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In Vitro Activity of Moxifloxacin against 923 Anaerobes Isolated from Human Intra-Abdominal Infections

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The in vitro activity of moxifloxacin against 923 recent anaerobic isolates obtained from pretreatment cultures in patients with complicated intra-abdominal infections was studied using the CLSI M11-A-6 agar dilution method. Moxifloxacin was active against 87% (96 of 110) *Bacteroides fragilis* strains at ≤1 μg/ml and 87% (79 of 90) *B. thetaiotaomicron* strains at ≤2 μg/ml. Species variation was seen, with *B. uniformis*, *B. vulgatus*, *Clostridium clostridioforme*, and *C. symbiosum* being least susceptible and accounting for most of the resistant isolates; excluding the aforementioned four resistant species, 86% (303 of 363) of *Bacteroides* species isolates and 94% (417 of 450) of all other genera and species were susceptible to ≤2 μg/ml of moxifloxacin. Overall, moxifloxacin was active against 763 of 923 (83%) of strains at ≤2 μg/ml, supporting its use as a monotherapy for some community-acquired intra-abdominal infections.

Intra-abdominal infections are known to be composed of mixed aerobic and anaerobic bacteria (9). Current guidelines (22) recommend combining a fluoroquinolone with metronidazole for therapy of community-acquired intra-abdominal infections. Moxifloxacin, an 8-methoxyquinolone, has been reported to have activity against a broad spectrum of both aerobic and anaerobic bacteria (1, 4–6, 10, 14, 15, 25) such as encountered in intra-abdominal infections. However, many older in vitro studies employed a variety of media and methods and utilized isolates collected from a wide range of clinical sources. Moreover, older isolates may not reflect potential resistance that has since developed from use of the fluoroquinolones. Moxifloxacin has been reported to penetrate and accumulate in the human gastrointestinal mucosa (24) and a comparative mouse model study (19) has supported its use as a single agent in intra-abdominal infections. Clinical studies performed to evaluate the efficacy of moxifloxacin in mixed aerobic/anaerobic intra-abdominal infections have been reported in abstract form (M. Malangoni, J. Song, S. Choudri, P. Potgieter, and P. Cyrus, 44th Intersci. Conf. Antimicrob. Agents Chemother., abstr. L-990, 2004). In order to further evaluate its potential for this indication, we studied the comparative activity of moxifloxacin against 923 sequential anaerobic strains isolated from pretherapy cultures of patients with complicated intra-abdominal infections.

MATERIALS AND METHODS

Isolates were collected between 2001 and April 2004 from pretherapy clinical specimens from patients with complicated community-acquired intra-abdominal infections, some as part of a 56-site United States clinical trial for which we were a reference laboratory. The primary specimens were sent by overnight courier and cultured in our laboratory. All isolates were identified by standard criteria (13, 16) and some, when required, were identified by sequencing of the 16S RNA gene.

Standard laboratory powders of the following antimcirobial agents were obtained as follows: moxifloxacin, Bayer Inc., West Haven, CT; levofloxacin, R.W. Johnson Pharmaceutical Research Institute, Raritan, NJ; cefoxitin, Merck Inc., West Point, PA; ampicillin-sulbactam and clindamycin, Pfizer Inc., New York, NY; and metronidazole, Searle, Skokie, IL.

Frozen cultures were transferred twice onto brucella agar supplemented with hemin, vitamin K_1 and 5% sheep blood to ensure purity and good growth. Susceptibility testing was performed according to CLSI standards (M11-A6) (17). Antimicrobial agents were reconstituted according to the manufacturers' instructions and serial twofold dilutions of antimicrobial agents were prepared on the day of the test and were added to the media at various concentrations. The agar plates were inoculated with a Steers replicator (Craft Machine Inc., Chester, PA) with an inoculum of 10^5 CFU/spot. Control plates without antimicrobial agents were inoculated before and after each set of drug-containing plates. Plates were incubated at 35°C for 48 h in an anaerobic chamber (Anaerobe Systems, CA) and were then examined. The control strains tested included *Bacteroides fragilis* strain ATCC 25285 and *B. thetaiotaomicron* strain ATCC 29741. The MIC was defined as the lowest concentration of an agent that yielded no growth or a marked change in the appearance of growth compared to the control plates.

RESULTS

The activities of the antimicrobial agents tested are shown in Table 1. Quality control results are reported in Table 2. Overall, 83% (763 of 923) of isolates were susceptible to ≤2 μg/ml of moxifloxacin. CLSI (formerly NCCLS) breakpoints have yet to be established for moxifloxacin against anaerobes, and we chose a conservative value of 2 μg/ml as a cutoff. For moxifloxacin and levofloxacin, isolates were considered susceptible if they had an MIC of ≤2 μg/ml and nonsusceptible if they had an MIC of ≥4 μg/ml. There was species variation in the *Bacteroides fragilis* group (species) as well as clusters of some isolates within a species, which required higher concentrations for inhibition. The MIC_{90} of the 110 *B. fragilis* strains to moxifloxacin was 8 μg/ml, but 96 (87%) were susceptible to ≤1 μg/ml with a geometric mean MIC of 0.69 μg/ml. Levofloxacin was generally twofold less active, with an MIC_{90} of >16 μg/ml and 14% resistant (MIC, ≥8 μg/ml); one isolate had a metronidazole MIC of 8 μg/ml and was susceptible to 0.25 μg/ml of

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TABLE 1. Comparative in vitro activities of moxifloxacin against 923 anaerobic strains obtained from pretreatment cultures from patients with community-acquired complicated intra-abdominal infections

Organism (no. of isolates) and antimicrobial agent	MIC (μg/ml)			% Susceptible[a]		
	Range	50%	90%	GM[b]	Breakpoint 1	Breakpoint 2
Bacteroides caccae (20)						
Moxifloxacin	1–>16	2	16	3.36	20	65
Levofloxacin	2–>16	8	>16	9.19	5	35
Clindamycin	≤0.06–>32	2	>32	3.96	70	75
Cefoxitin	4–32	16	32	16.56	75	100
Ampicillin-sulbactam	0.25–16	1	4	1.32	90	100
Metronidazole	≤0.06–2	1	2	0.92	100	
Bacteroides distasonis (40)						
Moxifloxacin	0.125–>16	0.5	8	0.63	85	87.5
Levofloxacin	0.5–>16	1	16	1.83	85	85
Clindamycin	≤0.06–>32	2	>32	2.88	50	77.5
Cefoxitin	4–64	16	32	17.15	60	92.5
Ampicillin-sulbactam	0.5–32	4	16	4.29	85	97.5
Metronidazole	0.125–4	1	2	0.84	100	
Bacteroides fragilis (110)						
Moxifloxacin	0.25–>16	0.5	8	0.69	84.5	88
Levofloxacin	0.5–>16	1	>16	1.97	81	85.5
Clindamycin	≤0.06–>32	0.5	2	0.85	90	90
Cefoxitin	2–64	8	16	6.88	94.5	98
Ampicillin-sulbactam	0.25–>32	1	4	1.18	96	99
Metronidazole	≤0.06–8	1	2	0.94	100	
Bacteroides merdae (12)						
Moxifloxacin	0.25–16	0.5	16	0.84	75	75
Levofloxacin	1–>16	1	>16	2.67	75	75
Clindamycin	≤0.06–>32	1	>32	3.85	58	67
Cefoxitin	8–64	16	32	21.36	58	92
Ampicillin-sulbactam	2–16	4	16	4.76	75	100
Bacteroides ovatus (50)						
Moxifloxacin	1–>16	2	16	2.91	14	70
Levofloxacin	2–>16	8	>16	9.19	4	22
Clindamycin	≤0.06–>32	2	>32	4.06	64	70
Cefoxitin	1–>128	16	32	21.41	56	90
Ampicillin-sulbactam	0.5–16	1	8	1.47	98	100
Metronidazole	0.125–2	1	2	0.95	100	
Bacteroides splanchnicus (30)						
Moxifloxacin	0.5–>16	2	2	1.66	37	97
Levofloxacin	0.2–16	2	2	1.82	90	97
Clindamycin	≤0.06–>32	≤0.06	32	0.19	83	83
Cefoxitin	0.25–32	2	8	2.41	97	100
Ampicillin-sulbactam	0.25–8	1	2	1.10	100	
Metronidazole	≤0.06–0.25	0.125	0.25	0.12	100	
Bacteroides stercoris (11)						
Moxifloxacin	0.25–>16	0.5	16	1.13	73	73
Levofloxacin	0.5–>16	1	16	2.27	73	73
Clindamycin	0.125–>32	2	>32	3.53	73	73
Cefoxitin	1–32	16	32	10.29	73	100
Ampicillin-sulbactam	0.5–2	2	2	1.37	100	
Metronidazole	0.125–1	1	1	0.57	100	
Bacteroides thetaiotaomicron (90)						
Moxifloxacin	0.5–>16	1	4	1.55	65.5	85.5
Levofloxacin	2–>16	4	16	4.42	24	79
Clindamycin	≤0.06–>32	4	>32	7.28	40	65.5
Cefoxitin	2–128	32	32	24.63	39	93
Ampicillin-sulbactam	0.5–32	1	8	1.78	94	98
Metronidazole	≤0.06–4	1	2	0.91	100	
Bacteroides uniformis (35)						
Moxifloxacin	0.125–>16	2	>16	3.09	31	54
Levofloxacin	0.25–>16	4	>16	6.06	21	51

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TABLE 1—*Continued*

Organism (no. of isolates) and antimicrobial agent	MIC (μg/ml)			% Susceptible[a]		
	Range	50%	90%	GM[b]	Breakpoint 1	Breakpoint 2
Clindamycin	≤0.06–>32	2	>32	9.44	54	60
Cefoxitin	1–128	16	32	11.89	77	94
Ampicillin-sulbactam	0.5–32	2	8	2.39	91	97
Metronidazole	≤0.06–2	1	1	0.80	100	
Bacteroides vulgatus (35)						
Moxifloxacin	0.125–>16	1	>16	2.12	54	60
Levofloxacin	0.5–>16	4	>16	4.08	46	60
Clindamycin	≤0.06–>32	1	>32	2.26	60	66
Cefoxitin	2–64	8	32	6.43	89	97
Ampicillin-sulbactam	0.25–16	2	8	2.08	97	100
Metronidazole	≤0.06–2	0.5	1	0.50	100	
Bilophila wadsworthia (33)						
Moxifloxacin	0.125–2	0.5	1	0.41	94	100
Levofloxacin	0.25–2	0.5	1	0.49	100	
Clindamycin	≤0.06–>32	0.25	0.5	0.37	97	97
Cefoxitin	2–>128	16	>128	24.35	54.5	79
Ampicillin-sulbactam	≤0.06–>32	2	>32	3.73	82	82
Metronidazole	≤0.06–0.25	0.125	0.25	0.11	100	100
Desulfovibrio spp. (13)[c]						
Moxifloxacin	≤0.06–>16	0.5	>16	0.78	69	77
Levofloxacin	≤0.06–>16	0.5	>16	1.09	69	77
Clindamycin	≤0.06–>32	0.25	1	0.36	92	92
Cefoxitin	1–128	64	128	25.85	31	46
Ampicillin-sulbactam	≤0.06–32	8	32	2.39	54	85
Metronidazole	≤0.06–1	0.25	0.5	0.21	100	100
Dialister-Sutterella group (10)[d]						
Moxifloxacin	≤0.06–>16	0.25	4	0.52	70	70
Levofloxacin	≤0.06–>16	0.25	8	0.65	70	80
Clindamycin	≤0.06–16	0.25	2	0.28	90	90
Cefoxitin	≤0.06–>128	0.5	4	0.98	90	90
Ampicillin-sulbactam	≤0.06–>32	0.125	2	0.26	90	90
Metronidazole	≤0.06–>32	1	8	0.87	90	90
Fusobacterium nucleatum (11)						
Moxifloxacin	0.125–0.5	0.125	0.25	0.18	100	100
Levofloxacin	0.5–1	1	1	0.78	100	100
Clindamycin	≤0.06–0.125	≤0.06	≤0.06	0.05	100	100
Cefoxitin	≤0.06–0.5	0.25	0.5	0.15	100	100
Ampicillin-sulbactam	≤0.06–≤0.06	≤0.06	≤0.06	0.05	100	100
Metronidazole	≤0.06–0.25	0.125	0.25	0.10	100	100
Fusobacterium spp. (14)[e]						
Moxifloxacin	0.125–>16	1	4	1.16	64	79
Levofloxacin	0.5–>16	2	8	2.10	71	86
Clindamycin	≤0.06–4	≤0.06	2	0.11	93	100
Cefoxitin	≤0.06–4	0.125	4	0.23	100	100
Ampicillin-sulbactam	≤0.06–1	≤0.06	1	0.13	100	100
Metronidazole	≤0.06–1	0.25	0.5	0.21	100	100
Porphyromonas asaccharolytica (11)						
Moxifloxacin	0.25–2	0.5	0.5	0.47	91	100
Levofloxacin	0.25–4	0.5	0.5	0.57	91	100
Clindamycin	≤0.06–≤0.06	≤0.06	≤0.06	0.05	100	100
Cefoxitin	0.125–0.5	0.25	0.25	0.21	100	100
Ampicillin-sulbactam	≤0.06–≤0.06	≤0.06	≤0.06	0.05	100	100
Metronidazole	0.125–0.25	0.125	0.25	0.17	100	100
Porphyromonas spp. (11)[f]						
Moxifloxacin	≤0.06–>16	0.5	1	0.45	91	91
Levofloxacin	≤0.06–>16	1	4	0.86	73	91
Clindamycin	≤0.06–>32	≤0.06	≤0.06	0.11	91	91
Cefoxitin	≤0.06–2	0.125	1	0.20	100	100

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TABLE 1—*Continued*

Organism (no. of isolates) and antimicrobial agent	MIC (μg/ml)			% Susceptible[a]		
	Range	50%	90%	GM[b]	Breakpoint 1	Breakpoint 2
Ampicillin-sulbactam	≤0.06–8	<0.06	0.5	0.11	100	100
Metronidazole	≤0.06–1	0.25	0.5	0.21	100	100
Prevotella intermedia (12)						
Moxifloxacin	0.5–8	0.5	0.5	0.63	92	92
Levofloxacin	0.5–2	0.5	1	0.59	100	100
Clindamycin	≤0.06–≤0.06	≤0.06	≤0.06	0.05	100	100
Cefoxitin	≤0.06–2	0.125	2	0.25	100	100
Ampicillin-sulbactam	≤0.06–1	≤0.06	0.5	0.15	100	100
Metronidazole	0.25–1	0.5	1	0.47	100	100
Prevotella melaninogenica (11)						
Moxifloxacin	0.25–>16	0.5	16	1.07	82	82
Levofloxacin	0.5–>16	1	>16	1.46	82	82
Clindamycin	≤0.06–≤0.06	≤0.06	≤0.06	0.05	100	100
Cefoxitin	0.125–4	0.5	1	0.57	100	100
Ampicillin-sulbactam	≤0.06–2	0.25	1	0.27	100	100
Metronidazole	≤0.06–1	0.5	1	0.49	100	100
Prevotella spp. (17)[g]						
Moxifloxacin	0.25–16	0.5	4	0.69	88	88
Levofloxacin	0.5–16	0.5	4	0.85	88	94
Clindamycin	≤0.06–>32	≤0.06	>32	0.37	76	76
Cefoxitin	0.125–4	1	4	0.72	100	100
Ampicillin-sulbactam	≤0.06–4	0.125	1	0.13	100	100
Metronidazole	≤0.06–4	0.5	2	0.63	100	100
Gram-negative cocci (14)[h]						
Moxifloxacin	≤0.06–8	0.5	2	0.45	71	93
Levofloxacin	0.125–16	2	8	1.10	64	86
Clindamycin	≤0.06–0.125	≤0.06	≤0.06	0.05	100	100
Cefoxitin	1–>128	4	16	5.12	93	93
Ampicillin-sulbactam	0.125–>32	1	4	1.10	93	93
Metronidazole	0.125–8	0.25	8	0.64	100	100
Actinomyces spp. (10)[i]						
Moxifloxacin	0.25–4	2	2	1.32	40	90
Levofloxacin	1–8	4	8	3.03	40	70
Clindamycin	≤0.06–0.5	0.25	0.5	0.14	100	100
Cefoxitin	≤0.06–0.5	0.125	0.5	0.14	100	100
Ampicillin-sulbactam	≤0.06–0.25	0.125	0.125	0.08	100	100
Metronidazole	1–>32	>32	>32	42.22	0	0
Clostridium clostridioforme group (30)						
Moxifloxacin	0.5–16	8	8	6.20	3	3
Levofloxacin	2–>16	16	>16	15.63	3	7
Clindamycin	≤0.06–4	1	2	0.71	90	100
Cefoxitin	1–32	4	16	6.35	97	100
Ampicillin-sulbactam	0.25–16	1	8	1.05	90	100
Metronidazole	≤0.06–1	0.125	0.25	0.11	100	100
Clostridium innocuum (46)						
Moxifloxacin	0.5–16	1	2	1.35	61	96
Levofloxacin	1–>16	4	4	3.24	41	93
Clindamycin	0.125–33	0.5	1	0.61	96	96
Cefoxitin	32–128	64	128	64.97	0	20
Ampicillin-sulbactam	≤0.06–0.5	0.125	0.25	0.16	100	100
Metronidazole	0.25–4	0.5	2	0.77	100	100
Clostridium perfringens (13)						
Moxifloxacin	0.25–1	0.5	0.5	0.47	100	100
Levofloxacin	0.25–0.5	0.25	0.5	0.31	100	100
Clindamycin	≤0.06–4	1	1	0.51	92	100
Cefoxitin	0.5–2	1	2	0.85	100	100
Ampicillin-sulbactam	≤0.06–0.125	≤0.06	0.125	0.06	100	100
Metronidazole	0.5–2	1	2	0.95	100	100

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TABLE 1—*Continued*

Organism (no. of isolates) and antimicrobial agent	MIC (μg/ml)			% Susceptible[a]		
	Range	50%	90%	GM[b]	Breakpoint 1	Breakpoint 2
Clostridium ramosum (10)						
Moxifloxacin	1–2	2	2	1.62	30	100
Levofloxacin	2–4	4	4	3.48	20	100
Clindamycin	1–>32	4	8	4.29	30	80
Cefoxitin	2–64	4	64	6.96	80	80
Ampicillin-sulbactam	≤0.06–0.5	≤0.06	0.5	0.08	100	100
Metronidazole	0.5–4	1	2	1.00	100	100
Clostridium symbiosum (10)						
Moxifloxacin	0.25–16	8	16	4.59	20	30
Levofloxacin	0.25–>16	16	>16	10.56	10	20
Clindamycin	0.125–2	1	2	0.76	100	100
Cefoxitin	0.5–8	2	4	2.14	100	100
Ampicillin-sulbactam	0.125–1	0.5	1	0.47	100	100
Metronidazole	≤0.06–0.25	≤0.06	0.25	0.08	100	100
Clostridium spp. (21)[j]						
Moxifloxacin	0.25–8	1	4	0.97	86	86
Levofloxacin	0.25–>16	2	8	2.14	52	76
Clindamycin	≤0.06–>32	2	16	2.49	52	67
Cefoxitin	≤0.06–128	4	128	4.37	76	76
Ampicillin-sulbactam	≤0.06–1	0.5	1	0.29	100	100
Metronidazole	≤0.06–1	0.25	1	0.31	100	100
Collinsella aerofaciens (10)						
Moxifloxacin	0.125–2	0.25	1	0.41	90	100
Levofloxacin	0.25–4	2	2	0.93	90	100
Clindamycin	≤0.06–4	≤0.06	0.25	0.09	90	100
Cefoxitin	≤0.06–32	4	16	1.82	90	100
Ampicillin-sulbactam	≤0.06–8	≤0.06	2	0.12	100	100
Metronidazole	0.25–1	0.5	1	0.54	100	100
Eubacterium alactolyticum (12)						
Moxifloxacin	0.125–2	1	2	0.63	83	100
Levofloxacin	0.5–2	0.5	1	0.75	92	100
Clindamycin	≤0.06–2	0.25	1	0.23	100	100
Cefoxitin	0.25–2	0.5	2	0.71	100	100
Ampicillin-sulbactam	≤0.06–0.125	≤0.06	0.125	0.07	100	100
Metronidazole	≤0.06–0.5	0.125	0.5	0.18	100	100
Eubacterium lentum (40)						
Moxifloxacin	0.125–16	0.25	4	0.44	85	90
Levofloxacin	0.125–>16	0.5	8	0.59	87.5	87.5
Clindamycin	≤0.06–16	0.25	1	0.23	97.5	97.5
Cefoxitin	2–16	8	8	5.96	100	100
Ampicillin-sulbactam	≤0.06–1	0.5	1	0.43	100	100
Metronidazole	0.125–4	0.5	1	0.41	100	100
Eubacterium limosum (11)						
Moxifloxacin	1–1	1	1	1.00	100	100
Levofloxacin	0.5–2	1	2	1.29	100	100
Clindamycin	≤0.06–>32	1	>32	1.62	73	73
Cefoxitin	0.5–2	1	2	1.29	100	100
Ampicillin-sulbactam	≤0.06–0.25	0.125	0.25	0.12	100	100
Metronidazole	0.125–0.5	0.25	0.5	0.27	100	100
Lactobacillus plantarum (20)						
Moxifloxacin	0.25–>16	2	4	1.80	30	85
Levofloxacin	0.5–>16	4	8	3.86	25	75
Clindamycin	≤0.06–>32	4	8	2.12	45	85
Cefoxitin	0.5–>128	4	32	6.96	70	70
Ampicillin-sulbactam	≤0.06–2	≤0.06	0.25	0.10	100	100
Metronidazole	0.5–>32	2	>32	2.55	85	85
Lactobacillus spp. (18)[k]						
Moxifloxacin	0.25–2	1	2	0.71	83	100

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TABLE 1—*Continued*

Organism (no. of isolates) and antimicrobial agent	MIC (μg/ml)			% Susceptible[a]		
	Range	50%	90%	GM[b]	Breakpoint 1	Breakpoint 2
Levofloxacin	0.25–>16	2	8	1.47	78	89
Clindamycin	≤0.06–4	0.125	4	0.22	89	100
Cefoxitin	0.25–>128	8	>128	7.13	83	89
Ampicillin-sulbactam	≤0.06–1	0.125	0.5	0.13	100	100
Metronidazole	0.25–>32	1	>32	2.33	83	83
Peptostreptococcus anaerobius (12)						
Moxifloxacin	≤0.06–0.5	0.125	0.25	0.14	100	100
Levofloxacin	0.125–1	0.25	0.5	0.30	100	100
Clindamycin	≤0.06–32	≤0.06	0.5	0.10	92	92
Cefoxitin	≤0.06–2	0.125	0.5	0.22	100	100
Ampicillin-sulbactam	≤0.06–0.125	≤0.06	≤0.06	0.05	100	100
Metronidazole	≤0.06–32	0.125	2	0.28	92	92
Peptostreptococcus magnus (10)						
Moxifloxacin	≤0.06–8	0.25	8	0.69	60	80
Levofloxacin	0.125–>16	4	>16	3.03	40	60
Clindamycin	≤0.06–32	≤0.06	2	0.24	90	90
Cefoxitin	≤0.06–2	0.5	2	0.48	100	100
Ampicillin-sulbactam	≤0.06–0.5	0.125	0.25	0.14	100	100
Metronidazole	0.25–4	0.5	2	0.71	100	100
Peptostreptococcus micros (50)						
Moxifloxacin	0.25–2	0.25	0.5	0.34	94	100
Levofloxacin	0.125–8	0.25	0.5	0.38	98	98
Clindamycin	≤0.06–0.5	0.125	0.25	0.16	100	100
Cefoxitin	0.25–8	0.5	1	0.54	100	100
Ampicillin-sulbactam	≤0.06–1	≤0.06	0.25	0.06	100	100
Metronidazole	≤0.06–>32	0.25	0.25	0.20	98	98
Peptostreptococcus spp. (10)[l]						
Moxifloxacin	0.125–16	0.25	2	0.50	80	90
Levofloxacin	0.5–>16	4	8	3.48	40	60
Clindamycin	≤0.06–>32	0.125	4	0.43	80	90
Cefoxitin	≤0.06–4	≤0.06	1	0.13	100	100
Ampicillin-sulbactam	≤0.06–0.125	≤0.06	≤0.06	0.05	100	100
Metronidazole	0.25–1	1	1	0.71	100	100

[a] Concentrations (μg/ml) used for breakpoints 1 and 2, respectively, were as follows: moxifloxacin, 1 and 2; levofloxacin, 2 and 4; clindamycin, 2 and 4; cefoxitin, 16 and 32; ampicillin-sulbactam, 8 and 16; metronidazole, 8 and 16.

[b] To calculate the geometric mean, all greater-than endpoints were adjusted to the next dilution higher, with the exception of clindamycin, where >32 was adjusted to 256, the more usual endpoint of clindamycin resistance.

[c] *Desulfovibrio desulfuricans* ($n = 1$), *D. fairfieldensis* ($n = 8$), *D. piger* ($n = 2$), and *D. vulgaris* ($n = 2$).

[d] *Dialister pneumosintes* ($n = 7$) and *Sutterella wadsworthensis* ($n = 3$).

[e] *Fusobacterium gonidiaformans* ($n = 2$), *F. mortiferum* ($n = 3$), *F. necrogenes* ($n = 1$) *F. necrophorum* ($n = 6$), and *F. varium* ($n = 2$).

[f] *Porphyromonas catoniae* ($n = 2$), *P. endodontalis* ($n = 2$), *P. gingivalis* ($n = 4$), and *P. levii* ($n = 3$).

[g] *Prevotella bivia* ($n = 1$), *P. buccae* ($n = 7$), *P. denticola* ($n = 1$), *P. oralis* ($n = 3$), *P. oris* ($n = 3$), and *P. tannerae* ($n = 2$).

[h] *Acidaminococcus fermentans* ($n = 9$) and *Veillonella* species ($n = 15$).

[i] *Actinomyces israelii* ($n = 1$), *A. meyeri* ($n = 2$), *A. odontolyticus* ($n = 3$), *A. turicensis* ($n = 3$), and *Actinomyces* species, No Good Fit ($n = 1$).

[j] *Clostridium butyricum* ($n = 2$), *C. cadaveris* ($n = 1$), *C. cochlearium* ($n = 2$), *C. difficile* ($n = 5$), *C. glycolicum* ($n = 1$), *C. hastiforme* ($n = 1$), *C. hathewayi* ($n = 1$), *C. hylemonae* ($n = 1$), *C. indolis* ($n = 1$), *C. paraputrificum* ($n = 1$), *C. sartagoforme* ($n = 1$), *C. sordelii* ($n = 1$), *C. sphenoides* ($n = 1$), and *C. tertium* ($n = 2$).

[k] *Lactobacillus acidophilus* ($n = 2$), *L. brevis* ($n = 1$), *L. catenaforme* ($n = 7$), *L. fermentum* ($n = 2$), *L. leichmannii* ($n = 2$), *L. rhamnosus* ($n = 3$), and *L. salivarius* ($n = 1$).

[l] *Peptostreptococcus asaccharolyticus* ($n = 6$) and *P. prevotii* ($n = 4$).

moxifloxacin. Clindamycin, cefoxitin and ampicillin-sulbactam were active against most *B. fragilis* isolates, with geometric mean MICs of 0.85, 6.88 and 1.18 μg/ml, respectively. For *B. thetaiotaomicron*, 79 of 90 (88%) isolates were susceptible to ≤2 μg/ml of moxifloxacin, with an MIC_{90} of 4 μg/ml and a geometric mean (GM) MIC of 1.55 μg/ml. For the other species, 88% of *B. distasonis* (GM MIC, 0.63 μg/ml), 54% of *B. uniformis* (GM MIC, 3.09 μg/ml), 63% of *B. vulgatus* (GM MIC, 2.12 μg/ml), and 70% of *B. ovatus* (GM MIC, 2.91 μg/ml) isolates were susceptible to ≤2 μg/ml of moxifloxacin. Among the *Clostridium* species, only *C. clostridioforme* and *C. symbiosum* were generally resistant to moxifloxacin, while all *C. perfringens* and *C. ramosum*, 96% of *C. innocuum*, and 86% of other *Clostridium* species tested were susceptible to ≤2 μg/ml of moxifloxacin. All clostridia were susceptible to metronidazole but showed variable susceptibilities to the other agents tested.

B. uniformis, *B. vulgatus*, *C. clostridioforme*, and *C. symbiosum* were the least susceptible and accounted for most of the resistant isolates; excluding the aforementioned four resistant species, 86% (303 of 363) of *Bacteroides* species isolates and 94% (417 of 450) of all other genera and species were suscep-

tible to ≤2 μg/ml of moxifloxacin. One of three strains of *Sutterella wadsworthensis* was resistant to all beta-lactams, clindamycin, and metronidazole. One of seven strains of *Dialister pneumosintes* was highly resistant to moxifloxacin and levofloxacin (MIC, >16 μg/ml)

Evaluating moxifloxacin at a breakpoint of ≤4 μg/ml, to match breakpoint 2 of levofloxacin and to compare our results with older studies, did not generally change the percentage of susceptible isolates and resulted in one or two more isolates becoming susceptible. The following changes were noted: *B. caccae* went from 65% to 75% susceptible, *B. ovatus* from 70% to 84%, *B. thetaiotaomicron* from 86% to 92% (6 of 90 more isolates susceptible), *B. uniformis* from 54% to 60%, *B. vulgatus* from 60% to 71%, *Fusobacterium* species from 79% to 93%, *Prevotella* species from 88% to 94%, *Actinomyces* species from 90% to 100%, *C. clostridioforme* from 3% to 30%, *Clostridium* species from 86% to 95%, *Eubacterium lentum* from 90% to 93%, and *Lactobacillus plantarum* from 85% to 95%. All the rest of the species within each genus maintained the same susceptibility levels.

DISCUSSION

Intra-abdominal infections result in approximately 2 million surgical procedures yearly in the United States (18). Complicated infections are those that require either surgical or radiological procedures plus broad-spectrum antimicrobial therapy, which must take into account the complex aerobic/anaerobic flora of the bowel. In our study, the high degree of clindamycin resistance for most species of the *B. fragilis* group suggests that it should be not be used empirically for patients with intra-abdominal infections.

Moxifloxacin has shown activity against a wide range of aerobic gram-positive and gram-negative bacteria (5, 10, 25). The studies of the in vitro activity of moxifloxacin against anaerobic bacteria have been based on strains from diverse sites of isolation and have shown disparate results (2, 3, 6, 7, 12, 14, 15, 21, 23). Snydman et al. (20) noted that different media resulted in higher geometric mean MICs for ciprofloxacin and trovafloxacin when tested on Wilkins-Chalgren agar compared to brucella blood agar. Hecht (11) recently reviewed the prevalence of antibiotic resistance in anaerobic bacteria and suggested that standardized methods of susceptibility testing, surveillance studies of antimicrobial activity and understanding of the mechanisms of resistance are important factors in the selection of the most appropriate antimicrobial agent for the treatment of patients. While methodologies and media used in more recent studies of moxifloxacin have been similar, it is possible that strain susceptibilities may also differ due to geographic factors, clonal populations, years of isolation or the source of the isolates.

Wexler et al. (23) tested 179 respiratory anaerobes, including 12 *B. fragilis* group species that had a geometric mean MIC of 0.8 μg/ml, and found that only one strain of *Clostridium clostridioforme* was resistant to moxifloxacin (MIC, 8 μg/ml). Using the NCCLS broth microdilution method, Aldridge et al. (3) studied 542 blood isolates obtained from 12 U.S. medical centers between 1987 and 1999 and found that of the 156 *Bacteroides* strains tested for susceptibility to trovafloxacin, 100% of *B. fragilis* and *B. distasonis* strains, 92% of the *B. thetaiotaomicron* and *B. vulgatus* and 90% of the *B. ovatus* strains were susceptible to ≤2 μg/ml. Studies have shown the activity of moxifloxacin to be similar to that of trovafloxacin (4, 15). Horn and Robson (12) also used a broth microdilution method and found 82% of 132 strains of *B. fragilis* and 85% of 20 strains of *B. thetaiotaomicron* but only 68% of 22 strains of *B. vulgatus* susceptible to ≤2 μg/ml of moxifloxacin, which is similar to our findings using the agar dilution method.

TABLE 2. Results of quality control tests done on NCCLS strains

Organism (strain)	Observed MIC (no. of tests)/mode	Expected range
B. fragilis (ATCC 25285)	0.125 (8), 0.5 (25)/0.25	0.125–0.5
B. thetaiotaomiocron (ATCC 29741)	1 (23), 2 (10)/1	1–4

Edmiston et al. (7) tested 350 aerobic and 550 anaerobic surgical isolates obtained from patients with intra-abdominal and diabetic foot infections between 1999 and 2002 and found that 97% of the anaerobes were susceptible to ≤4 μg/ml of moxifloxacin. This included 97% of the 130 strains of *B. fragilis*, 95% of 40 *B. thetaiotaomicron* strains, 100% of 40 *B. distasonis* strains, 93% of 30 *B. ovatus* and 30 *B. vulgatus* strains and 90% of 20 *B. uniformis* strains. They did not differentiate between the sources of the resistant isolates. In contrast, Golan et al. (8) reported on the increased resistance to moxifloxacin in 4,434 *Bacteroides* species isolated from 12 U.S. hospitals between 1994 and 2001. "The largest increase in moxifloxacin resistance (MIC breakpoint of 4 μg/ml) was among *B. distasonis*, from 22% in 1999 to 37% in 2001." Neither the number of *B. distasonis* isolates tested nor their sources were stated. They also noted that moxifloxacin resistance varies by sites of isolation "from 17% of *B. fragilis* from the female genital tract to 71% for *B. vulgatus* isolated from skin and soft tissue infections." Golan et al. (8) did note that "resistance patterns observed among different species and sites of isolation were consistent across different hospitals."

The current study shows that moxifloxacin was generally twofold more active than levofloxacin against most strains and that 88% of *B. fragilis* and 86% of *B thetaiotaomicron* were susceptible to ≤2 μg/ml of moxifloxacin. This is slightly less than that found by Edmiston et al. (7) at a breakpoint of 4 μg/ml and Aldridge et al. (3), similar to that found by Horn and Hobson (12), but much more susceptible than found by Snydman et al. (21). Aldridge et al. (3) and Horn and Robson (12) used a broth microdilution method as opposed to an agar dilution method. Also, Aldridge et al. (3) used strains isolated between 1987 and 1999 and Horn and Robson (12) used strains isolated between 1996 and 1997 as opposed to the other two studies (7, 21) that tested only more recent isolates. The four studies do not specifically report their quality control (QC) results that might aid in making comparisons. We have reported our QC results in Table 2 in order to show reproducibility and accuracy of our methods. In the future, it would be helpful if other investigators did the same.

Table 3 compares the MIC_{50}, MIC_{90}, and, where available, geometric mean MIC susceptibility data of the current study with those of Edmiston et al. (7) and Snydman et al. (21) for selected *B. fragilis* group species and highlights the marked

TABLE 3. Comparison of moxifloxacin susceptibilities of selected species of *Bacteroides* isolated from human intra-abdominal sources reported from four studies

Study[a]	Total no. of isolates	Yr range	MIC_{50}/MIC_{90} (GM MIC) (μg/ml) for:					
			B. fragilis	*B. thetaiotaomicron*	*B. ovatus*	*B. distasonis*	*B. uniformis*	*B. vulgatus*
RMA	360	2001–2004	0.5/8 (0.7)	1/4 (1.5)	2/16 (2.9)	0.5/8 (0.6)	2/16 (3.1)	1/16 (2.1)
Edmiston	290	1999–2002	0.5/1 (97%)[c]	2/2	2/2	0.5/2	0.5/4	0.5/2
Snydman	567	1999–2000	1/8 (1.5)	2/32 (4.2)	4/32 (4.1)	2/32 (2.8)	8/32 (6.2)	32/128 (15)
Horn	55/200[b]	1996–1997	0.25/8	2/4	NA[d]	NA	NA	2/64

[a] RMA, current study; Edmiston, reference 7; Snydman, reference 21; Horn, reference 12.
[b] Horn and Robson studied 200 isolates with sources as follows: surgical wounds, 57; abdominal fluids, 55; skin ulcers, 33; abscesses, 15; and other sites, 20.
[c] Percent susceptible at 4 μg/ml.
[d] NA, not available.

variation in susceptibilities among these studies. Of note, Snydman et al. (21) determined higher endpoints for the quinolones (0.06 to >64 μg/ml) while we tested a range of 0.06 to >16 μg/ml, so that the strict comparison of geometric mean MICs might be somewhat misleading.

Other factors that could account for differences in MICs are geographic variability with clonal populations and local antimicrobial usage patterns. Snydman et al. used isolates from 12 medical center laboratories across the United States, including some of our own strains that were not part of this current study. Edmiston et al. (7) collected isolates from Milwaukee, Wis. Our isolates came from 56 sites across the United States. Another possibility might be the site of isolation of the strains. All of our strains came from pretreatment cultures from patients with intra-abdominal infections. The isolates of Edmiston et al. (7) came from both diabetic foot infections and intra-abdominal infections, while neither Snydman et al. (21) nor Horn and Robson (12) specify the sites of isolation nor do they report on any prior history regarding antimicrobial utilization noted.

Moxifloxacin has been shown to be effective in animal studies for the therapy of mixed abdominal infections (19). Our in vitro data support the use of moxifloxacin for community-acquired intra-abdominal infections. The publication of clinical trial results will further define its clinical potential.

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