Oral Microbiology Immunology 2007: 22: 298–303
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ORAL MICROBIOLOGY
AND IMMUNOLOGY

Susceptibility of oral obligate anaerobes to telithromycin, moxifloxacin and a number of commonly used antibacterials

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Tomás I, Tomás M, Álvarez M, Velasco D, Potel C, Limeres J, Diz P. Susceptibility of oral obligate anaerobes to telithromycin, moxifloxacin and a number of commonly used antibacterials.
Oral Microbiol Immunol 2007: 22: 298–303. © 2007 The Authors. Journal compilation © 2007 Blackwell Munksgaard.

Introduction: Obligate anaerobes are closely involved in the pathogenesis of oral and focal infections. The objective of this study was to evaluate the susceptibility profiles of obligate anaerobes of oral origin to telithromycin (TLM), moxifloxacin (MXF), and other antibiotics that are commonly used in dentistry.
Methods: The study sample comprised 172 obligate anaerobes isolated from the saliva of 43 adult volunteers. The minimum inhibitory concentrations (MICs) were determined by the agar dilution technique in *Brucella* agar medium supplemented with vitamin K, haemin and 5% (volume/volume) laked sheep blood, and incubated under anaerobic conditions. The Clinical and Laboratory Standards Institute methodology was followed and its criteria were used for the qualitative interpretation of the results. The antibiotics evaluated were: amoxicillin (AMX), amoxicillin-clavulanic acid (AMX-CLA), clindamycin (CM), metronidazole (MTZ), azithromycin (AZM), TLM and MXF.
Results: Resistance to AMX ($MIC_{90} \geqslant 16$ mg/l) was observed in 45.3% of the obligate anaerobes and resistance to CM ($MIC_{90} \geqslant 16$ mg/l) was found in 18.6%. All the isolates were sensitive to MTZ ($MIC_{90} = 1$ mg/l) and 98.8% were sensitive to AMX-CLA ($MIC_{90} = 2$ mg/l). The MIC_{90} values for AZM, TLM and MXF were $\geqslant 16$, $\geqslant 8$ and $\geqslant 2$ mg/l, respectively.
Conclusion: Pathogenic, opportunistic and non-pathogenic obligate anaerobes showed high percentages of resistance to AMX and CM, and high MIC values for AZM in the absence of recently administered antibiotics. MXF showed a higher activity than TLM, similar to that detected for AMX-CLA and MTZ. In consequence, MXF could represent a possible alternative antimicrobial against obligate anaerobes of oral origin, particularly in those patients with allergy, intolerance or lack of response to AMX-CLA or MTZ.

Key words: moxifloxacin; obligate anaerobes; oral flora; telithromycin

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Accepted for publication November 13, 2006

The oral cavity constitutes one of the principal ecological niches for obligate anaerobic bacteria (33). These microorganisms play an important role in the pathogenesis of oral infections (3) and focal infections of oral origin (4).

In Spain, the antibiotics most widely used therapeutically in the dental setting include particularly amoxicillin (AMX), amoxicillin–clavulanic acid (AMX-CLA), metronidazole (MTZ), clindamycin (CM) and azithromycin (AZM) (3). In accordance with the latest guidelines for the prevention of focal infections of oral origin (mainly bacterial endocarditis and prosthetic joint infection) drawn up by Expert Committees, AMX continues to be the antibiotic of choice for patients 'at risk'

who are to undergo certain dental procedures. For patients who are allergic or intolerant to penicillin, the antibiotic of choice is CM and the alternative antibiotic is AZM (2, 7, 13).

Some published studies highlight the growing prevalence of obligate anaerobes of oral origin that are resistant to some of these antibiotics (5, 14, 16), giving rise to the need to investigate alternative antibiotics for therapeutic or prophylactic use.

Telithromycin (TLM) is a ketolide agent with a broad spectrum of activity, including activity against gram-positive and gram-negative cocci, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, intracellular pathogens, atypical microorganisms, toxoplasma and many obligate anaerobic bacteria (17). TLM is also highly active against beta-lactam, macrolide and fluoroquinolone reduced-susceptibility pathogens (32). Moxifloxacin (MXF) is an 8-methoxy-quinolone with a broad spectrum of activity, including activity against typical, atypical and intracellular respiratory pathogens, gram-negative pathogens and many obligate anaerobic bacteria (6). MXF is also highly active against strains that are resistant to penicillin, macrolides, tetracyclines, trimethoprim/sulfamethoxazole and some fluoroquinolones (24).

The objective of this study was to evaluate the susceptibility profiles of obligate anaerobes of oral origin to TLM and MXF, and to compare the results with those obtained for other antibiotics that are commonly used in dentistry.

Materials and methods

Forty-three Spanish adults with healthy periodontium or untreated moderate-to-severe chronic adult periodontitis were studied. Periodontal disease was diagnosed by applying the criteria used by Fosner et al. (10) and Kinane et al. (19). The following exclusion criteria were applied: under 18 years of age, possessing fewer than 20 teeth, the routine use of oral antiseptics, antibiotic treatment in the previous 3 months and/or suffering any disorder that affects salivary secretion. Informed consent was obtained from all patients before their participation in the study.

Non-stimulated samples of total saliva (2 ml) were collected from all the patients and were inoculated into BBL Port-A-Cul vials (Beckton Dickinson and Company, Sparks, MD) and transported to the laboratory. The samples were cultured on Schaedler agar with 5% sheep blood supplemented with vitamin K and haemin, and on Anaerobe Laked Sheep Blood Kanamycin Vancomycin Agar (Remel Inc., Santa Fe Drive, Lenexa, KS) and *Bacteroides* Bile Esculin agar (Remel Inc.); all were incubated at 37°C under anaerobic conditions for 48–72 h.

The anaerobic atmosphere was achieved using the 2.5-l or 7.0-l GENbox systems (bioMérieux Inc., Hazelwood, MO) with an oxygen concentration <0.1% and a carbon dioxide concentration >15%. An anaerobic indicator strip (bioMérieux Inc.) was always included.

In the present study, although a number of species were possibly missed, the major species were isolated. The four predominant colony types from each sample were individually subcultured. Anaerobic identification was performed by common microbiological methods (25). A Gram-stain and an aerotolerance test were performed on each isolate. Fluorescence was determined by the usual method with a Woods lamp (long-wave ultraviolet light, 366 nm). Vancomycin sensitivity was defined as yielding a $\geqslant$10 mm zone of inhibition around a 5-μg vancomycin disk on anaerobic blood agar. The catalase test used 10–15% hydrogen peroxide. *Clostridium* spp. were identified on the basis of the use of PRAS (pre-reduced anaerobically sterilized) media (Remel Inc.) for determination of fermentation profiles and other characteristics. *Peptostreptococcus* spp. were identified by a carbohydrate fermentation reaction and production of saccharolytic and proteolytic enzymes. *Eubacterium* spp. were negative for motility, catalase test, negative indole production, nitrate reduction and gelatin and were esculin hydrolysed. Gram-negative rods (*Bacteroides* spp., *Prevotella* spp. and *Fusobacterium* spp.) were identified on the basis of their sensitivity or resistance to kanamycin 1000 μg, vancomycin 5 μg, colistin 10 μg disks, growth in 20% bile, catalase test, indole test, lipase production, pigment presence, fluorescence, motility, nitrate reduction and urease activity. *Veillonella* spp. were identified on the basis of nitrate reduction, catalase test and non-fermentation of glucose. The species identification was carried out using PRAS media for the determination of fermentation profiles and other characteristics.

The 172 obligate anaerobes isolated included: 58 *Prevotella* spp., 30 *Peptostreptococcus* spp., 22 *Bacteroides* spp., 20 *Fusobacterium* spp., 20 *Veillonella* spp., 14 *Clostridium* spp. and eight *Eubacterium* spp. Antibiotic susceptibility was tested following the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) guidelines (27). The antibiotics evaluated were AMX, AMX-CLA, CM, MTZ, AZM, TLM and MXF. Minimum inhibitory concentrations (MICs) were determined by the agar dilution technique (with an inoculum of 10^5 colony-forming units per spot) using *Brucella* agar supplemented with vitamin K1 (1 mg/l), haemin (5 mg/l) and 5% (v/v) laked sheep blood, and incubated under anaerobic conditions. The lowest antibiotic concentration yielding no growth was read as the MIC. The control strains *Bacteroides fragilis* (ATCC 25285) and *Bacteroides thetaiotaomicron* (ATCC 29741) were included on each set of plates. To check the quality control for AZM and TLM *S. pneumoniae* (ATCC 49619) and *Staphylococcus aureus* (ATCC 29213) were included. These two strains were assayed in triplicate using the CLSI recommendations for aerobic bacteria (26) and anaerobic bacteria (27). The susceptibility breakpoints recommended by the CLSI (27) for obligate anaerobic bacteria are: ampicillin $\leqslant$0.5 mg/l (AMX breakpoints are considered equivalent to ampicillin breakpoints), AMX-CLA $\leqslant$4 mg/l, CM $\leqslant$2 mg/l and MTZ $\leqslant$8 mg/l. The AZM, TLM and MXF breakpoints for obligate anaerobes have not been established.

Results and discussion

The MIC_{50}, MIC_{90} and MIC range for the seven antibiotics evaluated, and the antimicrobial susceptibility profiles to AMX, AMX-CLA, CM and MTZ of the different genera of obligate anaerobes of oral origin are presented in Tables 1 and 2.

Susceptibility studies have documented the emergence of antimicrobial resistance in obligate anaerobic bacteria, revealing differences in their resistance patterns that are related to geographical regions and antibiotic prescribing regimens (28).

Resistance to AMX (MIC_{90} $\geqslant$ 16 mg/l) was observed in 45.3% of the obligate anaerobes. The highest MIC_{50} and MIC_{90} values and the highest percentages of isolates resistant to AMX were found in the *Bacteroides* spp. ($\geqslant$16 mg/l, $\geqslant$16 mg/l and 100%, respectively) and *Prevotella* spp. (8 mg/l, $\geqslant$16 mg/l and 82.8%, respectively). All the *Peptostreptococcus* spp., *Clostridium* spp. and *Eubacterium* spp. were sensitive to AMX (MIC range 0.008–0.512 mg/l). Sensitivity to AMX-CLA (MIC_{90} 2 mg/l) was observed in 98.8% of the obligate anaerobes. The highest MIC_{50} and MIC_{90} values for AMX-CLA were found in the genera *Bacteroides* spp. (2 and 8 mg/l, respectively);

Table 1. MIC_{50}, MIC_{90}, MIC ranges and sensitivity profile to amoxicillin, amoxicillin-clavulanic acid, clindamycin, metronidazole and azithromycin of the different genera of obligate anaerobes of oral origin ($n = 172$ isolates)

Antibiotic	Bacterial genera (n)[1]	MIC range (mg/l)[2]	MIC_{50} (mg/l)[3]	MIC_{90} (mg/l)[4]	S[5] (%)	IR[6] (%)	R[7] (%)
Amoxicillin	*Prevotella* spp. (58)	0.008 to ⩾16	8	⩾16	6 (10.3)	4 (6.9)	48 (82.8)
	Peptostreptococcus spp. (30)	0.032–0.512	0.256	0.512	30 (100)	–	–
	Bacteroides spp. (22)	4 to ⩾16	⩾16	⩾16	–	–	22 (100)
	Fusobacterium spp. (20)	0.032–2	0.256	2	16 (80)	2 (10)	2 (10)
	Veillonella spp. (20)	0.256–4	1	4	8 (40)	6 (30)	6 (30)
	Clostridium spp. (14)	0.016–0.512	0.128	0.512	14 (100)	–	–
	Eubacterium spp. (8)	0.008–0.512	0.512	–	8 (100)	–	–
Amoxicillin–clavulanic acid	*Prevotella* spp. (58)	0.016–2	1	1	58 (100)	–	–
	Peptostreptococcus spp. (30)	0.016–0.512	0.256	0.512	30 (100)	–	–
	Bacteroides spp. (22)	1–8	2	8	20 (90.9)	2 (9.1)	–
	Fusobacterium spp. (20)	0.016–1	0.128	1	20 (100)	–	–
	Veillonella spp. (20)	0.128–2	0.256	2	20 (100)	–	–
	Clostridium spp. (14)	0.128–0.512	0.512	0.512	14 (100)	–	–
	Eubacterium spp. (8)	0.128–4	1	–	8 (100)	–	–
Clindamycin	*Prevotella* spp. (58)	0.008 to ⩾16	0.256	16	46 (79.3)	–	12 (20.7)
	Peptostreptococcus spp. (30)	0.008–8	0.256	8	22 (73.3)	2 (6.7)	6 (20)
	Bacteroides spp. (22)	0.128 to ⩾16	⩾16	⩾16	10 (45.5)	–	12 (54.5)
	Fusobacterium spp. (20)	0.016–0.512	0.128	0.512	20 (100)	–	–
	Veillonella spp. (20)	0.016 to ⩾16	0.064	⩾16	18 (90)	–	2 (10)
	Clostridium spp. (14)	0.256–4	2	4	12 (85.7)	2 (14.3)	–
	Eubacterium spp. (8)	0.256–1	1	–	8 (100)	–	–
Metronidazole	*Prevotella* spp. (58)	0.016–4	0.512	2	58 (100)	–	–
	Peptostreptococcus spp. (30)	0.064–1	0.512	1	30 (100)	–	–
	Bacteroides spp. (22)	0.128–2	0.512	2	22 (100)	–	–
	Fusobacterium spp. (20)	0.032–0.512	0.064	0.512	20 (100)	–	–
	Veillonella spp. (20)	0.256–2	0.512	2	20 (100)	–	–
	Clostridium spp. (14)	0.128–1	1	1	14 (100)	–	–
	Eubacterium spp. (8)	0.256–0.512	0.512	–	8 (100)	–	–
Azithromycin	*Prevotella* spp. (58)		0.512	⩾16	NA[8]	NA	NA
	Peptostreptococcus spp. (30)		1	4	NA	NA	NA
	Bacteroides spp. (22)		8	⩾16	NA	NA	NA
	Fusobacterium spp. (20)		0.256	8	NA	NA	NA
	Veillonella spp. (20)		4	⩾16	NA	NA	NA
	Clostridium spp. (14)		0.256	2	NA	NA	NA
	Eubacterium spp. (8)		2	–	NA	NA	NA

[1]The species identified in the different bacterial genera were: 58 *Prevotella* spp. (24 *P. buccae*, 18 *P. intermedia*, six *P. bivia* and 10 *Prevotella* spp.); 30 *Peptostreptococcus* spp. (14 *P. micros*, 10 *P. magnus*, two *P. asaccharolyticus* and four *Peptostreptococcus* spp.); 22 *Bacteroides* spp. (10 *B. fragilis*, six *B. distasonis*, two *B. uniformis*, two *B. vulgatus* and two *B. thetaiotaomicron*); 20 *Fusobacterium* spp. (10 *F. necrophorum*, six *F. nucleatum* and four *Fusobacterium* spp.); 20 *Veillonella* spp. (six *V. parvula*, 14 *Veillonella* spp.); 14 *Clostridium* spp. (12 *C. perfringes* and two *C. innocuum*) and eight *Eubacterium* spp. (six *E. lentum* and two *Eubacterium* spp.).
[2]MIC, minimum inhibitory concentration;
[3]MIC_{50}, concentration that inhibits the growth of 50% of the bacterial population;
[4]MIC_{90}, concentration that inhibits the growth of 90% of the bacterial population;
[5]S, sensitive;
[6]IR, intermediate resistance;
[7]R, resistance;
[8]NA, not applicable.
The CLSI criteria were applied to perform the qualitative interpretation (25).

two isolates had intermediate resistance to this antimicrobial (9.1%). *Peptostreptococcus* spp. had low MIC_{50} and MIC_{90} values (0.256 and 0.512 mg/l, respectively) to AMX-CLA.

Eick et al. in 1999 (9) and Sobottka et al. in 2002 (31) detected high percentages of resistance to penicillin among obligate anaerobes isolated from dental abscesses (45% and 37%, respectively). In Spain, in a study published in 2006, Brescó et al. (5) found that 22% of obligate anaerobes of oral origin (isolated from periapical dental infections and pericoronitis) were resistant to AMX. In the present study, almost half of the isolates analysed were resistant to AMX, with the highest percentages being found for the genera *Bacteroides* spp. and *Prevotella* spp. However, practically 100% of the obligate anaerobes were sensitive to AMX-CLA; these findings are similar to those observed by other authors (18, 22, 23). Evidence confirms that the principal mechanism of bacterial resistance to AMX is the production of beta-lactamases (15).

Resistance to CM ($MIC_{90} \geqslant 16$ mg/l) was observed in 18.6% of the obligate anaerobes. *Bacteroides* spp. had higher MIC_{50} and MIC_{90} values to CM (both ⩾16 mg/l), and the highest percentage of resistance (54.5%). Between 90 and 100% of the isolates of *Veillonella* spp., *Fusobacterium* spp. and *Eubacterium* spp. were sensitive to CM (MIC range 0.016 to ⩾16 mg/l).

Kuriyama et al. (20, 21) and Eckert et al. (8) reported sensitivity to CM in 100% and 98.6%, respectively, of obligate anaerobes isolated from odontogenic infections (*Peptostreptococcus* spp., *Eubacterium* spp., *Prevotella* spp., *Fusobacterium* spp. and *Porphyromonas* spp.). In contrast, some Spanish authors have recently demonstrated that 18% of the obligate anaerobes isolated from periapical infections and pericoronitis were resistant to CM, particularly *Bacteroides forsythus* and *Prevotella intermedia* (5). These figures agree with the findings of

Table 2. MIC_{50}, MIC_{90}, MIC ranges and sensitivity profile to telithromycin and moxifloxacin of the different genera of obligate anaerobes of oral origin ($n = 172$ isolates)

Antibiotic	Bacterial genera (n)[1]	MIC range (mg/l)[2]	MIC_{50} (mg/l)[3]	MIC_{90} (mg/l)[4]
Telithromycin	*Prevotella* spp. (58)	0.008 to $\geqslant$16	0.256	2
	Peptostreptococcus spp. (30)	0.008–0.512	0.016	0.128
	Bacteroides spp. (22)	0.512 to $\geqslant$16	8	$\geqslant$16
	Fusobacterium spp. (20)	0.016 to $\geqslant$16	4	$\geqslant$16
	Veillonella spp. (20)	0.008–4	0.512	4
	Clostridium spp. (14)	0.016–0.512	0.128	0.512
	Eubacterium spp. (8)	0.064–0.512	0.512	–
Moxifloxacin	*Prevotella* spp. (58)	0.008–4	0.512	1
	Peptostreptococcus spp. (30)	0.032–2	0.256	1
	Bacteroides spp. (22)	0.256 to $\geqslant$16	2	$\geqslant$16
	Fusobacterium spp. (20)	0.008–0.256	0.128	0.256
	Veillonella spp. (20)	0.064–2	0.064	2
	Clostridium spp. (14)	0.256–1	0.500	1
	Eubacterium spp. (8)	0.008–0.256	0.128	–

[1]The species identified in the different bacterial genera were: 58 *Prevotella* spp. (24 *P. buccae*, 18 *P. intermedia*, six *P. bivia* and 10 *Prevotella* spp.); 30 *Peptostreptococcus* spp. (14 *P. micros*, 10 *P. magnus*, two *P. asaccharolyticus* and four *Peptostreptococcus* spp.); 22 *Bacteroides* spp. (10 *B. fragilis*, six *B. distasonis*, two *B. uniformis*, two *B. vulgatus* and two *B. thetaiotaomicron*); 20 *Fusobacterium* spp. (10 *F. necrophorum*, six *F. nucleatum* and four *Fusobacterium* spp.); 20 *Veillonella* spp. (six *V. parvula*, 14 *Veillonella* spp.); 14 *Clostridium* spp. (12 *C. perfringes* and two *C. innocuum*) and eight *Eubacterium* spp. (six *E. lentum* and two *Eubacterium* spp.).
[2]MIC, minimum inhibitory concentration;
[3]MIC_{50}, concentration that inhibits the growth of 50% of the bacterial population;
[4]MIC_{90}, concentration that inhibits the growth of 90% of the bacterial population.

the present study (*Bacteroides* spp. was the genus with the highest recorded resistance to CM).

All the isolates were sensitive to MTZ (MIC_{90} 1 mg/l), although significant differences in the MIC_{90} values were found between patients with a healthy periodontium and those with untreated moderate-to-severe chronic adult periodontitis (2 and 1 mg/l, respectively). *Fusobacterium* spp. had lower MIC_{50} and MIC_{90} values with MTZ (0.064 and 0.512 mg/l, respectively).

Eick et al. in 1999 (9) and Sixou et al. in 2003 (30), in two studies of obligate anaerobes isolated from odontogenic abscesses/periodontitis and from pericoronitis, respectively, found that 100% of the isolates were sensitive to MTZ. Likewise, Ready et al. (29), in a study of 35 healthy children, found no MTZ-resistant obligate anaerobes in the oral microflora, a result that coincides with the findings of the present study. In contrast, Goumas et al. (14), in a study of 52 Greek patients with periapical abscesses, detected a 20% mean rate of resistance to MTZ in 40 anaerobes isolates (*Peptococcus* spp., *Peptostreptococcus* spp., *Bacteroides* spp., *Propionibacterium* spp. and *Fusobacterium* spp.). In this study, 33% of the patients had been treated with various antibiotics 1 to 10 days before specimen collection. Other Spanish authors have recently reported a high prevalence of resistance to MTZ (85%) in obligate anaerobes isolated from periapical dental infections and pericoronitis, particularly *B. forsythus*, *Fusobacterium nucleatum* and *P. intermedia* (5).

The MIC_{50} of obligate anaerobes for AZM was 1 mg/l and the MIC_{90} was $\geqslant$16 mg/l. The highest MIC_{50} and MIC_{90} for AZM were found in *Bacteroides* spp. (8 and $\geqslant$16 mg/l, respectively) and *Veillonella* spp. (4 and $\geqslant$16 mg/l, respectively).

Van Winkelhoff et al. (34) detected significant percentages of some obligate anaerobes in samples from Spanish adults with untreated periodontitis growing on AZM-selective blood agar plates (2 mg/l), of the order of 25% for *B. forsythus* and 17.4% for *P. intermedia*. Jacinto et al. (16), in their study of obligate anaerobic bacteria isolated from the root canals of teeth with apical periodontitis, found that AZM showed low activity against certain bacterial genera such as *Fusobacterium* spp. and *Prevotella* spp. (MIC_{90} range 4–12 mg/l). In the present study, AZM showed low activity against obligate anaerobes, with only 18% inhibition of the strains at a concentration of 0.4 mg/l (mean plasma concentration obtained after the administration of a single dose of 500 mg AZM) (11); this low activity was most pronounced against *Bacteroides* spp. and *Veillonella* spp.

The MIC_{50} and MIC_{90} of obligate anaerobes for TLM were 0.256 and 8 mg/l, respectively. Significant differences in the MIC_{90} values were found between patients with a healthy periodontium and those with untreated moderate-to-severe chronic adult periodontitis (4 and 16 mg/l, respectively). The highest activity of TLM was observed against *Peptostreptococcus* spp. (MIC_{50} 0.016 mg/l and MIC_{90} 0.128 mg/l) and *Clostridium* spp. (MIC_{50} 0.128 mg/l and MIC_{90} 0.512 mg/l). The lowest activity of TLM was found against *Bacteroides* spp. (MIC_{50} 8 mg/l and $MIC_{90} \geqslant 16$ mg/l) and *Fusobacterium* spp. (MIC_{50} 4 mg/l and $MIC_{90} \geqslant 16$ mg/l).

No studies found in the literature have tested the activity of TLM against obligate anaerobes of oral origin. Goldstein et al. (12) showed that TLM had very good activity against *Prevotella* spp. (MIC_{90} range 0.25–0.5 mg/l), *Propionibacterium* spp. ($MIC_{90} \leqslant 0.015$ mg/l), and *Peptostreptococcus* spp. (MIC_{90} range 0.03–0.06 mg/l) isolated from antral puncture specimens taken from patients with sinusitis; in this study, however, TLM presented low activity against *Fusobacterium* spp. (MIC_{90} 16 mg/l) and *Veillonella* spp. (MIC_{90} 8 mg/l). In the study published by Wexler et al. (35), TLM demonstrated good activity against certain groups of obligate anaerobes (*Porphyromonas* spp., *Prevotella* spp., *Peptostreptococcus* spp., non-*fragilis* group *Bacteroides* spp. and *Clostridium perfringens*), though it only inhibited 10% of *B. fragilis*, 50% of other *B. fragilis* group organisms, and was not active against the *Fusobacterium mortiferum/varium* group. In the present study, 80% of the strains were inhibited at a concentration of 2 mg/l (mean plasma concentration obtained after the administration of a single dose of 800 mg TLM) (11). TLM demonstrated low activity against *Bacteroides* spp. and *Fusobacterium* spp., but good activity against *Prevotella* spp., *Peptostreptococcus* spp., *Clostridium* spp. and *Eubacterium* spp.

The MIC_{50} and MIC_{90} of obligate anaerobes for MXF were 0.256 and 2 mg/l, respectively. Significant differences in the MIC_{90} values were found between patients with a healthy periodontium and those with untreated moderate-to-severe chronic adult periodontitis (8 and 1 mg/l, respectively). The highest activity of MXF was found against *Fusobacterium* spp. (MIC_{50} 0.128 mg/l and MIC_{90} 0.256 mg/l) and the lowest activity of MXF was found against *Bacteroides* spp. (MIC_{50} 2 mg/l and $MIC_{90} \geqslant 16$ mg/l).

Ackerman et al. (1) concluded that MXF has a high level of activity against the clinically most important obligate anaerobic pathogens because it inhibited 97% of the 292 strains studied at a concentration of 4 mg/l. In 2002, Milazzo et al. (23) demonstrated that MXF presented a high activity against *Bacteroides* spp., *Prevotella* spp. and *Fusobacterium* spp. (MIC_{90} range 0.12–0.5 mg/l) isolated from periodontal infections; and Sobottka et al. (31) also found this high activity against *Prevotella* spp. (MIC_{90} 1 mg/l) isolated from odontogenic abscesses. In the present study, consistent with the results described above, MXF was active against all the genera of obligate anaerobes studied: 94% of the strains were inhibited at a concentration of 3 mg/l (the mean plasma concentration obtained after the administration of a single dose of 400 mg of MXF) (11), with the exception of *Bacteroides* spp.

In conclusion, pathogenic, opportunistic and non-pathogenic obligate anaerobes demonstrated high percentage resistance to AMX and CM, and high MIC values for AZM in the absence of recent antibiotic treatment. MXF had a higher activity than TLM, similar to that detected for AMX-CLA and MTZ. In consequence, MXF could represent a possible antimicrobial alternative against obligate anaerobes of oral origin, particularly in those patients with allergy, intolerance or lack of response to AMX-CLA or MTZ.

Acknowledgments

Financial support for this study was received from the Galician Regional Government (Grant PXIB92501PR), Spain. M. del Mar Tomás Carmona is in receipt of a post-MIR research contract from the Instituto de Salud Carlos III, Spain.

References

1. Ackerman G, Schaumann R, Pless B, Claros MC, Goldstein EJ, Rodloff AC. Comparative activity of moxifloxacin *in vitro* against obligate anaerobic bacteria. Eur J Clin Microbiol Infect Dis 2000: **19**: 228–232.
2. American Dental Association, American Academy of Orthopaedic Surgeons. Antibiotic prophylaxis for dental patients with total joint replacements. J Am Dent Assoc 2003: **134**: 895–899.
3. Bascones A, Aguirre JM, Bermejo A et al. Consensus statement on antimicrobial treatment of odontogenic bacterial infections. Med Oral Patol Oral Cir Bucal 2004: **9**: 363–376.
4. Bisharat N, Goldstein L, Raz R, Elias M. Gram-negative anaerobic endocarditis: two case reports and review of the literature. Eur J Clin Microbiol Infect Dis 2001: **20**: 651–654.
5. Brescó M, Costa N, Berini L, Gay C. Antibiotic susceptibility of the bacteria causing odontogenic infections. Med Oral Pathol Oral Cir Bucal 2006: **11**: E70–E75.
6. Caeiro JP, Iannini PB. Moxifloxacin (Avelox): a novel fluoroquinolone with a broad spectrum of activity. Expert Rev Anti-Infect Ther 2003: **1**: 363–370.
7. Dajani AS, Taubert KA, Wilson W et al. Prevention of bacterial endocarditis: recommendations by the American Heart Association. J Am Med Assoc 1997: **277**: 1794–1801.
8. Eckert AW, Mauere P, Wilhelms D, Schubert J. Bacterial spectra and antibiotics in odontogenic infections. Renaissance of the penicillins? Mund Kiefer Gesichts Chir 2005: **9**: 377–383.
9. Eick S, Pfister W, Straube E. Antimicrobial susceptibility of anaerobic and capnophilic bacteria isolated from odontogenic abscesses and rapidly progressive periodontitis. Int J Antimicrob Agents 1999: **12**: 41–46.
10. Fosner L, Larsen T, Kilian M, Holmstrup P. Incidence of bacteremia after chewing, tooth brushing and scaling in individuals with periodontal inflammation. J Clin Periodontol 2006: **33**: 401–407.
11. Gilbert DN, Moellering RC, Eliopoulos GM, Sande MA. The Sanford guide to antimicrobial therapy, 35th edn. Sperryville, VA: Antimicrobial Therapy, Inc., 2005.
12. Goldstein EJC, Citron DM, Merriam CV, Warren Y, Tyrrel KL, Fernandez H. *In vitro* activities of telithromycin and 10 oral agents against aerobic and anaerobic pathogens isolated from antral puncture specimens from patients with sinusitis. Antimicrob Agents Chemother 2003: **47**: 1963–1967.
13. Gould FK, Elliot TSJ, Foweraker J et al. Guidelines for the prevention of endocarditis: report of the Working Party of the British Society for Antimicrobial Chemotherapy. J Antimicrob Chemother 2006: **57**: 1035–1042.
14. Goumas PD, Naxakis SS, Papavasiliou DA, Moschovakis ED, Tsintsos SJ, Skoutelis A. Periapical abscesses: causal bacteria and antibiotic sensitivity. J Chemother 1997: **9**: 415–419.
15. Handal T, Olsen I, Walker CB, Caugant DA. β-Lactamase production and antimicrobial susceptibility of subgingival bacteria from refractory periodontitis. Oral Microbiol Immunol 2004: **19**: 303–308.
16. Jacinto RC, Gomes BP, Ferraz CC, Zaia AA, Filho FJ. Microbiological analysis of infected root canals from symptomatic and asymptomatic teeth with periapical periodontitis and the antimicrobial susceptibility of some isolated anaerobic bacteria. Oral Microbiol Immunol 2003: **18**: 285–292.
17. Johnson AP. Telithromycin. Aventis Pharma. Curr Opin Investig Drugs 2001: **2**: 1691–1701.
18. Khemaleelakul S, Baumgartner C, Pruksakorn S. Identification of bacteria in acute endodontic infections and their antimicrobial susceptibility. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002: **94**: 746–755.
19. Kinane DF, Riggio MP, Walker KF, MacKenzie D, Shearer B. Bacteraemia following periodontal procedures. J Clin Peridontol 2005: **32**: 708–713.
20. Kuriyama T, Karasawa T, Nakagawa K, Saiki Y, Yamamoto E, Nakamura S. Bacteriologic features and antimicrobial susceptibility in isolates from orofacial odontogenic infections. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000: **90**: 600–608.
21. Kuriyama T, Karasawa T, Nakagawa K, Yamamoto E, Nakamura S. Bacteriology and antimicrobial susceptibility of gram-positive cocci isolated from pus specimens of orofacial odontogenic infections. Oral Microbiol Immunol 2002: **17**: 132–135.
22. Lewis MAO, Parkhurst CL, Douglas CWI et al. Prevalence of penicillin resistant bacteria in acute suppurative oral infection. J Antimicrob Chemother 1995: **35**: 785–791.
23. Milazzo I, Blandino G, Musumeci R, Nicoletti G, Lo Bue AM, Speciale A. Antibacterial activity of moxifloxacin against periodontal anaerobic pathogens involved in systemic infections. Int J Antimicrob Agents 2002: **20**: 451–456.
24. Miravitlles M. Moxifloxacin in respiratory tract infections. Expert Opin Pharmacother 2005: **6**: 283–293.
25. Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, ed. Manual of clinical microbiology, 7th edn. Washington, DC: American Society for Microbiology, 1999.
26. NCCLS. Performance standards for antimicrobial susceptibility testing, 14th informational supplement. NCCLS document M100-S14 (ISBN 1-56238-516-X). Wayne, PN: NCCLS, 2004.
27. NCCLS. Methods for antimicrobial susceptibility testing of anaerobic bacteria, approved standard, 6th edn. NCCLS document M11-A6 (ISBN 1-56238-517-8). Wayne, PA: NCCLS, 2004.
28. Rasmussen BA, Bush K, Tally FP. Antimicrobial resistance in anaerobes. Clin Infect Dis 1997: **24** (suppl 1): S110–S120.
29. Ready D, Bedi R, Spratt DA, Mullany P, Wilson M. Prevalence, proportions, and identities of antibiotic-resistant bacteria in the oral microflora of healthy children. Microb Drug Resist 2003: **9**: 367–372.
30. Sixou JL, Magaud C, Jolivet-Gougeon A, Cormier M, Bonnaure-Mallet M. Evaluation of the mandibular third molar pericoronitis flora and its susceptibility to different antibiotics prescribed in France. J Clin Microbiol 2003: **41**: 5794–5797.

31. Sobottka I, Cachovan G, Stürenburg E et al. *In vitro* activity of moxifloxacin against bacteria isolated from odontogenic abscesses. Antimicrob Agents Chemother 2002: **46**: 4019–4021.
32. Spiers KM, Zervos MJ. Telithromycin. Expert Rev Anti-Infect Ther 2004: **2**: 685–693.
33. Tanner A, Stillman N. Oral and dental infections with anaerobic bacteria: clinical features, predominant pathogens, and treatment. Clin Infect Dis 1993: **16** (suppl 4): S304–S309.
34. Van Winkelhoff AJ, Gonzales DH, Winkel EG, Dellemijn-Kippuw N, Vandenbroucke-Grauls CMJE, Sanz M. Antimicrobial resistance in the subgingival microflora in patients with adult periodontitis. J Clin Periodontol 2000: **27**: 79–86.
35. Wexler HM, Molitoris E, Molitoris D, Finegold SM. *In vitro* activity of telithromycin (HMR 3647) against 502 strains of anaerobic bacteria. J Antimicrob Chemother 2001: **47**: 467–469.