)	2-8, 4, 4 (0)	1-4, 2, 4 (0)	0.5-2, 1, 2 (0)
Ofloxacin	≥8	NT	NT	4-32, 8, 16 (86)	4 -128, 8, 16 (91)	NT
Tosufloxacin	≥8	NT	NT	0.5-8, 1, 4 (4)	1-16, 2, 4 (9)	NT

*: Based on the criteria of the National Committee for Clinical Laboratory Standards (NCCLS, 1995); aerobic or arbitrary resistant breakpoints were used for cefepime, meropenem, ofloxacin and tosufloxacin.

†: Not tested.

†: The results were for amoxicillin/clavulanate (resistance breakpoint, ≥16/8 μg/mL) not for ampicillin/sulbactam.

Table 4. Antimicrobial susceptibility of other species of *Bacteroides fragilis* group isolated from 1989 to 1996

Antimicrobial agents	Resistance breakpoint* (μg/mL)	MIC range, MIC_{50}, MIC_{90} (μg/mL) (% of isolates resistant)				
		1989−1990 (n = 34)	1991 (n = 49)	1992−1993 (n = 52)	1994 (n = 15)	1995−1996 (n = 20)
Piperacillin	≥128	1->256, 32, >256 (44)	4->256, 32, >256 (33)	8->256, 64, >256 (50)	16->256, 64, >256 (47)	4->256, 128, >256 (55)
Ampicillin/ sulbactam	≥32/16	NT†	NT	0.25-32, 2, 16 (11)‡	1-64, 8, 32 (13)	1-32, 4, 32 (15)
Cefotaxime	≥64	1->256, 64, 256 (62)	0.5->256, 32, >256 (41)	2->256, 128, >256 (73)	8->128, 64, >128 (60)	0.5->128, 64, >128 (65)
Cefepime	≥32	NT	NT	NT	NT	8->128, >128, >128 (95)
Cefoxitin	≥64	2-128, 16, 64 (12)	4-64, 16, 32 (4)	4-64, 32, 64 (13)	4-32, 16, 32 (0)	4-64, 16, 32 (10)
Cefotetan	≥64	2->256, 64, 128 (65)	2-256, 64, 128 (67)	2->256, 128, 256 (67)	2->128, 32, 128 (47)	2->128, 64, 128 (85)
Imipenem	≥16	≤0.06-8, 0.25, 4 (0)	0.12-8, 1, 2 (0)	≤0.06-4, 0.5, 1 (0)	0.06-2, 0.5, 2 (0)	0.06-8, 0.25, 2 (0)
Meropenem	≥16	NT	0.12-2, 0.25, 1 (0)	0.12-8, 0.5, 2 (0)	0.12-4, 0.25, 1 (0)	NT
Chloramphenicol	≥32	1-8, 4, 4 (0)	2-8, 4, 8 (0)	2-8, 4, 8 (0)	4-8, 8, 8 (0)	2-8, 4, 4 (0)
Clindamycin	≥8	≤0.06->256, 2, >256 (38)	≤0.06->256, 64, >256 (51)	0.25->256, 4, >256 (48)	≤0.06->256, 8, >256 (60)	0.12->128, >128, >128 (70)
Metronidazole	≥32	0.12-4, 2, 4 (0)	0.5-4, 2, 4 (0)	1-16, 4, 8 (0)	0.5-4, 2, 4 (0)	0.12-2, 1, 2 (0)
Ofloxacin	≥8	NT	NT	1-256, 8, 128 (65)	2-16, 4, 16 (47)	NT
Tosufloxacin	≥8	NT	NT	0.25->256, 2, 16 (11)	0.5-4, 2, 4 (0)	NT

*: Based on the criteria of the National Committee for Clinical Laboratory Standards (NCCLS, 1995); aerobic or arbitrary resistant breakpoints were used for cefepime, meropenem, ofloxacin and tosufloxacin.

†: Not tested.

‡: The results were for amoxicillin/clavulanate (resistance breakpoint, ≥16/8 μg/mL) not for ampicillin/sulbactam.

A combination of β-lactamase inhibitors such as clavulanate, sulbactam, and tazobactam with β-lactams leads to the enhancement of antimicrobial activity to such a degree that MICs of β-lactams are lowered to susceptible levels for the majority of the *Bacteroides* spp. In our studies (Chong *et al.* 1995; Lee *et al.* 1996; Shin *et al.* 1998), the resistance rates of *B. fragilis* to amoxicillin/clavulanate or ampicillin/sulbactam were less than 5% (Table 2), and those of the non-*fragilis* of *B. fragilis* group organisms were slightly higher (about 10%) (Tables 3, 4).

Piperacillin and ticarcillin are more active than penicillin G against *B. fragilis* group organisms. This increased activity was considered somewhat artificial since the cumulative MICs of these drugs were very similar to those of penicillin G (Rosenblatt, 1989). The patterns seen by this investigator were similar to those of our studies (Tables 2-4). However, they used a much higher breakpoint (≥128 μg/mL) than that of penicillin G (≥2 μg/mL) because of the higher blood levels (Rosenblatt, 1989; NCCLS, 1995). In our studies (Lee *et al.* 1992; Lee *et al.* 1993; Chong *et al.* 1995; Lee *et al.* 1996; Shin *et al.* 1998), the piperacillin resistance rate of *B. fragilis* rose from 12% in 1989−1990 to 25% in 1995−1996 (Table 2). The resistance rates of the non-*fragilis* of *B. fragilis* group oragnisms were higher than those of *B. fragilis,* although the change over time was not remarkable (Tables 3, 4).

Cefoxitin was found to be considerably more active against β-lactamase-producing *Bacteroides* than the penicillins and cephalosporins. This superior activity is attributable to the resistance of cefoxitin to hydrolysis by β-lactamases (Rosenblatt, 1989). The resistance rates of *B. fragilis* to cefoxitin remained unchanged and were less than 5% in this study (Table 2), while those of the non-*fragilis* of *B. fragilis* group organisms fluctuated between 0−23% from 1989 to 1996 (Tables 3, 4). These resistance rates are similar to those of another report (Snydman *et al.* 1996). Cefotetan, another cephamycin, is more active than cefoxitin against most aerobic gram-negative bacilli. The resistance rates (5−10%) to cefotetan of *B. fragilis* were similar to those to cefoxitin (Table 2), but the resistance rates of *B. thetaiotaomicron* (73−96%) and other species of the *B. fragilis* group (47−85%) were much higher than those of *B. fragilis.*

The activity of cefotaxime was unimpressive against *Bacteroides* spp. in our studies. Cefotaxime resistance rates of the non-*fragilis* of *B. fragilis* group organisms were higher than those of *B. fragilis.* The resistance rate of *B. fragilis* rose from 17% in 1989−1990 to over 50% in 1991−1993, and then declined to about 35% in 1994−1996. A fourth generation cephalosporin such as cefepime was introduced recently, which is very useful for the treatment of aerobic gram-negative bacilli infections. Although tested only in 1995−1996 in our studies, the MIC_{50} of cefepime and resistance rates of the *B. fragilis* group were 64->128 μg/mL and >85%, respectively. This result suggested that it would not be useful for the treatment of anaerobic infections due to *B. fragilis* group organisms.

No imipenem-resistant strains of *B. fragilis* group organisms have yet been isolated in Korea, although such strains have been reported in other countries (Bandoh *et al.* 1993; Snydman *et al.* 1996). The increase in resistance is probably due to the increase of drug utilization. In Japan, imipenem is used commonly for the treatment of several kinds of infections. The in vitro activity of meropenem paralleled that of imipenem, although it was tested only in 1992−1994.

In vitro activity of non-β-lactam agent

Clindamycin was one of the active agents against anaerobes, and has been recommended for the treatment of anaerobic infections. However, several investigators reported a dramatic rise in the clindamycin resistance rate. The rate varied greatly depending on the studies. In Spain, quite different clindamycin resistance rates of 6−7% and 45% were reported depending on the hospital (Garcia-Rodriguez and Garcia-Sanchez, 1990; Pelaez *et al.* 1991). In our studies, the clindamycin resistance rate of *B. fragilis* increased remarkably from 18% in 1989−1990 to 43% in 1995−1996 (Table 2). The resistance rate of the non-*fragilis* of *B. fragilis* group organisms rose from 32−38% in 1989−1990 to 70−75% in 1995−1996 (Tables 3, 4).

Clindamycin resistance of anaerobes is due to a nonenzymatic mechanism, alteration in the target site, and is similar to the mechanism of macrolide-

lincosamide-streptogramin resistance of staphylococci (Rasmussen *et al.* 1997). Many plasmid-free strains of *B. fragilis* are capable of clindamycin resistance transfer by conjugative transposon (Hecht *et al.* 1989; Salyers and Shoemaker, 1995). In our previous study (Chong *et al.* 1995), resistance transfer from clindamycin-resistant isolates was relatively common (24%), and the resistance was also transferred from the strains without a plasmid.

Chloramphenicol and metronidazole are still the most active non-β-lactam agents against anaerobic bacteria. No chloramphenicol- or metronidazole-resistant strains were isolated in Korea. With the exception of the gram-positive nonspore-forming rods, all groups of anaerobes are highly susceptible to metronidazole, but reports of resistant strains are very rare. However, in Spain, 2% of *B. fragilis* strains were reported to be resistant to metronidazole (Pelaez *et al.* 1991). They reported that all of the 14 resistant isolates of the *B. fragilis* group organisms were inhibited by ≥ 16 μg/mL of metronidazole. For nine of the 14 strains, the MICs were 32->128 μg/mL.

Fluoroquinolones such as ofloxacin and ciprofloxacin are generally inactive against anaerobic bacteria and have little or no clinically useful activity against *B. fragilis* group organisms (Goldstein and Citron, 1985; Nord *et al.* 1993). Although tested only from 1992 to 1994 in our studies, tosufloxacin was more active than ofloxacin, i.e. the MIC_{50} and MIC_{90} values were two- to eight-fold lower. Recently, new fluoroquinolones such as DU-6859a and trovafloxacin with improved in vitro activity against anaerobic bacteria were introduced (Goldstein, 1996; Kato *et al.* 1996).

The medium used for testing susceptibility of anaerobe can have an effect on the results (Wexler, 1991). NCCLS recommended Wilkins-Chalgren agar for use as a reference agar dilution procedure. In this study, supplemented Brucella blood agar was used from 1989 to 1994, and Wilkins-Chagren agar from 1995 to 1996 (NCCLS, 1993). In our previous study which determined the effect of media on the susceptibilities of *Bacteroides fragilis* group organisms, MICs of many antimicrobial agents tested were slightly higher on Brucella blood agar than on Wilkins-Chagren agar. However, 98% or more of the MIC results were within two $\log_2$ dilution except for metronidazole, and no significant difference was noted in the resistance rate (Shin *et al.* 1997). Therefore, use of Wilkins-Chalgren agar from 1995 to 1996 may have slightly lowered the MIC results of some antimicrobial agents tested.

Recently, breakpoints for resistance have changed. In 1993, the intermediate range was established because of the difficulty in reading end-points and the clustering of MICs at breakpoint concentrations (NCCLS, 1993). In 1995, the resistance breakpoint for penicillin G changed from ≥ 8 μg/mL to ≥ 2 μg/mL (NCCLS, 1995). We used the most recently published breakpoints of the NCCLS (1995).

NCCLS recommended that reading end-points is to examine the plates against a dark, nonreflecting background and to read the end-point at that concentration where a marked change occurs in the appearance of growth as compared to the control plate (NCCLS, 1993). The marked change in growth might be to no growth or lighter growth, to a haze, multiple tiny colonies, or one to several normal-sized colonies. However, we did not ignore the several normal-sized colonies during the study from 1989 to 1993, therefore those MIC results might be slightly higher than those of study from 1994 to 1996.

Although we did not correlate these in vitro data with the clinical outcome, the resistance rates of *B. fragilis* group organisms to some commonly used antimicrobial agents increased, and it may lead to an increase in failures of therapy. Therefore, periodic monitoring of susceptibility of *B. fragilis* group organisms is considered necessary to guide proper selection of suitable antimicrobial agents.

CONCLUSION

Among the 913 clinical isolates of *B. fragilis* group organisms isolated during an 8-year period in Korea, the resistances to antimicrobial agents such as piperacillin, third-generation cephalosporins, and clindamycin were not uncommon, and antimicrobial suceptibility testing of these drugs is necessary before using them. Carbapenem-, chloramphenicol- and metronidazole-resistant strains were not detected. β-lactam and β-lactamase inhibitor combina-

tions and cefoxitin-resistance were not common. Therefore, these agents may be considered when empirical selection of an antimicrobial agents is required to treat severe anaerobic infections.

REFERENCES

Bandoh K, Ueno K, Watanabe K, Kato N: Susceptibility patterns and resistance to imipenem in the *Bacteroides fragilis* group species in Japan: a 4-year study. *Clin Infect Dis 16(Suppl 4): 382-386, 1993*

Baron EJ, Citron DM, Wexler HM: Son of anaerobic susceptibility testing-revisited. *Clin Microbiol Newsletter 12: 69-72, 1990*

Betriu C, Cabronero C, Gomez M, Picazo JJ: Changes in the susceptibility of *Bacteroides fragilis* group organisms to various antimicrobial agents 1979–1989. *Eur J Clin Microbiol Infect Dis 11: 352-356, 1992*

Chong Y, Lee K, Jeong SH, Won DI, Kwon OH, Uh Y, Jang IH, Yoon KJ: Antimicrobial resistance patterns of *Bacteroides* species and the transferability of the resistance by conjugation procedure. *Korean J Infect Dis 27: 181-191, 1995*

Chong Y, Lee K, Kwon OH: Antimicrobial resistance patterns in Korea. *Int J Antimicrob Agents 3: 211-214, 1993*

Chong Y, Lee K, Suh JT, Kim EC, Pai CH, Lee KM, Choi TY: Antimicrobial resistance of aerobic gram-negative bacilli in different sizes of hospitals in Korea. *Korean J Infect Dis 28: 131-141, 1996*

Dubreuil L, Breuil J, Dublanchet A, Sedallian A: Survey of the susceptibility patterns of *Bacteroides fragilis* group strains in France from 1977 to 1992. *Eur J Clin Microbiol Infect Dis 11: 1094-1099, 1992*

Finegold SM: Anaerobic infection-An overview. *Korean J Clin Pathol 11: 507-511, 1991*

Finegold SM, National Committee for Clinical Laboratory Standards Working Group on Anaerobic Susceptibility Testing: susceptibility testing of anaerobic bacteria. *J Clin Microbiol 26: 1253-1256, 1988*

Finegold SM, Wexler HM: Therapeutic implications of bacteriologic findings in mixed aerobic-anaerobic infections. *Antimicrob Agents Chemother 32: 611-616, 1988*

Garcia-Rodriguez JE, Garcia-Sanchez JE: Evolution of antimicrobial susceptibility in isolates of the *Bacteroides fragilis* group in Spain. *Rev Infect Dis 12 (Suppl 2): 142-151, 1990*

Goldstein EJC: Possible role for the new fluoroquinolones (levofloxacin, grepafloxacin, trovafloxacin, clinafloxacin, sparfloxacin, and DU-6859a) in the treatment of anaerobic infections: Review of current information on efficacy and safety. *Clin Infect Dis 23(Suppl 1): 25-30, 1996*

Goldstein EJC, Citron DM: Comparative activity of the quinolones against anaerobic bacteria isolated at community hospitals. *Antimicrob Agents Chemother 27: 657-659, 1985*

Hecht DW, Malamy MH, Tally FP: *Mechanisms of resistance and resistance transfer in anaerobic bacteria.* In Finegold SM, ed. *Anaerobic infections in humans.* San Diego, Academic Press, Inc., *1989, 755-769*

Holdeman LV, Cato EP, Moore WEC: Anaerobe laboratory manual. 4th ed. Blacksburg, Virginia: Virginia Polytechnic Institute and State University, *1977*

Kato N, Kato H, Tanaka-Bandoh K, Watanabe K, Ueno K: Comparison of in vitro activities of DU-6859a and other fluoroquinolones against Japanese isolates of anaerobic bacteria. *Clin Infect Dis 23(Suppl): 31-35, 1996*

Kim HK, Lee K, Chong Y, Kwon OH, Kim JM, Kim DS: Blood culture results at the Severance Hospital during 1984–1993. *Korean J Infect Dis 28: 151-165, 1996*

Lee K, Chong Y, Jeong SH, Xu XS, Kwon OH: Emerging resistance of anaerobic bacteria to antimicrobial agents in South Korea. *Clin Infect Dis 23(suppl 1): 73-77, 1996*

Lee K, Chong Y, Kwon OH, Jang IH, Yoon KJ, Kim SJ: In vitro susceptibilities of *Bacteroides fragilis* group organisms: comparison of the strains isolated in 1990 with 1991. *Korean J Infect Dis 25: 27-32, 1993*

Lee K, Jang IH, Kim YJ, Chong Y: In vitro susceptibilities of the *Bacteroides fragilis* group to 14 antimicrobial agents in Korea. *Antimicrob Agents Chemother 36: 195-197, 1992*

Lee K, Jang IH, Song W, Kim YJ: Evaluation of the anaerobic bacteria from the clinical specimens. *Korean J Clin Pathol 11: 615-625, 1991*

Livermore DM: β-lactamases in laboratory and clinical resistance. *Clin Microbiol Rev 8: 557-584, 1995*

National Committee for Clinical Laboratory Standards: Methods for antimicrobial susceptibility testing of anaerobic bacteria: approved standard. 3rd ed. NCCLS document M11-A3. Villanova, Pa, National Committee for Clinical Laboratory Standards, *1993*

National Committee for Clinical Laboratory Standards: Performance standards for antimicrobial susceptibility testing: sixth informational supplement. NCCLS document M100-S6. Villanova, Pa, National Committee for Clinical Laboratory Standards, *1995*

Nord CE, Lindmark A, Persson I: In vitro activity of the new quinolone BAY y 3118 against anaerobic bacteria. *Eur J Clin Microbiol Infect Dis 12: 640-642, 1993*

Pelaez MT, Cercenado E, Rodriguez-Creixems M, Bouza E: Resistance of anaerobic bacteria to antimicrobial agents. *Rev Infect Dis 13: 183, 1991*

Rasmussen BA, Bush K, Tally FP: Antimicrobial resistance in anaerobes. *Clin Infect Dis 24(Suppl 1): 110-120, 1997*

Redondo MC, Arbo MDJ, Grindlinger J, Snydman DR:

Attributable mortality of bacteremia associated with *Bacteroides fragilis* group. *Clin Infect Dis 20: 1492-1496, 1995*

Rosenblatt JE: *Antimicrobial susceptibility of anaerobic bacteria.* In Finegold SM, ed *Anaerobic infections in humans.* San Diego, Academic Press, *1989, 731-753*

Salyers AA, Shoemaker NB: Conjugative transposons: The force behind the spread of antibiotic resistance genes among *Bacteroides* clinical isolates. *Anaerobe 1: 143-150, 1995*

Shin HJ, Xu XS, Lee J, Lee K, Chong Y, Kwon OH: Effect on the susceptibilities of *Bacteroides fragilis* group organisms by the use of Wilkins-Chalgren agar. *Korean J Clin Pathol Quality Control 19: 191-196, 1997*

Shin JW, Park NJ, Lee K, Chong Y, Cho JW: In vitro susceptibilities of *Bacteroides fragilis* group organisms to several antimicrobial agents, including cefepime. *J Korean Soc Chemother 16: 23-31, 1998*

Snydman DR, McDermott L, Cuchural GJ Jr, Hecht DW, Iannini PB, Harrell LJ, Jenkins SG, O'Keefe JP, Pierson CL, Rihs JD, Yu VL, Finegold SM, Gorbach SL: Analysis of trends in antimicrobial resistance patterns among clinical isolates of *Bacteroides fragilis* group species from 1990 to 1994. *Clin Infect Dis 23(Suppl 1): 54-65, 1996*

Summanen P, Baron EJ, Citron DM, Strong C, Wexler HM, Finegold SM: Wadsworth anaerobic bacteriology manual. 5th ed. Belmont, California, Star Publishing, *1993*

Tanaka-Bandoh K, Kato N, Watanabe K, Ueno K: Antibiotic susceptibility profiles of *Bacteroides fragilis* and *Bacteroides thetaiotaomicron* in Japan from 1990 to 1992. *Clin Infect Dis 20(suppl 2): 352-355, 1995*

Wexler HM: Susceptibility testing of anaerobic bacteria: myth, magic, or method? *Clin Microbiol Rev 4: 470-484, 1991*

Wexler HM, Molitoris E, Finegold SM: Effect of β-lactamase inhibitors on the activities of various β-lactam agents against anaerobic bacteria. *Antimicrob Agents Chemother 35: 1219-1224, 1991*