

Table 3. MIC Data (MIC<sub>50</sub>, MIC<sub>90</sub>, MIC Ranges and Susceptibility Rates)

Organism	Antimicrobial	N	MIC (µg/ml)			%S	%I	%R
			MIC <sub>50</sub>	MIC <sub>90</sub>	Range			
<i>B. fragilis</i>	AMOXICA 2 <sup>1st</sup>	192	0.25	4	<0.06–>128	NA	NA	NA
	AMOXICA 2 <sup>1st</sup>	259	0.5	4	<0.125–>128	94.6	1.2	4.2
	Amoxicillin	293	32	>128	<0.125–>128	NA	NA	NA
	Clindamycin	293	1	64	<0.016–>256	79.5	6.8	13.7
	Imipenem	293	0.25	1	<0.016–>128	98.3	0.0	1.7
	Levofloxacin	293	2	8	<0.125–>16	NA	NA	NA
	Metronidazole	293	1	1	<0.06–>16	99.7	0.3	0.0
<i>Prevotella</i> spp.	AMOXICA 2 <sup>1st</sup>	218	0.125	0.5	<0.016–>32	NA	NA	NA
	AMOXICA 2 <sup>1st</sup>	259	0.125	1	0.125–4	100	0	0
	Amoxicillin	303	1	64	<0.016–>128	NA	NA	NA
	Clindamycin	303	<0.016	2	<0.016–>256	92.1	1.3	6.6
	Imipenem	303	0.63	0.25	<0.016–>2	100	0	0
	Levofloxacin	303	1	8	<0.06–>64	NA	NA	NA
	Metronidazole	303	0.5	2	0.06–>4	100	0	0
<i>F. nucleatum</i>	AMOXICA 2 <sup>1st</sup>	46	0.125	0.5	<0.06–>2	NA	NA	NA
	AMOXICA 2 <sup>1st</sup>	144	0.125	0.25	0.03–1	100	0	0
	Amoxicillin	157	0.125	1	0.03–>128	NA	NA	NA
	Clindamycin	157	0.06	0.125	<0.016–>8	99.4	0.0	0.6
	Imipenem	157	0.015	0.25	<0.016–>2	100	0	0
	Levofloxacin	157	0.5	2	<0.06–>16	NA	NA	NA
	Metronidazole	157	0.125	1	0.06–>2	100	0	0
<i>E. corrodens</i>	AMOXICA 2 <sup>1st</sup>	21	0.25	2	<0.016–>2	NA	NA	NA
	AMOXICA 2 <sup>1st</sup>	70	0.5	1	0.06–2	NA	NA	NA
	Amoxicillin	83	1	2	0.06–32	NA	NA	NA
	Clindamycin	83	>32	128	0.016–256	NA	NA	NA
	Imipenem	83	0.125	0.25	<0.016–>8	NA	NA	NA
	Levofloxacin	83	<0.06	0.125	<0.06–>0.125	NA	NA	NA
	Metronidazole	83	>32	>64	16–>64	NA	NA	NA
<i>P. anaerobius</i>	AMOXICA 2 <sup>1st</sup>	40	0.125	8	<0.06–>32	NA	NA	NA
	AMOXICA 2 <sup>1st</sup>	83	0.25	8	0.03–32	84.3	7.2	8.4
	Amoxicillin	92	0.25	16	0.06–32	NA	NA	NA
	Clindamycin	92	0.06	0.25	<0.016–>32	98.9	0.0	1.1
	Imipenem	92	0.05	1	<0.016–>8	98.9	1.1	0.0
	Levofloxacin	92	0.5	1	0.125–32	NA	NA	NA
	Metronidazole	92	0.5	1	0.06–>2	100	0	0
<i>F. (P.) magna</i>	AMOXICA 2 <sup>1st</sup>	40	0.125	0.5	<0.06–>1	NA	NA	NA
	AMOXICA 2 <sup>1st</sup>	90	0.25	0.5	0.125–1	100	0	0
	Amoxicillin	98	0.25	0.5	0.06–1	NA	NA	NA
	Clindamycin	98	0.5	32	<0.016–>256	84.7	2.0	13.3
	Imipenem	98	0.06	0.125	<0.016–>0.5	100	0	0
	Levofloxacin	98	1	16	<0.125–>64	NA	NA	NA
	Metronidazole	98	0.5	1	0.06–>64	96.9	0.0	3.1
<i>P. micros</i>	AMOXICA 2 <sup>1st</sup>	78	0.125	0.125	<0.06–>1	NA	NA	NA
	AMOXICA 2 <sup>1st</sup>	142	0.125	0.5	0.03–2	100	0	0
	Amoxicillin	146	0.125	0.5	0.03–>128	NA	NA	NA
	Clindamycin	146	0.125	0.5	<0.016–>8	99.3	0.0	0.7
	Imipenem	146	<0.016	0.06	<0.016–>0.5	100	0.0	0.0
	Levofloxacin	146	0.5	2	0.125–>16	NA	NA	NA
	Metronidazole	146	0.25	0.5	0.06–>64	99.3	0.0	0.7
<i>Porphyromonas</i> spp.	AMOXICA 2 <sup>1st</sup>	66	0.125	0.125	<0.06–>0.5	NA	NA	NA
	AMOXICA 2 <sup>1st</sup>	119	0.125	0.125	0.03–0.5	100	0	0
	Amoxicillin	125	0.125	0.25	0.03–16	NA	NA	NA
	Clindamycin	125	<0.016	0.06	<0.016–>32	96.8	0.0	3.2
	Imipenem	125	<0.016	0.5	<0.016–>0.5	100	0	0
	Levofloxacin	125	0.5	2	0.125–8	NA	NA	NA
	Metronidazole	125	0.125	0.5	0.06–>2	100	0	0

%S, percentage susceptible; %I, percentage intermediate; %R, percentage resistant; NA, not available

AMOXICA, amoxicillin/clavulanic acid

\*Amoxicillin/clavulanic acid MIC is expressed in terms of amoxicillin concentration

†Tested at German and French sites

‡Tested at US and German sites

## B. fragilis

Metronidazole, imipenem and amoxicillin/clavulanic acid were the most active agents. A total of 75% (9/12) of isolates with amoxicillin/clavulanic acid MICs  $\geq 16$  µg/ml were from one European site (Cardiff, Wales, UK). The less active agents against *B. fragilis* were amoxicillin, clindamycin and levofloxacin.

## Prevotella spp.

All strains were susceptible to amoxicillin/clavulanic acid 2:1, imipenem and metronidazole. Of the 303 isolates tested, 20 were resistant to clindamycin. Amoxicillin and levofloxacin demonstrated weak activity.

## F. nucleatum

Amoxicillin/clavulanic acid 2:1, imipenem and metronidazole were active against all the isolates against which they were tested. Only one strain was resistant to clindamycin, four strains had amoxicillin MICs  $\geq 4$  µg/ml and four strains had levofloxacin MICs  $\geq 2$  µg/ml.

## E. corrodens

Clindamycin and metronidazole were not active against the 83 strains tested; the other agents tested showed good activity.

## P. anaerobius

Clindamycin, imipenem and metronidazole were the most active agents. A total of 13/83 strains were intermediate or resistant to amoxicillin/clavulanic acid 2:1. Amoxicillin and amoxicillin/clavulanic acid MICs were similar. All 13 of these strains were from the USA (three from Hershey, PA, and 10 from Los Angeles, CA). Seven strains had levofloxacin MICs  $\geq 2$  µg/ml.

## F. (P.) magna

All strains were susceptible to amoxicillin/clavulanic acid 2:1 and imipenem. Amoxicillin was as active as amoxicillin/clavulanic acid. Only three of the 98 strains were resistant to metronidazole (all three of these strains were from Lille, France). A total of 13.3% of the strains were resistant to clindamycin (10 strains were from the USA and three were from Europe). Levofloxacin demonstrated weak activity.

## P. micros

All agents showed similar activity against the strains tested. However, 12/146 strains had levofloxacin MICs  $\geq 2$  µg/ml.

## Porphyromonas spp.

All agents were very active against the strains tested, with the exception of four out of 125 strains that were resistant to clindamycin (all four were from Los Angeles, CA) and 10 strains that had levofloxacin MICs  $\geq 2$  µg/ml.

## Amoxicillin/Clavulanic Acid Test Concentrations

With the exception of *B. fragilis* and *Prevotella* spp., the MICs for amoxicillin/clavulanic acid 2 correlated with those for amoxicillin/clavulanic acid 2:1. A total of 77.2% of *B. fragilis* with amoxicillin/clavulanic acid MICs  $\leq 2$  µg/ml had lower MICs (by 1–4 dilutions) with amoxicillin/clavulanic acid 2 compared with amoxicillin/clavulanic acid 2:1. However, 52.4% of *B. fragilis* with amoxicillin/clavulanic acid MICs  $\geq 4$  µg/ml had higher MICs (by 1–2 dilutions) with amoxicillin/clavulanic acid 2 compared with amoxicillin/clavulanic acid 2:1. A total of 68.3% of *Prevotella* spp. with amoxicillin MICs  $\geq 0.5$  µg/ml had lower MICs with amoxicillin/clavulanic acid 2 compared with amoxicillin/clavulanic acid 2:1.

## Discussion and Conclusions

- Amoxicillin/clavulanic acid was very active against all species, with the exception of 12 *B. fragilis* (nine of which were isolated from one site in Cardiff, Wales, UK) and 13 *P. anaerobius* strains (all USA isolates). Similar amoxicillin MICs for these 13 *P. anaerobius* strains would indicate a non- $\beta$ -lactamase-resistant mechanism (probable penicillin-binding protein).
- With the exception of *B. fragilis* and *Prevotella* spp., MICs for amoxicillin/clavulanic acid 2 and amoxicillin/clavulanic acid 2:1 were similar. Amoxicillin/clavulanic acid 2 was more active than amoxicillin/clavulanic acid 2:1 against *B. fragilis* with MICs  $\geq 2$  µg/ml, and less active than amoxicillin/clavulanic acid 2:1 against *B. fragilis* with MICs  $\geq 4$  µg/ml. Amoxicillin/clavulanic acid 2 was more active than amoxicillin/clavulanic acid 2:1 against *Prevotella* spp. with amoxicillin MICs  $\geq 0.5$  µg/ml.
- Metronidazole was very active against all species except the micro-aerophilic *E. corrodens*, and imipenem was highly active against all species.
- Levofloxacin, clindamycin and amoxicillin were the least active agents. Levofloxacin was least active against *F. (P.) magna*, *B. fragilis* and *Prevotella* spp., and clindamycin was least active against *E. corrodens*, *B. fragilis* and *F. (P.) magna*. Amoxicillin was least active against *B. fragilis*, *Prevotella* spp. and *P. anaerobius*.
- These data suggest that amoxicillin/clavulanic acid remains an effective agent for the treatment and prophylaxis of anaerobic infections.

## Reference

- National Committee for Clinical Laboratory Standards. Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria, 4<sup>th</sup> edn. Approved Standard M11-A4. Wayne, PA, USA: NCCLS, 1997.