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Recent evolution of antibiotic resistance in the anaerobes as compared to previous decades

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ABSTRACT

Evolution of antibiotic resistance in the anaerobes was reviewed using recent data covering 2000–2013 as compared to previous years. All studies reported growing moxifloxacin resistance in *Bacteroides*/*Parabacteroides* spp. in Europe and USA and in *Clostridium difficile* in Europe. In half or more studies, the resistance rates in *Bacteroides*/*Parabacteroides* spp. to amoxicillin–clavulanate or ampicillin–sulbactam and clindamycin rose. In some studies, an increase in resistance was found in *Bacteroides*/*Parabacteroides* spp. to cefoxitin/cefotetan and carbapenems, in *Prevotella* spp. to penicillins, in anaerobic cocci to clindamycin and in *Bacteroides*/*Parabacteroides* spp. and *C. difficile* to metronidazole. Decreasing resistance was also observed, e.g. in *Bacteroides*/*Parabacteroides* spp. to cephalosporins, in *Prevotella* spp. and *C. difficile* to tetracyclines and in *C. difficile* to rifampin. No resistance changes were found to tigecycline, in *Bacteroides*/*Parabacteroides* spp. to chloramphenicol and in *C. difficile* to vancomycin. Factors influencing the resistance were the species, ribotype, country, hospital centre, antibiotic consumption and specimen type. In conclusion, the antibiotic resistance changes in the anaerobes are diverse and dynamic. Regular national surveys of resistance and both anaerobic microbiology and susceptibility testing of the isolates become more and more valuable.

1. Introduction

As yet, not many laboratories perform anaerobic microbiology and test the susceptibility of anaerobic isolates. In the USA, 89% of the laboratories performed anaerobic culture but only 21% tested in-house the susceptibility of the isolates; another 20% of the laboratories contacted the reference centers for this purpose [1,2]. In Scotland, UK, 19% of the laboratories did not identify anaerobes routinely [3]. Quality control for diagnostic oral microbiology laboratories in European countries revealed that only half of the laboratories isolated and identified the anaerobes from patients with periodontitis [4]. For this reason, the treatment of anaerobic infections in many hospital centers not only starts but remains empirical based on published surveys. However, both the global and local changes in resistance rates over time should be considered to provide optimal treatment of the patients.

Susceptibility testing of anaerobes is crucial in serious infections such as bloodstream infection and those isolates from normally sterile body sites as well as in those not responsive to empirical therapy. It is strongly recommended that anaerobes that should be considered for susceptibility testing are the highly virulent pathogens and those with unpredictable susceptibility patterns including the Gram-negative species *Bacteroides* spp., *Prevotella* spp., *Fusobacterium* spp., *Bilophila wadsworthia* and *Sutterella wadsworthensis* as well as the Gram-positive *Clostridium* spp. [5].

Current susceptibility testing methods for anaerobes include agar dilution technique with supplemented Brucella agar (the reference method), broth microdilution with supplemented Brucella broth (for *Bacteroides* and *Parabacteroides* spp.,) E test, β-lactamase test (with limited usefulness) and the spiral gradient endpoint system [2,5]. Importantly, the disk diffusion method is unsuitable for anaerobes. Different antibiotic breakpoints are used, mostly those of Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing

Abbreviations: ADM, agar dilution method; BMM, broth microdilution method; CA-SFM, Antibiogram Committee of the French Society of Microbiology; CLSI, Clinical and Laboratory Standards Institute; ET, E test; EUCAST, European Committee on Antimicrobial Susceptibility Testing; SGE, spiral gradient endpoint analysis.

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Table 1
Examples of evolution of antibiotic resistance in anaerobes according to data from publications in the last six years.

Agent[a]	Anaerobic species[b]	Country/ region	No. of strains (specimen type[c])	Method[d]	Resistance rate % (years)[e]		Resistance trend	Breakpoint MIC (mg/L)[f]	Reference
Penicillins									
Ampicillin (HLR)	*Bacteroides*/*Parabacteroides* spp.	Europe	2113 (V)	ADM	16.0 (1988–89)	44.5 (2008–09)	Increase	≥64	[19]
Penicillin	*B. fragilis*	Kuwait	831 (V)	ET	100.0 (2002–04)	100.0 (2005–07)	None	CLSI	[20]
	Prevotella spp.	Bulgaria	133 (O)	BSTM	15.4 (2003–04)	60.6 (2007-09)	Increase	CLSI	[9]
	P. intermedia/*P. nigrescens*	Switzerland	326 (O)	ET	14.0 NS (1991–94)	14.7 NS (2001–04)	None	CLSI	[13]
	Prevotella spp.	Taiwan	248 (V)	ADM	62.0 (2002)	94.0 (2006)	Increase	CLSI	[10]
	Anaerobic cocci	Belgium	119 (V)	ET	15.0 NS (1987)	12.0 NS (2011–12)	None	EUCAST	[14,16]
Cephalosporins									
Cefoxitin	*Bacteroides*/*Parabacteroides* spp.	Canada	735 (V)	BMM	26.0 (1992)	15.2 (2010–11)	Decrease	CLSI	[18]
	Bacteroides/*Parabacteroides* spp.	Belgium	418 (V)	ET	38.0 NS (2004)	44.0 NS (2011–12)	None	CLSI	[16]
	Bacteroides/*Parabacteroides* spp.	Europe	2113 (V)	ADM	3.0 (1988–89)	17.2 (2008–09)	Increase	CLSI	[19]
	Bacteroides/*Parabacteroides* spp.	Spain	286 (V)	ADM	3.4 (1999)	27.1 (2006)	Increase	CLSI	[7]
	Bacteroides/*Parabacteroides* spp.	Spain	830 (V)	ET	37.6–38.0 NS (2006–07)	22.1–36.5 NS (2008–10)	None	CLSI	[22]
	Bacteroides/*Parabacteroides* spp.	USA	4369 (V)	ADM	4–8.0 (1981–89)	9.0 (2000–07)	None	CLSI	[21]
Cefotetan	*B. fragilis*	Korea	276 (V)	ADM	15.0 (1997)	29.0 (2004)	Increase	CLSI	[17]
	B. thetaiotaomicron	Korea	106 (V)	ADM	100.0 (1997)	27.0 (2004)	Decrease	CLSI	[17]
BL-BLI									
Amoxicillin-clavulanate	*Bacteroides*/*Parabacteroides* spp.	Canada	735 (V)	BMM	0.8 (1992)	6.2 (2010–11)	Increase	CLSI	[18]
	Bacteroides/*Parabacteroides* spp.	Europe	2113 (V)	ADM	1.0 (1988–89)	10.4 (2008–09)	Increase	CLSI	[19]
	Bacteroides/*Parabacteroides* spp.	Spain	1343 (V)	ADM	5.0–8.9 (1997–99)	2.2–20.9 (2000–06)	Slight increase	CLSI	[7]
	Bacteroides/*Parabacteroides* spp.	Spain	830 (V)	ET	5.9–14.8 NS (2006–07)	7.4–13.8 NS (2008–10)	None	CLSI	[22]
	Fusobacterium spp.	Kuwait	75 (V)	ET	0.0 (2002–04)	0.0 (2005–07)	None	CLSI	[20]
	Anaerobic cocci	Belgium	119 (V)	ET	2.0 NS (1987)	3.0 NS (2011–12)	None	EUCAST	[14,16]
	GPAC	Kuwait	496 (V)	ET	0.0 (2002–04)	0.0 (2005–07)	None	CLSI	[20]
Ampicillin-sulbactam	*B. fragilis*	Taiwan	1605 (V)	ADM	<30.0 NS (2000–03)	48.0 NS (2007)	Increase	CLSI	[10]
Piperacillin-tazobactam	*Bacteroides*/*Parabacteroides* spp.	USA	5220 (V)	ADM	<1 (1990–99)	<1 (2000–07)	None	CLSI	[21]
	Bacteroides/*Parabacteroides* spp.	Canada	735 (V)	BMM	0.0 (1992)	0.5 (2010–11)	None	CLSI	[18]
	Bacteroides/*Parabacteroides* spp.	Europe	2108 (V)	ADM	<1.0 (1999–01)	3.1 (2008–09)	None	CLSI	[19]
	Bacteroides/*Parabacteroides* spp.	Spain	830 (V)	ET	10.0–11.9 NS (2006–07)	4.4–8.1 NS (2008–10)	None	CLSI	[22]
	B. fragilis	Kuwait	831 (V)	ET	0.0 (2002–04)	0.0 (2005–07)	None	CLSI	[20]
Carbapenems									
Imipenem	*Bacteroides*/*Parabacteroides* spp.	Europe	2113 (V)	ADM	0.0 (1988–89)	1.2 (2008–09)	None	CLSI	[19]
	Bacteroides/*Parabacteroides* spp.	USA	4369 (V)	ADM	<1.0 (1981–89)	<1.0 (2000–07)	None	CLSI	[21]
	Bacteroides/*Parabacteroides* spp.	Canada	735 (V)	BMM	0.0 (1992)	0.5 (2010–11)	None	CLSI	[18]
	Bacteroides/*Parabacteroides* spp.	Spain	1343 (V)	ADM	≤1.5 (1997)	≤1.5 (2006)	None	CLSI	[7]
	Bacteroides/*Parabacteroides* spp.	Spain	830 (V)	ET	0–1.0 NS (2006–07)	1.2–4.2 NS (2008–10)	Slight increase	CLSI	[22]
	Prevotella spp.	Kuwait	532 (V)	ET	0.0 (2002–04)	0.0 (2005-07)	None	CLSI	[20]
	Fusobacterium spp.	Kuwait	75 (V)	ET	0.0 (2002–04)	0.0 (2005–07)	None	CLSI	[20]
Meropenem	*B. fragilis*	Kuwait	96 (V)	ET	1.0 (1999)	7.9 (2007)	Increase	CLSI	[20]
Lincosamides									
Clindamycin	*Bacteroides*/*Parabacteroides* spp.	Canada	735 (V)	BMM	8.9 (1992)	34.1 (2010–11)	Increase	CLSI	[18]
	Bacteroides/*Parabacteroides* spp.	Europe	2113 (V)	ADM	9.0 (1988–89)	32.4 (2008–09)	Increase	CLSI	[19]
	Bacteroides/*Parabacteroides* spp.	France	1347 (V)	NA[h]	17.0 (1992–96)	30.4 (2000–03)	Increase	CLSI	[8]
	B. fragilis	Kuwait	299 (V)	ET	43.0 (2002)	60.0 (2007)	Increase	CLSI	[20]
	Bacteroides/*Parabacteroides* spp.	Spain	358 (V)	ADM	33.5 (1997)	47.9 (2006)	Increase	CLSI	[7]
	B. fragilis	Spain	830 (V)	ET	47.2–54.0 NS (2006–07)	37.1–47.5 NS (2009–10)	None	CLSI	[22]
	Bacteroides/*Parabacteroides* spp.	USA	4369 (V)	ADM	5.0–6.0 (1981–89)	31.0->35.0 (2000–07)	Increase	CLSI	[21]
	B. thetaiotaomicron	Korea	106 (V)	ADM	67.0 (1997)	91.0 (2004)	Increase	CLSI	[17]
	Prevotella spp.	Bulgaria	131 (O)	BSTM	7.7 (2003–04)	13.0 (2007–09)	None	CLSI	[9]
	Prevotella, *Porphyromonas*, *Campylobacter* and *Sutterella* spp.	Belgium	91 (V)	ET	8.0 NS (1987)	31.0 NS (2011–12)	Increase	EUCAST	[14–16]
	C. difficile	UK	179	ADM	97.1 (1979–86)	91.8 (1996–04)	None	CLSI	[24]
	Anaerobic cocci	Belgium	119 (V)	ET	6.0 NS (1987)	17.0 NS (2011–12)	None	EUCAST	[14,16]
	Anaerobic cocci	Bulgaria	78 (V)	BSTM	8.6 (1996–99)	30.2 (2011–12)	Increase	CLSI	[23],B[g]

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