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Changes in the antibiotic susceptibility of anaerobic bacteria from 2007–2009 to 2010–2012 based on the CLSI methodology

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Abstract

Antimicrobial susceptibility testing of anaerobic isolates was conducted at four independent sites from 2010 to 2012 and compared to results from three sites during the period of 2007–2009. This data comparison shows significant changes in antimicrobial resistance in some anaerobic groups. Therefore, we continue to recommend institutions regularly perform susceptibility testing when anaerobes are cultured from pertinent sites. Annual generation of an institutional-specific antibiogram is recommended for tracking of resistance trends over time.

Keywords

Antimicrobial susceptibility; Anaerobe; Antibiogram

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1. Introduction

Anaerobic resistance to antimicrobial agents has continuously increased over recent decades [1,2]. Furthermore, resistance has been shown to vary in the same region from institution to institution [3,4]. Predictably, many commonly used antimicrobials have seen significant increases in resistance. The resistance of the *Bacteroides fragilis* group to clindamycin has steadily increased over the past three decades from 5 to 6% in the 1980s to 30–40% presently [2]. Other anaerobes, such as *Clostridium perfringens*, have also shown increased clindamycin resistance rates [1]. However, emerging resistance is not limited to clindamycin, and resistance against many active agents such as carbapenems, piperacillin-tazobactam, tigecycline, ampicillin-sulbactam, moxifloxacin, and metronidazole has also been reported [5–7]. Significant antimicrobial resistance has been identified in many different anaerobic species including *Prevotella* spp., *Fusobacterium* spp. and other anaerobic Gram-positive cocci, in addition to those listed above. With the increase in antimicrobial resistance among anaerobes, annual surveillance assessment of antimicrobial resistance in selected anaerobes continues to be recommended by the Clinical and Laboratory Standards Institute (CLSI) [8], and its necessity cannot be overstated. Here, we compare cumulative antibiograms from independent sites during two consecutive time periods and present resistance trends of selected anaerobic isolates.

2. Materials and methods

Isolates were collected and identified at four different sites including Loyola University Medical Center, Maywood, IL; International Health Management Associates, Inc. (IHMA), Schaumburg, IL; R.M. Alden Research Laboratory, Culver City, CA; and Tufts New England Medical Center, Boston, MA, between the years of 2007–2009 and 2010–2012. No data were obtained from IHMA during 2007–2009. The inclusion of IHMA data provides an opportunity to survey global resistance rates as IHMA is an independent contract research company that currently manages three of the largest antimicrobial susceptibility surveillance studies in the world and tests over 100,000 clinical isolates each year with isolates collected in the United States and abroad. For the data from 2010 to 2012, the isolate breakdown per site was 1742 isolates (54% of total) from Loyola University Medical Center, 792 isolates (24% of total) from IHMA, 163 isolates (5% of total) from R.M. Alden Research Laboratory and 557 isolates (17% of total) from Tufts New England Medical Center. Growth conditions and agar dilution susceptibility testing were conducted in accordance with CLSI guidelines described in M11-A8 [8]. No broth microdilution testing was included in this study. The antimicrobials assayed were: ampicillin-sulbactam (A/S), piperacillin-tazobactam (P/T), cefoxitin (FOX), ertapenem (ETP), imipenem (IPM), meropenem (MEM), penicillin (PEN), ampicillin (AMP), clindamycin (CC), moxifloxacin (MXF), and metronidazole (MTZ). Quality control (QC) testing was performed with at least two of the following four QC organisms *Bacteroides fragilis* ATCC 25285, Bacteroides *thetaiotaomicron* ATCC 29741, *Eggerthella lenta* ATCC 43055, or *Clostridium difficile* ATCC 700057 following guidelines in CLSI M11-A8 [8]. However, not all isolates were tested on all of the above listed antimicrobials. Proportions were analyzed using a chi-square test with use significance determined by $p < 0.05$ to distinguish susceptibility differences.

3. Results/discussion

In general, increased resistance led to most of the significant changes noted between the two time periods (Tables 1–4). From 2007–2009 to 2010–2012, significant increases in antimicrobial resistance can be seen overall anaerobic gram-positive cocci to ampicillin/sulbactam, cefoxitin, and moxifloxacin. Small increases in resistance rates were noted for meropenem against the *B. fragilis* group without *B. fragilis*, and for metronidazole against the *B. fragilis* group (all 7 species), while moderate increases in resistance rates were seen in both for ampicillin-sulbactam and piperacillin-tazobactam. For organisms other than *B. fragilis*, there was a similar pattern of moderate increases in resistance to ampicillin-sulbactam and ertapenem but smaller increases in metronidazole resistance rates. However, the resistance rate decreased in the *B. fragilis* group without *B. fragilis* for cefoxitin. Moxifloxacin resistance rates were also lower in the recent time period analyzed for some *B. fragilis* group isolates and for certain other anaerobes such as *Prevotella* spp. The reason behind such differences in resistance over time may include the addition of IHMA data, as well as changes in antimicrobial usage over time which can shift the antimicrobial pressures on organisms and lead to changes in antimicrobial susceptibilities [9,10].

Low frequencies of resistance were observed in most anaerobic bacteria species tested against metronidazole, with the expected exception of high resistance in *Propionibacterium acnes* (Table 4) and a slight but significant increase in resistance of *B. fragilis* over time (Table 2). The *B. fragilis* group (all 7 species) remained susceptible to imipenem with no significant changes from 2007 to 2012 (Tables 1 and 2). Overall, high rates of resistance were noted against clindamycin for isolates from *B. fragilis* group as well as most of the other anaerobes tested (Tables 1–4), and in some cases significantly lower in Clostridium perfringens and *Veillonella* spp. in 2010–2012 (Tables 3 and 4). Additional antimicrobial/organism combinations of an epidemiological interest, such as *Clostridium difficile* and the selected antimicrobials from Tables 3 and 4, can be found in the CLSI M100-S25 [11] as well as the CLSI M11-A8 [8].

As resistance rates can vary from region to region even institution to institution [3,4], internal institution susceptibility tracking is an important tool and should be established to assist empirical antimicrobial treatment for anaerobes. The 2010−2012 data provides a global survey of anaerobic antibiotic resistance rates however susceptibility surveys of frequently isolated species should be established and reviewed regularly by the local institution or sent to a reference laboratory. Standards and instructional use on susceptibility testing of anaerobes [8] and antibiograms [12] have been published by CLSI to aid clinical laboratories in this endeavor. In doing so, clinicians will be equipped with current information on relevant resistance patterns, resulting in improved patient care.

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Table 1

Antimicrobial susceptibility and resistance of *Bacteroides fragilis* group to selected antimicrobials from 2007 to 2009.

Percent Susceptible (%S) and Percent Resistant (%R)[b]	A/S[a]			P/T			FOX			ETP			IPM			MEM			CC			MXF			MTZ		
	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R
Breakpoints in µg/mL	–	≤8/4	≥32/16	–	≤32/4	≥128/4	–	≤16	≥64	–	≤ 4	≥16	–	≤ 4	≥16	–	≤ 4	≥16	–	≤2	≥8	–	≤2	≥8	–	≤ 8	≥32
B. fragilis	872	89	4	872	98	1	872	85	6	872	96	2	872	98	2	872	97	2	872	64	28	872	53	38	872	100	0
B. thetaiotaomicron	342	86	3	342	92	2	342	32	13	342	96	2	342	99	0	342	99	1	342	27	56	342	44	34	342	100	0
B. ovatus	67	93	2	67	93	2	67	37	15	67	98	0	67	100	0	67	100	0	67	54	39	67	43	39	67	100	0
B. vulgatas	70	67	6	70	100	0	70	83	4	70	98	2	70	98	2	70	98	2	70	49	51	70	43	46	70	100	0
B. uniformis	60	87	2	60	93	0	60	42	13	60	97	0	60	100	0	60	98	0	60	35	52	60	35	50	60	100	0
B. eggerchii	58	95	0	58	100	0	58	98	2	58	100	0	58	100	0	58	100	0	58	29	55	58	28	55	58	100	0
Parabacteroides distasonis	111	69	11	111	91	2	111	41	16	111	97	0	111	100	0	111	99	0	111	30	41	111	54	38	111	100	0
B. fragilis group without *B. fragilis*	708	83	4	708	93	1	708	40	12	708	97	1	708	99	0	708	99	0	708	33	42	708	43	40	708	100	0
All 7 species listed	1580	86	4	1580	95	2	1580	65	9	1580	97	1	1580	98	1	1580	98	1	1580	50	39	1580	49	39	1580	100	0

[a]The following antimicrobials were tested: Ampicillin-sulbactam (A/S), Piperacillin-Tazobactam (P/T), Cefoxitin (FOX), Ertapenem (ETP), Imipenem (IPM), Meropenem (MEM), Clindamycin (CC), Moxifloxacin (MXF), Metronidazole (MTZ).

[b]Intermediate category is not shown, but can be derived by subtraction of %S and %R for each antimicrobial agent from %100.

Table 2

Antimicrobial susceptibility and resistance of *Bacteroides fragilis* group to selected antimicrobials from 2010 to 2012.

Percent susceptible (%S) and percent resistant (%R)[b]	A/S[a]			P/T			FOX			ETP			IPM			MEM			CC			MXF			MTZ		
	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R
Breakpoints in µg/mL	–	≤8/4	≥32/16	–	≤32/4	≥128/4	–	≤16	≥64	–	≤4	≥16	–	≤4	≥16	–	≤4	≥16	–	≤2	≥8	–	≤2	≥8	–	≤8	≥32
B. fragilis	768	90	3	1497	98	1	1403	87	3	770	97	2	234	98	1	1503	96	1	1423	72	23	769	65	26	1503	96	2
B. thetaiotaomicron	349	80	4	467	79	8	469	48	8	348	98	1	134	99	1	470	98	1	469	32	55	348	47	34	470	100	0
B. ovatus	77	88	1	127	95	4	130	58	9	77	95	1	52	100	0	130	98	0	129	43	46	77	32	40	130	99	0
B. vulgatus	106	70	5	174	97	2	153	82	7	106	99	1	56	100	0	153	98	1	152	47	52	92	20	76	174	100	0
B. uniformis	94	88	4	128	95	2	129	60	9	94	100	0	24	100	0	128	99	0	121	44	40	94	27	53	128	99	0
B. eggerthii	60	93	0	70	89	11	73	34	21	60	100	0	–	–	–	72	100	0	72	29	63	61	25	38	72	100	0
Parabacceroides distasonis	220	66	20	265	56	30	265	42	15	220	97	2	33	97	0	265	97	2	265	25	57	220	69	27	265	100	0
B. fragilis group without *B. fragilis*	906	78[c]	8	1231	81	11	1219	53	10	905	98	1	299	99	0	1218	98	1	1208	35	53	892	45	40	1239	100	0
All 7 species listed	2580	82	6	3959	87	7	3841	65	7	2580	98	1	832	99	1	3939	98	1	3839	48	42	2553	51	36	3981	98	1

[a] The following antimicrobials were used: Ampicillin-sulbactam (A/S), Piperacillin-Tazobactam (P/T). Cefoxitin (FOX), Ertapenem (ETP), Imipenem (IPM), Meropenem (MEM), Clindamycin (CC), Moxifloxacin (MXF), Metronidazole (MTZ).

[b] Intermediate category is not shown, but can be derived by subtraction of %S and %R for each antimicrobial agent from %100.

[c] Underlined values designate significant changes in %S and %R compared to Table 1 data as determined by chi-square test.

Table 3

Antimicrobial susceptibility and resistance of anaerobic organisms other than *B. fragilis* to selected antimicrobials from 2007 to 2009.

Percent susceptible (%S) and percent resistant (%R)[b]	A/S[a]			P/T			FOX			ETP			IPM			MEM			PEN/AMP			CC			MXF			MTZ		
	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R
Breakpoints in µg/mL	–	≤8/4	≥32/16	–	≤32/4	≥128/4	–	≤16	≥64	–	≤4	≥16	–	≤4	≥16	–	–	≥16	–	≤0.5	≥2	–	≤2	≥8	–	≤2	≥8	–	≤8	≥32
Prevotella spp.	173	98	1	173	99	1	173	99	1	173	100	0	173	100	0	173	–	1	173	40	49	173	66	30	173	59	24	173	100	0
Fusobacterium nucleatum-necrophorum	44	100	0	44	100	0	44	100	0	44	100	0	44	100	0	44	–	0	44	100	0	44	100	0	44	95	5	44	100	0
Anaerobic gram-positive cocci	168	98	1	168	100	0	168	100	0	168	100	0	168	100	0	168	–	0	168	96	3	168	78	20	168	82	11	168	98	1
Veillonella spp.	28	100	0	28	61	7	28	100	0	28	100	0	28	100	0	28	–	0	28	57	28	28	89	7	28	79	14	28	86	11
Propionibacterium acnes	34	100	0	34	100	0	34	100	0	34	100	0	34	100	0	34	–	0	34	100	0	34	91	3	34	100	0	34	3	97
Clostridium perfringens	73	100	0	73	100	0	73	100	0	73	100	0	73	100	0	73	–	0	73	100	0	73	96	0	73	99	1	73	100	0
Other *Clostridium* spp.[c]	43	100	0	43	100	0	43	47	26	43	100	0	43	100	0	43	–	0	43	79	9	43	56	21	43	74	12	43	100	0

[a] The following antimicrobials were used: Ampicillin-sulbactam (A/S), Piperacillin-Tazobactam (P/T), Cefoxitin (FOX), Ertapenem (ETP), Imipenem (1PM), Meropenem (MEM), Penicillin/Ampicillin (PEN/AMP), Clindamycin (CC), Moxifloxacin (MXF), Metronidazole (MTZ).

[b] Intermediate category is not shown, but can be derived by subtraction of %S and %R for each antimicrobial agent from %100.

[c] *Clostridium* spp. excludes *Clostridium difficile.*

Table 4

Antimicrobial susceptibility and resistance of anaerobic organisms other than *B. fragilis* to selected antimicrobials from 2010 to 2012.

Percent susceptible (%S) and percent resistant (%R)[b]	A/S[a]			P/T			FOX			ETP			IPM			MEM			PEN/AMP			CC			MXF			MTZ		
	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R	N	%S	%R
Breakpoints in µg/mL	–	≤8/4	≥32/16	–	≤32/4	≥128/4	–	≤16	≥64	–	≤4	≥16	–	–	–	–	<4	>16	–	–	–	–	≤2	≥8	–	≤2	≥8	–	≤8	≥32
Prevotella spp.	229	99	0	800	100	0	806	97	1	196	100	0	–	–	–	234	100	0	–	–	–	800	72	26	196	73	24	571	97	0
Fusobacterium nucleatum-necrophorum	27	100	0	27	100	0	27	100	0	15	100	0	–	–	–	27	100	0	–	–	–	27	100	0	15	100	0	27	100	0
Anaerobic gram-positive cocci	150	88[c]	9	614	99	0	148	94	3	150	83	9	–	–	–	614	98	1	–	–	–	614	79	16	150	63	20	611	96	3
Veillonella spp.	31	90	6	32	84	16	32	97	0	26	85	8	–	–	–	32	97	0	–	–	–	32	66	34	26	81	12	32	97	0
Propionibacterium acnes	58	100	0	58	100	0	58	100	0	58	100	0	–	–	–	58	100	0	–	–	–	58	91	9	58	93	3	58	9	91
Clostridium perfringens	108	100	0	348	100	0	108	99	0	69	100	0	–	–	–	348	100	0	–	–	–	348	86	7	69	100	0	348	100	0
Other *Clostridium* spp.[d]	71	100	0	266	98	2	77	70	17	39	100	0	–	–	–	266	99	0	–	–	–	266	66	21	45	74	20	266	98	1

[a]The following antimicrobials were used: Ampicillin-sulbactam (A/S), Piperacillin-Tazobactam (P/T), Cefoxitin (FOX). Ertapenem (ETP), Imipenem (IPM), Meropenem (MEM). Penicillin/Ampicillin (PEN/AMP), Clindamycin (CC), Moxifloxacin (MXF), Metronidazole (MTZ).

[b]Intermediate category is not shown, but can be derived by subtraction of %S and %R for each antimicrobial agent from %100.

[c]Underlined values designate significant changes in %S and %R compared to Table 3 data as determined by chi-square test.

[d]*Clostridium* spp. excludes *Clostridium difficile.*