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Prevalence of Antimicrobial Resistance among Clinical Isolates of *Bacteroides fragilis* Group in Canada in 2010-2011: CANWARD Surveillance Study

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Clinical isolates of the *Bacteroides fragilis* group ($n = 387$) were collected from patients attending nine Canadian hospitals in 2010-2011 and tested for susceptibility to 10 antimicrobial agents using the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method. *B. fragilis* (59.9%), *Bacteroides ovatus* (16.3%), and *Bacteroides thetaiotaomicron* (12.7%) accounted for ~90% of isolates collected. Overall rates of percent susceptibility were as follows: 99.7%, metronidazole; 99.5%, piperacillin-tazobactam; 99.2%, imipenem; 97.7%, ertapenem; 92.0%, doripenem; 87.3%, amoxicillin-clavulanate; 80.9%, tigecycline; 65.9%, cefoxitin; 55.6%, moxifloxacin; and 52.2%, clindamycin. Percent susceptibility to cefoxitin, clindamycin, and moxifloxacin was lowest for *B. thetaiotaomicron* ($n = 49$, 24.5%), *Parabacteroides distasonis*/*P. merdae* ($n = 11$, 9.1%), and *B. ovatus* ($n = 63$, 31.8%), respectively. One isolate (*B. thetaiotaomicron*) was resistant to metronidazole, and two isolates (both *B. fragilis*) were resistant to both piperacillin-tazobactam and imipenem. Since the last published surveillance study describing Canadian isolates of *B. fragilis* group almost 20 years ago (A.-M. Bourgault et al., Antimicrob. Agents Chemother. 36:343–347, 1992), rates of resistance have increased for amoxicillin-clavulanate, from 0.8% (1992) to 6.2% (2010-2011), and for clindamycin, from 9% (1992) to 34.1% (2010-2011).

Members of the *Bacteroides fragilis* group are important human pathogens and are most frequently associated with intra-abdominal, pelvic, complicated skin and soft tissue, and bloodstream infections (6). The *B. fragilis* group is comprised of >20 species, which are commonly isolated from patient specimens as a component of a mixed infection. The susceptibility of isolates of the *B. fragilis* group has been demonstrated to vary for individual species (6, 15) and by geographic location (5), and *in vitro* antimicrobial susceptibility testing results have been shown to be relevant to determining patient outcome, even in the presence of mixed infections (13). For example, in one study of 128 patients with *Bacteroides* bacteremia that assessed the correlation between *in vitro* antimicrobial susceptibility testing results and clinical outcome, the investigators reported a 30-day mortality rate of 45% for patients with inactive antimicrobial therapy, compared with a rate of only 16% ($P = 0.04$) for patients receiving active therapy (13). Further, inactive therapy was associated with a rate of treatment failure of 82%, compared with a rate of 22% ($P = 0.002$) for patients receiving active therapy, and microbiological persistence was found to be 42% for patients receiving inactive therapy versus 12% for patients receiving active therapy ($P = 0.06$) (13). Unfortunately, even in 2011, anaerobic antimicrobial susceptibility testing is not routinely performed in many clinical laboratories and physicians are forced to rely on published surveillance studies to help guide their empirical antimicrobial prescribing decisions (6, 8).

Antimicrobial susceptibility testing data for clinical isolates of the *B. fragilis* group collected from Canadian patients have not been published in almost 20 years (2). During this time, *B. fragilis* group isolates have been reported to have evolved in other locations from relatively susceptible organisms to pathogens that now may potentially demonstrate resistance to all classes of antianaerobe agents, including carbapenems and metronidazole (6, 10, 15). Investigators in the United States have reported resistance among *B. fragilis* group organisms to be high and increasing with agents such as cefoxitin, clindamycin, and moxifloxacin (8, 15, 17). The goal of the current study was to assess the *in vitro* activities of 10 frequently tested antimicrobial agents with antianaerobe activity against *B. fragilis* group organisms isolated from patients in Canadian hospitals in 2010-2011.

MATERIALS AND METHODS

B. fragilis group isolates were collected by nine Canadian hospital laboratories from January 2010 to August 2011 and shipped to the coordinating laboratory (Health Sciences Centre, Winnipeg, Manitoba, Canada). Each laboratory was asked to collect 50 consecutive *B. fragilis* group isolates. Each isolate was deemed clinically significant by individual clinical microbiology laboratory algorithms; isolates were limited to one per patient. Isolate inclusion was independent of patient age. The coordinating laboratory confirmed the identities of all isolates using Vitek ANC identification cards and a Vitek 2 instrument (bioMérieux, Durham, NC) and ancillary tests as required (12). In total, 387 *B. fragilis* group isolates were available for antimicrobial susceptibility testing. These included 232 *B. fragilis* (59.9%), 63 *Bacteroides ovatus* (16.3%), 49 *Bacteroides thetaiotaomicron* (12.7%), 24 *Bacteroides stercoris* (6.2%), 11 *Parabacteroides distasonis*/*P. merdae* (2.8%), and 6 *Bacteroides vulgatus* (1.6%) isolates, 1 *Bacteroides uniformis* (0.3%) isolate, and 1 *Bacteroides caccae* (0.3%) isolate.

In vitro susceptibilities to 10 antimicrobial agents were determined using the broth microdilution method recommended by the Clinical and Laboratory Standards Institute (CLSI) (3). In-house-prepared broth microdilution panels included amoxicillin-clavulanate, cefoxitin, clindamy-

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cin, doripenem, ertapenem, imipenem, piperacillin-tazobactam, metronidazole, moxifloxacin, and tigecycline. MICs were interpreted using breakpoints published in the M100-S21 (2011) document (4) for all agents except doripenem (Doribax package insert, 2007) and tigecycline (Tygacil package insert, 2011), for which the U.S. Food and Drug Administration (FDA)-recommended MIC breakpoints were used. *B. fragilis* ATCC 25285 and *B. thetaiotaomicron* ATCC 29741 served as quality control strains and were run with each batch of isolates tested (4). Statistical analyses were performed by χ^2 testing with the EpiInfo Statcalc (version 6.0) program (Centers for Disease Control and Prevention). Uncorrected *P* values of <0.05 were considered statistically significant.

RESULTS

The nine participating laboratories submitted 387 isolates of the *B. fragilis* group (range, 7 to 70 isolates; mean, 43.0 isolates; standard deviation, ±16.3 isolates). *B. fragilis* was the most frequent isolate submitted by all nine participating laboratories and accounted for 51.1 to 67.4% of isolates in the seven laboratories submitting 40 or more isolates; isolates of other *B. fragilis* group species were relatively evenly distributed across the nine participating laboratories (data not shown). The *B. fragilis* group isolates submitted were from wound ($n = 255$), blood ($n = 130$), and respiratory ($n = 2$) sources. The isolates were from patients that ranged in age from 1 to 98 years, with 14 isolates (3.6%) from patients aged ≤17 years, 222 isolates (57.4%) from patients aged 18 to 64 years, and 151 isolates (39.0%) from patients aged ≥65 years; 61.2% of isolates were from male patients. Significant ($P < 0.5$) associations between species of *Bacteroides* isolated and specimen source, between species of *Bacteroides* isolated and patient age, and between species of *Bacteroides* isolated and patient gender were not observed (data not shown).

Susceptibility rates for the 10 antimicrobial agents tested against *B. fragilis* group isolates are presented in Table 1. Metronidazole, piperacillin-tazobactam, imipenem, and ertapenem were the agents to which the isolates had the highest *in vitro* susceptibilities (>97%). One isolate (*B. thetaiotaomicron* isolated from blood) was resistant to metronidazole, and two isolates (one blood isolate, one wound isolate), both *B. fragilis*, were resistant to both piperacillin-tazobactam and imipenem; an additional isolate (*B. vulgatus*) was imipenem intermediate. Three isolates (two *B. fragilis*, one *B. vulgatus*) were resistant to ertapenem, and six isolates (five *B. fragilis*, one *B. thetaiotaomicron*) were ertapenem intermediate. Thirty-one isolates were nonsusceptible to doripenem; however, the doripenem susceptibility breakpoint (≤1 μg/ml; Doribax package insert, 2007) is 2 doubling dilutions lower than the CLSI breakpoints for ertapenem and imipenem (≤4 μg/ml, susceptible) (4) and is not an indicator of vastly different *in vitro* potencies for these three carbapenems (Table 2). Percent susceptibility to cefoxitin, clindamycin, and moxifloxacin was lowest for *B. thetaiotaomicron* ($n = 49$, 24.5%), *P. distasonis*/*P. merdae* ($n = 11$, 9.1%), and *B. ovatus* ($n = 63$, 31.8%), respectively. MIC distributions for the 10 antimicrobial agents tested against *B. fragilis* group isolates are presented in Table 2.

Geographic variation in the susceptibilities of isolates to cefoxitin, clindamycin, moxifloxacin, and tigecycline was not observed; however, the numbers of isolates tested per site may have been too low for differences to be apparent. The percentages of isolates of *B. ovatus* and *B. thetaiotaomicron*, the species most frequently associated with resistance, were consistent across submitting laboratories. Significant differences ($P < 0.5$) in rates of susceptibility were not observed for any antimicrobial agent tested when isolates were grouped by specimen source (i.e., blood isolates compared with isolates from wounds) (data not shown).

Of the 387 *B. fragilis* group isolates tested, 26.1, 25.8, 23.8, and 24.3%, respectively, were resistant to 0, 1, 2, and ≥3 antimicrobial agent classes (Table 3). Among multidrug-resistant isolates (isolates resistant to ≥3 antimicrobial agent classes), 93.6% (88/94) were resistant to clindamycin, 88.3% (83/94) were resistant to moxifloxacin, 72.3% (68/94) were resistant to cefoxitin, 55.3% (52/94) were resistant to tigecycline, and 38.3% (36/94) were resistant to amoxicillin-clavulanate. Isolates of *B. ovatus* (47.6%, 30/63) and *B. thetaiotamicron* (49.0%, 24/49) were more frequently multidrug resistant than were isolates of *B. fragilis* (12.5%, 29/232).

DISCUSSION

The most recently published studies describing antimicrobial susceptibility testing data for *B. fragilis* group isolates from Canadian patients were both authored by Bourgault and coworkers in 1992 (2) and 1986 (1). The study published in 1992 reported on 348 *B. fragilis* group isolates collected from six medical centers in 1990 (2); the MIC resistance breakpoints listed in that paper for amoxicillin-clavulanate, piperacillin-tazobactam, cefoxitin, imipenem, clindamycin, and metronidazole were identical to those recommended by CLSI in 2011 (4). The study published in 1986 described 260 *B. fragilis* group isolates collected in 1984 by five medical centers (1); the MIC resistance breakpoints listed in that paper (which were referred to as higher breakpoints by the authors) for cefoxitin and metronidazole were identical to those recommended by CLSI in 2011 (4), while the MIC resistance breakpoint for clindamycin was 1 doubling dilution higher (16 μg/ml) than that currently recommended (4). Between 1986 and 1992, Bourgault et al. reported that there was an increase in resistance to clindamycin, from 0.6 to 8.9% (some of this change may have been attributable to the difference in breakpoints), and to cefoxitin, from 2 to 26% (1, 2). In the current study, rates of resistance to clindamycin were higher (34.1%) and those to cefoxitin were lower (15.2%) than in the 1992 study (2). The decrease in cefoxitin resistance from 26% (1992) to 15.2% (present study) is initially perplexing, as the resistance breakpoint (≥64 μg/ml) was identical in the two studies but may be explained by the clustering of MICs close to the resistance breakpoint, differences in species composition of the *Bacteroides* isolates tested in the different studies (15), and/or differences in cefoxitin use over time. The rate of resistance for amoxicillin-clavulanate also increased from 0.8% (1992) (2) to 6.2% in the current study. No metronidazole-resistant isolates were reported in the 1986 (1) and 1992 (2) publications; piperacillin-tazobactam-resistant and imipenem-resistant isolates of *B. fragilis* group were not reported in the 1992 report (2).

In 2011, *B. fragilis* group isolates may demonstrate resistance to all classes of antianaerobe agents, including carbapenems and metronidazole (6, 10). Metronidazole-resistant isolates, although very rare in North America (15, 16), have been reported to arise via chromosomal or plasmid carriage of one of nine known *nim* genes (*nimA* to *nimI*); *nim* genes code for a nitroimidazole reductase that may be expressed at very low levels (15). Currently, metronidazole resistance has been reported to occur in <1% of *B. fragilis* group isolates in the United States; however, as many as 3% of *Bacteroides* isolates are suspected of harboring one of the *nim*

TABLE 1 *In vitro* activities of antimicrobial agents tested against 387 isolates of *Bacteroides* spp.

Organism (no. of isolates tested)/antimicrobial agent	MIC (μg/ml)			%		
	50%	90%	Range	Susceptible	Intermediate	Resistant
All *Bacteroides* spp.[a] (387)						
Amoxicillin-clavulanate	1	8	0.25–32	87.3	6.5	6.2
Piperacillin-tazobactam	0.25	8	≤0.015–>256	99.5	0	0.5
Cefoxitin	16	64	≤1–>128	65.9	18.9	15.2
Ertapenem	0.5	2	0.12–>32	97.7	1.5	0.8
Imipenem	0.25	1	0.06–>32	99.2	0.3	0.5
Doripenem[b]	≤0.25	1	≤0.25–>2	92.0	NA[c]	NA
Clindamycin	2	>16	≤0.25–>16	52.2	13.7	34.1
Metronidazole	1	4	≤0.12–32	99.7	0	0.3
Moxifloxacin	2	>16	0.12–>16	55.6	10.6	33.8
Tigecycline[b]	1	8	≤0.06–32	80.9	11.1	8.0
Bacteroides fragilis (232)						
Amoxicillin-clavulanate	0.5	8	0.25–32	89.2	5.2	5.6
Piperacillin-tazobactam	0.12	1	≤0.015–>256	99.1	0	0.9
Cefoxitin	8	32	2–>128	82.8	7.7	9.5
Ertapenem	0.25	2	0.12–>32	97.0	2.1	0.9
Imipenem	0.12	1	0.06–>32	99.1	0	0.9
Doripenem	≤0.25	1	≤0.25–>2	90.1	NA	NA
Clindamycin	1	>16	≤0.25–>16	66.4	6.0	27.6
Metronidazole	1	2	0.25–8	100	0	0
Moxifloxacin	1	16	0.12–>16	65.5	7.8	26.7
Tigecycline	1	8	0.25–16	85.8	9.9	4.3
Bacteroides ovatus (63)						
Amoxicillin-clavulanate	1	16	0.25–32	77.8	9.5	12.7
Piperacillin-tazobactam	2	16	≤0.015–32	100	0	0
Cefoxitin	32	128	4–>128	42.9	27.0	30.1
Ertapenem	1	4	0.12–4	100	0	0
Imipenem	0.25	0.5	0.12–2	100	0	0
Doripenem	0.5	1	≤0.25–2	96.8	NA	NA
Clindamycin	4	>16	1–>16	28.6	27.0	44.4
Metronidazole	1	4	≤0.12–8	100	0	0
Moxifloxacin	4	>16	0.5–>16	31.8	20.6	47.6
Tigecycline	1	16	≤0.06–32	71.4	11.1	17.5
Bacteroides thetaiotaomicron (49)						
Amoxicillin-clavulanate	1	8	0.25–32	87.8	8.2	4.0
Piperacillin-tazobactam	8	16	≤0.015–32	100	0	0
Cefoxitin	32	64	8–>128	24.5	61.2	14.3
Ertapenem	1	2	0.12–8	98.0	2.0	0
Imipenem	0.25	0.5	0.06–2	100	0	0
Doripenem	0.5	1	≤0.25–2	95.9	NA	NA
Clindamycin	8	>16	≤0.25–>16	22.5	26.5	51.0
Metronidazole	1	4	≤0.12–32	98.0	0	2.0
Moxifloxacin	4	>16	0.5–>16	34.7	20.4	44.9
Tigecycline	2	16	0.5–16	69.4	18.4	12.2
Bacteroides stercoris (24)						
Amoxicillin-clavulanate	0.5	4	0.25–16	91.7	4.1	4.2
Piperacillin-tazobactam	0.25	8	≤0.015–16	100	0	0
Cefoxitin	8	64	≤1–>128	62.5	16.7	20.8
Ertapenem	0.5	2	0.12–4	100	0	0
Imipenem	0.25	1	0.06–1	100	0	0
Doripenem	≤0.25	1	≤0.25–>2	91.7	NA	NA
Clindamycin	2	>16	≤0.25–>16	58.3	20.8	20.9
Metronidazole	2	4	0.5–8	100	0	0
Moxifloxacin	2	16	0.25–>16	62.5	0	37.5
Tigecycline	1	16	0.5–32	70.8	12.5	16.7
Parabacteroides distasonis/P. merdae (11)						
Amoxicillin-clavulanate	2	4	0.25–8	90.9	9.1	0
Piperacillin-tazobactam	4	4	1–8	100	0	0
Cefoxitin	32	64	16–>128	36.4	36.3	27.3
Ertapenem	1	1	0.5–2	100	0	0
Imipenem	0.5	1	0.06–2	100	0	0
Doripenem	≤0.25	1	≤0.25–1	100	NA	NA
Clindamycin	8	>16	1–>16	9.1	36.3	54.6
Metronidazole	1	2	0.25–2	100	0	0
Moxifloxacin	1	>16	0.5–>16	72.7	0	27.3
Tigecycline	1	4	0.25–4	100	0	0

[a] The 387 isolates included 232 *B. fragilis*, 63 *B. ovatus*, 49 *B. thetaiotamicron*, 24 *B. stercoris*, 11 *Parabacteroides distasonis/merdae*, and 6 *B. vulgatus* isolates, 1 *B. uniformis* isolate, and 1 *B. caccae* isolate. Individual species data are presented only where isolate numbers were ≥10.

[b] Clinical and Laboratory Standards Institute (M100-S21, 2011) MIC interpretative breakpoints not available. FDA MIC interpretative breakpoints used.

[c] NA, not available.

TABLE 2 Distributions of MICs for antimicrobial agents tested against 387 isolates of *Bacteroides* spp.

Antimicrobial agent	No. of isolates (cumulative % inhibition) for which the antimicrobial agent MIC (μg/ml) was[a]:												
	≤0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	≥64
Piperacillin-tazobactam	35 (9.0)	13 (12.4)	16 (16.5)	77 (36.4)	65 (53.2)	24 (59.4)	29 (66.9)	27 (73.9)	31 (81.9)	46 (93.8)	20 (99.0)	**2 (99.5)**	2[b] (100)
Imipenem			79 (20.4)	108 (48.3)	85 (70.3)	66 (87.3)	31 (95.4)	13 (98.7)	**2 (99.2)**	1 (99.5)	1 (99.7)	1 (100)	
Ertapenem				57 (14.7)	106 (42.1)	55 (56.3)	96 (81.1)	38 (90.9)	**26 (97.7)**	6 (99.2)	1 (99.5)	2 (100)	
Doripenem					246 (63.4)	82 (84.5)	**28 (92.0)**	12[c] (95.1)					
Metronidazole				2 (0.5)	9 (2.8)	45 (14.5)	170 (58.4)	122 (89.9)	34 (98.7)	**4 (99.7)**	0 (99.7)	1 (100)	
Tigecycline			1 (0.3)	4 (1.3)	17 (5.7)	87 (28.2)	135 (63.0)	38 (72.9)	**31 (80.9)**	43 (92.0)	29 (99.5)	2 (100)	
Amoxicillin-clavulanate					35 (9.0)	138 (44.7)	63 (61.0)	66 (78.0)	**36 (87.3)**	25 (93.8)	19 (98.7)	5 (100)	
Moxifloxacin				1 (0.3)	15 (4.1)	92 (27.9)	50 (40.8)	**57 (55.5)**	41 (66.1)	49 (78.8)	33[d] (87.6)		
Clindamycin					41 (10.6)	29 (18.1)	79 (38.5)	**53 (52.2)**	53 (65.9)	10 (68.5)	4[d] (69.6)		
Cefoxitin							2 (0.5)	1 (0.8)	42 (11.6)	136 (46.8)	**74 (65.9)**	73 (84.8)	59[b] (100)

[a] Susceptible MIC breakpoint is indicated in bold type for each antimicrobial agent.
[b] Two/2 (piperacillin-tazobactam) and 21/59 (cefoxitin) isolate MICs were >64 μg/ml.
[c] Nineteen/31 (doripenem) isolate MICs were >2 μg/ml; concentrations of doripenem of >2 μg/ml were not tested.
[d] Forty-nine/82 (moxifloxacin) and 118/122 (clindamycin) isolate MICs were >16 μg/ml; concentrations of moxifloxacin and clindamycin of >16 μg/ml were not tested.

genes (15). In the current study, one isolate (*B. thetaiotaomicron*) was resistant to metronidazole.

In Taiwan, rates of nonsusceptibility to imipenem and meropenem for *B. fragilis* isolates have been reported to be 7% and 12%, respectively (10). In the current study, 3 isolates were nonsusceptible to imipenem (0.8%), 9 isolates (2.3%) were nonsusceptible to ertapenem, and 31 isolates (8.0%) were nonsusceptible to doripenem. Table 2 suggests that the differences in susceptibility for the three carbapenems tested arose because of the differences in their respective breakpoints and were not due to differences in their

TABLE 3 Distribution of resistance and MDR[a] phenotypes for 387 isolates of *Bacteroides* spp.

No. of agents to which isolate was resistant	No. of isolates	% of all isolates	% of MDR isolates	Most frequent resistance phenotypes (no. of isolates, %)
0	101	26.1	0	None
1	100	25.8	0	Moxifloxacin (36, 36.0)
				Clindamycin (31, 30.0)
				Cefoxitin (20, 20.0)
				Tigecycline (9, 9.0)
				Amoxicillin-clavulanate (4, 4.0)
2	92	23.8	0	Clindamycin, moxifloxacin (33, 35.9)
				Cefoxitin, clindamycin (25, 27.2)
				Cefoxitin, moxifloxacin (13, 14.1)
				Clindamycin, tigecycline (5, 5.4)
				Moxifloxacin, tigecycline (5, 5.4)
				Amoxicillin-clavulanate, cefoxitin (4, 4.3)
				Amoxicillin-clavulanate, clindamycin (3, 3.3)
				Cefoxitin, tigecycline (2, 2.2)
				Amoxicillin-clavulanate, moxifloxacin (1, 1.1)
				Amoxicillin-clavulanate, tigecycline (1, 1.1)
3	55	14.2	58.5	Cefoxitin, clindamycin, moxifloxacin (20, 36.4)
				Clindamycin, moxifloxacin, tigecycline (13, 23.6)
				Amoxicillin-clavulanate, cefoxitin, clindamycin (7, 12.7)
				Amoxicillin-clavulanate, clindamycin, moxifloxacin (6, 10.9)
				Cefoxitin, moxifloxacin, tigecycline (5, 9.1)
				Cefoxitin, clindamycin, tigecycline (2, 3.6)
				Amoxicillin-clavulanate, moxifloxacin, tigecycline (1, 1.8)
				Clindamycin, imipenem, moxifloxacin (1, 1.8)
4	30	7.8	31.9	Cefoxitin, clindamycin, moxifloxacin, tigecycline (17, 56.7)
				Amoxicillin-clavulanate, cefoxitin, clindamycin, moxifloxacin (7, 23.3)
				Amoxicillin-clavulanate, clindamycin, moxifloxacin, tigecycline (4, 13.3)
				Amoxicillin-clavulanate, clindamycin, metronidazole, moxifloxacin (1, 3.3)
				Amoxicillin-clavulanate, cefoxitin, clindamycin, tigecycline (1, 3.3)
5	7	1.8	7.4	Amoxicillin-clavulanate, cefoxitin, clindamycin, moxifloxacin, tigecycline (7, 100)
6	1	0.3	1.1	Amoxicillin-clavulanate, cefoxitin, clindamycin, imipenem, piperacillin-tazobactam, tigecycline (1, 100)
7	1	0.3	1.1	Amoxicillin-clavulanate, cefoxitin, clindamycin, imipenem, moxifloxacin, piperacillin-tazobactam, tigecycline (1, 100)

[a] MDR, multidrug resistance, defined as resistance to ≥3 antimicrobial classes (amoxicillin-clavulanate, cefoxitin, clindamycin, imipenem, metronidazole, moxifloxacin, piperacillin-tazobactam, tigecycline).

relative *in vitro* activities (11). MIC data interpreted by use of EUCAST breakpoints (doripenem and ertapenem susceptible MIC breakpoint, ≤1 μg/ml; imipenem susceptible MIC breakpoint, ≤2 μg/ml) would generate different rates of susceptibility (doripenem, 92.0%; ertapenem, 81.2%; imipenem, 98.7%) than those reported here using CLSI interpretations. Previous studies have shown some imipenem- and meropenem-resistant isolates of the *B. fragilis* group to harbor genes for metallo-β-lactamases, specifically, *ccrA* or *cfiA* (7, 18). The *cfiA* gene may not be highly expressed in many isolates of *Bacteroides* species in which it is found, and carbapenem-susceptible isolates have been reported to harbor the *cfiA* gene (18). A study of South Korean clinical isolates of *B. fragilis* recovered from 1997 to 2004 found 3 of 276 (1.1%) isolates to be carbapenem resistant, with 4.0% of isolates harboring *cfiA* (14). The regulation of expression of *cfiA* in *B. fragilis* has been shown to involve insertion sequence elements (18), and isolates not expressing a resident *cfiA* gene may convert to a resistant phenotype by a one-step mutation in the region upstream of the gene (15). A DNA typing study indicates that *cfiA*-positive isolates may encompass a distinct subgroup of *B. fragilis*; this group appears to be identical to the chromosomal DNA homology group II of *B. fragilis* (9, 18).

In the current study, only 55.6% of all *B. fragilis* group isolates tested were susceptible to moxifloxacin; susceptibilities to moxifloxacin were highest for *P. distasonis*/*P. merdae* (72.7%), *B. fragilis* (65.5%), and *B. stercoris* (62.5%) and lowest for *B. thetaiotaomicron* (34.7%) and *B. ovatus* (31.8%). In 2011, Goldstein and Citron summarized results from published studies testing moxifloxacin against members of the *B. fragilis* group and found rates of susceptibility to range from 32 to 90% (7). Snydman et al. (17) also reported that resistance to fluoroquinolones differed for various species of *Bacteroides*, with *B. fragilis* being the most susceptible to moxifloxacin and *B. vulgatus* the most resistant (>50% of isolates). Cumulatively, these data suggest that if moxifloxacin is to be considered for therapy, it needs to be tested against the patient's isolate (7). It has also been suggested that differences in fluoroquinolone susceptibilities may exist in isolates of the *B. fragilis* group, as well as other pathogens, due to differences in patterns of fluoroquinolone use in different centers and their surrounding communities (16).

Previous descriptions of multidrug-resistant isolates of *B. fragilis* group have not been published. Among the multidrug-resistant isolates in this study, most were resistant to clindamycin (93.6%), moxifloxacin (88.3%), and cefoxitin (72.3%). Isolates of *B. ovatus* (47.6%, 30/63) and *B. thetaiotaomicron* (49.0%, 24/49) were more frequently multidrug resistant than were isolates of *B. fragilis* (12.5%, 29/232). Metronidazole, piperacillin-tazobactam, imipenem, and ertapenem were highly active *in vitro* against current clinical isolates of *B. fragilis* group species, regardless of resistance to other frequently tested antimicrobial agents; however, it was interesting to note that the one metronidazole-resistant isolate identified and the two isolates resistant to both imipenem and piperacillin-tazobactam demonstrated multidrug-resistant phenotypes (Table 3).

One limitation of the current study that exists in most other surveillance initiatives as well is that our results may underestimate rates of susceptibility because only larger tertiary care academic hospitals were included in the study and rates of antimicrobial susceptibility tend to be lower in larger centers than smaller centers because of the greater complexity of patients admitted.

In conclusion, carbapenems (imipenem, ertapenem), metronidazole, and piperacillin-tazobactam continue to provide predictably effective *in vitro* activity against all species of the *B. fragilis* group in Canada. The selection of agents such as fluoroquinolones, clindamycin, and cefoxitin for the treatment of serious infections should be based upon the results of individual susceptibility tests and not upon institutional antibiograms (if available) or national surveillance studies (16). The propensity for non-*B. fragilis Bacteroides* species to more frequently demonstrate antimicrobial-resistant phenotypes underscores the need to determine the species of *B. fragilis* group isolates, particularly from serious infections (17). Continued surveillance is warranted, as many laboratories do not perform antimicrobial susceptibility testing on anaerobes, and broader surveillance data provide information that may lead to improved empirical antimicrobial prescribing and may potentially increase treatment effectiveness (17).

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