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In Vitro Activity of Moxifloxacin against Bacteria Isolated from Odontogenic Abscesses

Ingo Sobottka,[1]* Georg Cachovan,[2] Enno Stürenburg,[1] M. Oliver Ahlers,[2] Rainer Laufs,[1] Ursula Platzer,[2] and Dietrich Mack[1]

Institute of Medical Microbiology and Immunology[1] and Department of Operative Dentistry and Periodontology, School of Dentistry,[2] University Hospital Eppendorf, Hamburg, Germany

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We evaluated the antimicrobial susceptibility of 87 pathogens isolated from 37 patients with odontogenic abscesses. The most prevalent bacteria were viridans group streptococci and *Prevotella* species. Considering all bacterial isolates, 100% were susceptible to amoxicillin-clavulanic acid, 98% were susceptible to moxifloxacin and to levofloxacin, 76% were susceptible to doxycycline, 75% were susceptible to clindamycin, and 69% were susceptible to penicillin.

Dentoalveolar abscesses are almost always caused by a polymicrobial flora of aerobic, facultatively anaerobic, and anaerobic bacteria (7, 20). Abscesses in the maxillofacial region result either from infections around the apices of teeth via a necrotic pulp or from bacterial invasion of the surrounding tissues via the periodontal margin (9, 22). They also can develop after the extraction of teeth (9). The predominant bacteria in odontogenic infections such as periapical abscesses or deep fascial space infections are reported to be *Fusobacterium nucleatum*, pigmented *Bacteroides* spp., *Peptostreptococcus* spp., *Actinomyces* spp., and viridans group streptococci (4, 14). Even though many patients with odontogenic abscesses show improvement following incision and drainage or tooth extraction, antibiotic therapy can be indicated, especially in acute infections without localized accumulation of pus or in rapidly spreading infections (6, 7). Penicillin (PEN) is the preferred drug in most cases of odontogenic infection, but PEN-resistant organisms have increasingly been isolated from abscesses of odontogenic origin (7, 21). Therefore, other antibiotics such as clindamycin (CLI), erythromycin, tetracyclines, and levofloxacin (LVX) have been considered as alternative regimens for patients for whom PEN therapy has failed or for patients allergic to PEN (7, 19). However, the routine use of CLI is limited by its propensity to cause antibiotic-induced colitis (12), whereas erythromycin, tetracycline, and LVX have not been recommended for treatment of severe orofacial odontogenic infections (5, 12). Thus, alternative compounds for treatment of odontogenic abscesses are desirable. The aim of our study was to compare the in vitro activity of moxifloxacin (MXF), a new 8-methoxyquinolone, against odontogenic pathogens with those of the antibiotics usually employed and to evaluate its potential role in the treatment of odontogenic abscesses.

Forty-one swabs of odontogenic abscesses were obtained from 37 patients, 26 males and 11 females. The mean age of the patients was 39.6 years (range, 8 to 80 years). None of the patients received antimicrobial therapy before specimen collection. Prior to the collection of specimens, the mucosa had been disinfected with a tincture of povidone-iodine to avoid salivary contamination of the specimen. Swabs of odontogenic abscesses were obtained immediately after surgical incision and were placed in Amies charcoal medium (Transwab; Medical Wire & Equipment Co. Ltd., Corsham Wiltshire, England) and cultured within 6 h (1). All bacterial isolates were identified to the species level by standard laboratory methods. The MICs of PEN, amoxicillin-clavulanic acid (AMX-CLA), CLI, doxycycline (DOX), LVX, and MXF for all bacterial isolates were determined with Etest (AB Biodisk, Solna, Sweden) according to the manufacturer's instructions. The MICs of PEN, AMX-CLA, CLI, DOX, LVX, and MXF were interpreted according to actual NCCLS and U.S. Food and Drug Administration recommendations (11, 15, 16).

The acceptable quality control limits of MICs for *Bacteroides thetaiotaomicron* ATCC 29741, *Haemophilus influenzae* ATCC 49257, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, and *Staphylococcus aureus* ATCC 29213 were obtained according to NCCLS performance standards (15, 16).

A total of 90 bacterial strains (52 aerobes and facultative anaerobes and 38 anaerobes) were isolated following cultivation of 41 swabs from 37 patients. Eighty-seven of these isolates could be subcultivated for MIC determination. Aerobes and facultative anaerobes were recovered from 100% of the specimens, and anaerobes were recovered from 73% of the specimens. Eighty-three percent of the abscesses were polymicrobial, with an average of 2.2 isolates per specimen. The most prevalent bacteria were different viridans group streptococci (38 isolates) and *Prevotella* spp. (31 isolates). Only a few other facultative anaerobes and other anaerobes were isolated (Table 1).

Table 1 shows the in vitro activity of MXF compared with those of LVX and the antibiotics usually employed against odontogenic infections. Specifically, against the viridans group streptococci, MXF, LVX, AMX-CLA, and PEN were the most active antibiotics, with 100, 100, 100, and 90% of the isolates being susceptible, respectively, whereas CLI and DOX were less active, with 74 and 61% of the isolates being susceptible,

* Corresponding author. Mailing address: Institute of Medical Microbiology and Immunology, University Hospital Eppendorf, Martinistr. 52, D-20246 Hamburg, Germany. Phone: 49-40-42803-3157. Fax: 49-40-42803-4881. E-mail: sobottka@uke.uni-hamburg.de.

TABLE 1. In vitro susceptibility of 87 bacterial isolates obtained from 41 swabs from 37 patients with odontogenic abscesses

Microorganism and antibiotic	MIC (mg/liter)[e]			% Susceptible[f]
	Range	50%	90%	
Viridans group streptococci (n = 38)[a]				
PEN	0.008–1	0.032	0.25	90
AMX-CLA	0.016–1	0.016	0.125	100
CLI	0.016–>256	0.125	>256	74
DOX	0.032–16	4	16	61
LVX	0.5–2	1	2	100
MXF	0.064–0.5	0.125	0.5	100
Other aerobes and facultative anaerobes (n = 13)[b]				
PEN	<0.002–>32	0.25	16	46
AMX-CLA	0.016–2	0.125	0.5	100
CLI	0.016–>256	16	>256	31
DOX	0.016–32	2	16	85
LVX	<0.002–2	0.125	1	100
MXF	<0.002–1	0.125	0.25	100
Prevotella spp. (n = 29)[c]				
PEN	<0.002–>32	0.125	>32	55
AMX-CLA	0.016–0.25	0.064	0.25	100
CLI	0.016–>256	0.016	8	90
DOX	0.016–16	0.25	8	90
LVX	0.064–2	0.5	2	100
MXF	0.032–2	0.25	1	97
Other anaerobes (n = 7)[d]				
PEN	0.004–>32			57
AMX-CLA	0.016–2			100
CLI	0.016–0.125			100
DOX	0.016–8			86
LVX	0.125–8			71
MXF	0.032–8			86
All bacterial isolates (n = 87)				
PEN	<0.002–>32	0.064	8	69
AMX-CLA	<0.016–2	0.032	0.5	100
CLI	0.016–>256	0.125	>256	75
DOX	0.016–32	1	16	76
LVX	<0.002–8	1	2	98
MXF	<0.002–8	0.25	0.5	98

[a] *Streptococcus mitis* (17), *S. oralis* (4), *S. equinus* (4), *S. salivarius* (3), *S. sanguis* (2), *S. mutans* (1), *S. vestibularis* (1), *S. acidominimus* (1), *S. bovis* (1), and nontypeable viridans group streptococci (4).

[b] *Gemella haemolysans* (2), *Staphylococcus haemolyticus* (2), *Neisseria* spp. (2), *Haemophilus parainfluenzae* (1), *Staphylococcus aureus* (1), *Aerococcus viridans* (1), *Streptococcus pyogenes* (1), *Enterococcus faecalis* (1), *Klebsiella pneumoniae* (1), and *Stomatococcus* sp. (1).

[c] *P. melaninogenica* (6), *P. denticola* (5), *P. intermedia* (5), *P. oralis* (5), *P. buccae* (4), *P. loeschii* (2), *P. oris* or *P. buccae* (1), and *Prevotella* sp. (1).

[d] *Fusobacterium nucleatum* (2), *Fusobacterium* sp. (1), *Bacteroides ovatus* (1), *Bacteroides stercoris* (1), *Bacteroides uniformis* (1), and *Peptostreptococcus micros* (1).

[e] 50% and 90%, MICs at which 50 and 90% of isolates are inhibited, respectively.

[f] The susceptibility and resistance breakpoint concentrations (mg/liter) of the antibiotics were as follows. PEN: for *Staphylococcus* spp., ≤0.12 and ≥0.25, respectively; for *Enterococcus* spp., ≤8 and ≥16, respectively; for *Neisseria* spp., ≤0.06 and ≥2, respectively; for *Streptococcus* spp., ≥0.12 susceptibility. AMX-CLA: for *Staphylococcus* spp. and *Haemophilus* spp., ≤4 (AMX) and ≤2 (CLA) and ≥8 (AMX) and ≥4 (CLA), respectively; for *Enterobacteriaceae,* ≤8 (AMX) and ≤4 (CLA) and ≥ 32 (AMX) and ≥16 (CLA), respectively. CLI: for *Staphylococcus* spp., ≤0.5 and ≥4, respectively; for *Streptococcus* spp., ≤0.25 and ≥1, respectively. DOX: for *Staphylococcus* spp., *Enterococcus* spp., and *Enterobacteriaceae,* ≤4 and ≥16, respectively; for *Haemophilus* spp. and *Streptococcus* spp., ≤2 and ≥8, respectively (breakpoint concentrations of tetracycline); for *Neisseria* spp., ≤0.25 and ≥2, respectively (breakpoint concentrations of tetracycline). LVX: for *Staphylococcus* spp., *Enterococcus* spp., *Streptococcus* spp., and *Enterobacteriaceae,* ≤2 and ≥8, respectively; for *Haemophilus* spp., ≤2 (susceptibility) (16). MXF: for *Staphylococcus* spp. and *Enterobacteriaceae,* ≤2 and ≥8, respectively; for *Haemophilus* spp., ≤1 (susceptibility); for *Streptococcus* spp., ≤1 and ≥4, respectively (11). For anaerobic bacteria, the susceptibility and resistance breakpoint concentrations were as follows (15). PEN, ≤0.5 and ≥2, respectively; AMX-CLA, ≤4 (AMX) and ≤2 (CLA) and ≥16 (AMX) and ≥8 (CLA), respectively; CLI, ≤2 and ≥8, respectively; and DOX, ≤4 and ≥16, respectively (breakpoint concentrations of tetracycline).

respectively. Accordingly, MXF, LVX, and AMX-CLA showed the best activity against other aerobes and facultative anaerobes, with 100% of isolates being susceptible to each drug, followed by DOX, PEN, and CLI, with 85, 46, and 31% of isolates being susceptible, respectively. Among the second most prevalent isolates, *Prevotella* spp., 100% were susceptible to AMX-CLA and to LVX, 97% were susceptible to MXF, and 90% were susceptible to CLI and to DOX, but only 55% were susceptible to PEN. The best activity against other anaerobes was achieved by AMX-CLA and CLI, with 100% of isolates being susceptible to each, followed by MXF and DOX, with 86% of isolates being susceptible to each, and LVX and PEN, with 71 and 57% of isolates being susceptible, respectively. Taking account of all bacterial isolates (Table 1), the lowest MICs at which 90% of the isolates tested were inhibited (MIC_{90}s) were obtained with MXF and AMX-CLA (0.5 mg/liter each), followed by LVX (2 mg/liter), PEN (8 mg/liter), DOX (16 mg/liter), and CLI (>256 mg/liter). One hundred

percent of the isolates were susceptible to AMX-CLA. Comparable activity was observed with MXF and LVX, with 98% of isolates being susceptible to each, whereas a lower activity was observed with DOX, CLI, and PEN, with only 76, 75, and 69% of isolates being susceptible, respectively.

Our observations are in agreement with the results of other studies, in which the number of isolates per specimen ranged from 2.4 to 5 (2, 3, 12), that also reported that abscesses consist of a polymicrobial flora of anaerobic, aerobic, and facultatively anaerobic bacteria. Thus, antimicrobial therapy for odontogenic abscesses should provide equivalent effectiveness against both viridans group streptococci and anaerobes such as *Prevotella* spp. that have also been found by Kuriyama et al. (12) to be prevalent in odontogenic infections.

Determination of MICs for viridans group streptococci and *Prevotella* spp. revealed conflicting results with regard to the preferably administered antibiotics PEN and CLI (Table 1). Ninety percent of viridans group streptococci were found to be susceptible to PEN, with an MIC_{90} of 0.25 mg/liter, but only 74% were susceptible to CLI, with an MIC_{90} of >256 mg/liter. In contrast, 90% of the *Prevotella* spp. were susceptible to CLI, with an MIC_{90} of 8 mg/liter, but only 55% were susceptible to PEN, with an MIC_{90} of >32 mg/liter. This correlates well with the findings of other researchers who also reported a reduced activity of penicillins against oral anaerobes such as *Prevotella* spp. (8, 12, 13). With regard to all pathogens in our study (Table 1), the best in vitro activities were found with AMX-CLA, MXF, and LVX, with 100, 98, and 98% of isolates being susceptible, respectively, and with MIC_{90}s of 0.5, 0.5, and 2 mg/liter, respectively. A significantly lower activity was obtained with PEN, CLI, and DOX, with only 69, 75, and 76% of isolates being susceptible, respectively, and with MIC_{90}s of 8, >256, and 16 mg/liter, respectively. Based on the reduced susceptibility of odontogenic pathogens to PEN, CLI, and DOX, as observed in our study, these antibiotics seem to be of dubious benefit for empirical therapy of odontogenic abscesses. However, a better activity may be achieved by combination therapy regimens, e.g., with PEN and CLI (87.4% of isolates were susceptible in our study) or with PEN and metronidazole as recommended in the United States.

Because MIC determination alone cannot sufficiently characterize an antibiotic's effectiveness, pharmacokinetic and pharmacodynamic parameters are of particular importance for the assessment of clinical efficacy. In particular, MXF provides high bioavailability, a long half-life, and good penetration into tissues (11), including the spongy and compact tissues of bone, achieving site concentrations exceeding the plasma concentrations (23). Moreover, various methods have been analyzed to find the pharmacodynamic parameter that best correlates with clinical efficacy. As fluorochinolones have concentration-dependent killing, a value of ≥8 for the ratio of the maximum concentration of the drug in serum (C_{max}) to the MIC was found to be predictive of clinical cure (10, 17, 18). In our study, a high C_{max}/MIC_{90} ratio of 9, which is predictive of clinical cure, was found for MXF, compared with a lower C_{max}/MIC_{90} ratio of 2.9 for LVX (the C_{max}s following oral administration of 400 mg of MXF [C_{max}, 4.5 mg/liter] and 500 mg of LVX [C_{max}, 5.7 mg/liter] were obtained from the study by Pickerill et al. [18]).

In conclusion, we found that MXF has good in vitro activity against odontogenic pathogens compared with the activities of the antibiotics usually administered. MXF provides promising pharmacokinetic and pharmacodynamic properties that may justify clinical trials to assess whether MXF is a rational choice for the treatment of odontogenic abscesses.

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