Comparative Efficacies of Amoxicillin, Clindamycin, and Moxifloxacin in Prevention of Bacteremia following Dental Extractions

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We evaluated the efficacies of oral prophylactic treatment with amoxicillin (AMX), clindamycin (CLI), and moxifloxacin (MXF) in the prevention of bacteremia following dental extractions (BDE). Two hundred twenty-one adults who required dental extractions under general anesthesia were randomly assigned to a control group, an AMX group, a CLI group, and an MXF group (the individuals in the drug treatment groups received 2 g, 600 mg, and 400 mg, respectively, 1 to 2 h before anesthesia induction). Venous blood samples were collected from each patient at the baseline and 30 s, 15 min, and 1 h after the dental extractions. The samples were inoculated into BACTEC Plus aerobic and anaerobic blood culture bottles and were processed in a BACTEC 9240 instrument. Subculture and the further identification of the isolated bacteria were performed by conventional microbiological techniques. The prevalences of BDE in the control group, AMX group, CLI group, and MXF group were 96, 46, 85, and 57%, respectively, at 30 s; 64, 11, 70, and 24%, respectively, at 15 min; and 20, 4, 22, and 7%, respectively, at 1 h. Streptococcus spp. were the most frequently identified bacteria in all groups (44 to 68%), with the lowest percentage being detected in the AMX group (44%). AMX and MXF prophylaxis showed high efficacies in reducing the prevalence and duration of BDE, but CLI prophylaxis was noneffective. As a consequence, MXF prophylaxis is a promising antibiotic alternative for the prevention of BDE when beta-lactams are not indicated.

The controversy over bacterial endocarditis (BE) of oral origin has intensified during the past decade, based principally on estimates of the incidence (18) and on case-control studies which exclude dental treatment as a risk factor (45). Concerning bacteremia following dental manipulations, the small size of the bacterial inoculum, its transient nature, and the concept of cumulative exposure associated with “everyday” events have also been discussed (34). As a consequence, Durack (12) suggested that the indications for the administration of antibiotic prophylaxis (AP) for BE should be restricted. Furthermore, as there is no evidence of the efficacy of AP for the prevention of BE related to dental manipulations in patients “at risk” (31), some experts are starting to question whether the routine use of AP is necessary and whether the guidelines should be updated (32). However, the use of AP in patients “at risk” of BE who undergo “at-risk” dental procedures is a relatively widely accepted practice (48).

In accordance with the latest AP guidelines drawn up by expert committees, amoxicillin (AMX) continues to be the antibiotic of choice for patients “at risk” of BE and who are to undergo certain dental procedures; for patients allergic or intolerant to penicillin (PEN), the antibiotic of choice is clindamycin (CLI) (3, 9, 20).

The effect of CLI prophylaxis on the prevention of bacteremia following dental procedures has been evaluated in very few studies, and the results of those studies do not confirm the efficacy of CLI (1, 17, 19). Moreover, increasing resistance to CLI among streptococci isolated from the bloodstream after dental extractions has been found (47); this could limit its use as a prophylactic drug.

Moxifloxacin (MXF) is a broad-spectrum antibacterial agent approved for use for the treatment of acute exacerbations of chronic bronchitis, community-acquired pneumonia, acute bacterial sinusitis, and uncomplicated skin and skin structure infections (22). This fluoroquinolone shows good in vitro activity against odontogenic pathogens (23, 27, 43). Recently, we have found that all the streptococci isolated from a series of patients with iatrogenic bacteremia of oral origin showed a low MIC to MXF (47). Furthermore, we have demonstrated its efficacy in vivo for the treatment of submucous layer dental abscesses, confirming its penetration into tissue in the oral cavity (24).

The objective of this prospective, double-blind, randomized study was to investigate the efficacies of the prophylactic administration of AMX, CLI, and MXF for the prevention of bacteremia following dental extractions (BDE).

MATERIALS AND METHODS

Selection of study group. The study group comprised patients who, for behavioral reasons (autism, learning disabilities, phobias, etc.), underwent dental extractions under general anesthesia in the Santiago de Compostela University Hospital (Santiago de Compostela, Spain) from January 2003 to December 2004. The following exclusion criteria were applied: age under 18 years; receipt of antibiotics in the previous 3 months; routine use of oral antiseptics; a history of allergy or intolerance to AMX, CLI, or MXF; any type of congenital or acquired immunodeficiency; or any known risk factor for BE. By applying these criteria, 221 patients were selected and were randomly distributed into four study groups:

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the control group comprised 53 patients who did not receive any type of prophylaxis before the surgical procedure; the AMX group comprised 56 patients who received a standard prophylactic regimen of 2 g of AMX (Clamoxyl; Smith-Kline Beecham, Madrid, Spain) orally 1 to 2 h before anesthesia induction; the CLI group comprised 54 patients who received a standard prophylactic regimen of 600 mg of CLI (Dalaciñ; Upjohn Farmoquímica, Madrid, Spain) orally 1 to 2 h before anesthesia induction; and the MXF group comprised 56 patients who received a prophylactic regimen of 400 mg of MXF (Actira; Quimica Farmaceútica, Solna, Sweden) on Mueller-Hinton agar medium supplemented with 5% horse blood and incubation in 5% CO₂ (for aerobes, Streptococcus spp., and other facultative anaerobes), and on brucella agar medium supplemented with vitamin K and hemin with incubation in an anaerobic atmosphere (for obligate anaerobes). The readings were made according to the manufacturer’s recommendations. The criteria of the Clinical and Laboratory Standards Institute (CLSI; formerly NCCLS) were applied for the qualitative interpretation of the MICs for Streptococcus spp. and obligate anaerobic bacteria (29, 30). The antibiotics evaluated were PEN, AMX, ampicillin (AMP), erythromycin (EM), CLI, and MXF. The control microorganisms used were Streptococcus pneumoniae ATCC 49619 and Bacteroides fragilis ATCC 25285.

Sensitivity to antibiotics. The MIC was determined by the Etest (AB Biodisk, Solna, Sweden) on Mueller-Hinton agar medium supplemented with 5% horse blood and incubation in 5% CO₂ (for aerobes, Streptococcus spp., and other facultative anaerobes) and on brucella agar medium supplemented with vitamin K and hemin with incubation in an anaerobic atmosphere (for obligate anaerobes). The readings were made according to the manufacturer’s recommendations. The criteria of the Clinical and Laboratory Standards Institute (CLSI; formerly NCCLS) were applied for the qualitative interpretation of the MICs for Streptococcus spp. and obligate anaerobic bacteria (29, 30). The antibiotics evaluated were PEN, AMX, ampicillin (AMP), erythromycin (EM), CLI, and MXF. The control microorganisms used were Streptococcus pneumoniae ATCC 49619 and Bacteroides fragilis ATCC 25285.

**TABLE 1. Age, sex, oral health grade, and number of teeth extracted for the different study groups**

<table>
<thead>
<tr>
<th>Variable analyzed</th>
<th>Control group</th>
<th>AMX group</th>
<th>CLI group</th>
<th>MXF group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>26.1 ± 7.3</td>
<td>23.8 ± 5.7</td>
<td>24 ± 5.9</td>
<td>22.4 ± 4.3</td>
<td>NS³</td>
</tr>
<tr>
<td>Sex (no. [%] of patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>29 (55)</td>
<td>34 (61)</td>
<td>34 (63)</td>
<td>29 (50)</td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>24 (45)</td>
<td>22 (39)</td>
<td>20 (37)</td>
<td>29 (50)</td>
<td>NS</td>
</tr>
<tr>
<td>Oral health grade (no. [%]) of patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grades 0 and 1</td>
<td>10 (19)</td>
<td>16 (29)</td>
<td>8 (15)</td>
<td>12 (21)</td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>21 (40)</td>
<td>17 (30)</td>
<td>28 (52)</td>
<td>18 (31)</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>22 (41)</td>
<td>23 (41)</td>
<td>18 (33)</td>
<td>28 (48)</td>
<td>NS</td>
</tr>
<tr>
<td>No. of dental extractions³</td>
<td>4 (7)</td>
<td>4 (6)</td>
<td>3 (5)</td>
<td>4 (6)</td>
<td>NS</td>
</tr>
</tbody>
</table>

¹ The mean and standard deviation are shown.
² NS, not significant.
³ The median (interquartile range) are shown.

**FIG. 1. Prevalence of bacteremia at the baseline and postextraction**

Statistical analysis. The results were analyzed by using the SPSS (version 12.0) statistical package for Windows (SPSS Inc., Chicago, IL). Analysis of variance and the Kruskal-Wallis test were used to compare the ages of the patients in the different study groups and the number of dental extractions performed between the different study groups, respectively. The chi-square test was used to compare the genders and the oral health grades between the different study groups. Fisher’s exact test was used to compare the prevalence of bacteremia at the different study groups. BASELINE, blood sample drawn under basal conditions (after nasotracheal intubation and before any dental manipulation; these samples were obtained only from the 40 patients in the AMX, CLI, and MXF groups); 30 SEC, blood sample drawn 30 s after the final dental extraction; 15 MIN, blood sample drawn 15 min after completion of the surgical procedure; 1 H, blood sample drawn 1 h after completion of the surgical procedure (for purely technical reasons, it was possible to obtain the sample from 50 patients in the control group, 54 patients in the AMX group, and 56 patients in the MXF group).
TABLE 2. Bacteria identified in the positive blood cultures in the different study groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Streptococcus spp.</th>
<th>Staphylococcus spp.</th>
<th>Neisseria spp.</th>
<th>Obligate anaerobic bacteria</th>
<th>HACEK group</th>
<th>Other bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n = 133)$^a$</td>
<td>63.1</td>
<td>11.3</td>
<td>7.5</td>
<td>9.8</td>
<td>1.5</td>
<td>6.8</td>
</tr>
<tr>
<td>Amoxicillin (n = 36)$^b$</td>
<td>44.4</td>
<td>10.0</td>
<td>7.3</td>
<td>5.8</td>
<td>1.5</td>
<td>6.8</td>
</tr>
<tr>
<td>Clindamycin (n = 135)$^c$</td>
<td>58.5</td>
<td>4.4</td>
<td>14.8</td>
<td>13.4</td>
<td>1.5</td>
<td>7.4</td>
</tr>
<tr>
<td>Oxacillin (n = 62)$^d$</td>
<td>67.7</td>
<td>9.7</td>
<td>3.2</td>
<td>9.7</td>
<td>0</td>
<td>9.7</td>
</tr>
</tbody>
</table>

$^a$ The isolates recovered from the control group comprised 84 Streptococcus spp. (facultative anaerobes; 73 viridans group streptococci isolates [44 isolates in the S. mitis group, 21 isolates in the S. anginosus group, 4 isolates in the S. salivarius group, 3 isolates in the S. bovis group, and 1 isolate in the S. mutans group] and 11 unusual Streptococcus spp. and other gram-positive cocci in chains); 15 coagulase-negative staphylococci; 4 coagulase-negative staphylococci [the results were not sufficiently conclusive to ascribe the isolates at any coagulase-negative staphylococcal species]; 3 Staphylococcus capitis isolates, 3 S. aureus isolates, 2 S. schleiferi isolates, 1 S. epidermidis isolate, 1 S. sanguinis isolate, and 1 S. haemolyticus isolate]; 10 Neisseria spp. (8 N. cinerea isolates, 1 N. mucosa isolate, and 1 N. sulfusa isolate); 13 obligate anaerobic bacteria (3 Peptostreptococcus spp. [2 P. asaccharolyticum isolates and 1 P. nucleatum isolate]; 2 Peptostreptococcus spp. [2 P. micros isolates]; 2 Bacteroides spp. [1 R. fragilis isolate and 1 B. distans isolate]; 2 Prevotella spp. [2 P. corporis isolates]; 1 Eubacterium spp. [1 E. aerofaciens isolate]; 1 Veillonella spp. [1 V. parvula isolate]; 1 Bifidobacterium sp., and 1 obligate anaerobic Streptococcus sp.); 2 HACEK group (Haemophilus influenzae, H. parainfluenzae, H. aphrophilus, H. paraaphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae) isolates (2 Haemophilus spp. [2 H. parainfluenzae isolates]); and 9 other bacteria (2 Actinomyces spp. [2 A. odontolyticus isolates]; 2 Gemella spp. [2 G. morbillorum isolates]; 2 Lactobacillus spp. [2 L. acidophilus isolates]; 1 Enterococcus sp. [1 E. gallinarum isolate]; 1 Pantoea sp. [1 P. aglomerans isolate]; and 1 Enterobacter sp. [1 E. aerogenes isolate]).

$^b$ The isolates recovered from the amoxicillin group comprised 16 Streptococcus spp. (facultative anaerobes; 16 viridans group streptococci [16 S. mitis group isolates]); 2 Neisseria spp.; 8 obligate anaerobic bacteria (4 Peptostreptococcus spp. and 4 Prevotella spp.); 2 HACEK group isolates (2 Eikenella spp. [2 E. corrodens isolates]); and 8 other bacteria (2 Enterococcus spp. [2 E. faecalis isolates]; 2 Providencia spp.; 2 Leuconostoc spp.; and 2 nonfermenting gram-negative bacilli).

$^c$ The isolates recovered from the clindamycin group comprised 79 Streptococcus spp. (facultative anaerobes; 75 viridans group streptococci [42 S. mitis group isolates, 19 S. anginosus group isolates, 4 S. salivarius group isolates, and 10 S. mutans group isolates] and 4 unusual Streptococcus spp. and other gram-positive cocci in chains); 6 coagulase-negative staphylococci (the results were not sufficiently conclusive to ascribe the isolates to any coagulase-negative staphylococcal species); 20 Neisseria spp. (10 S. corneal isolates, 8 S. sanguinis isolates, and 2 Neisseria spp.); 18 obligate anaerobic bacteria (8 Prevotella spp., 4 Peptostreptococcus spp., 2 Fusobacterium spp., 2 Veillonella spp. and 2 obligate anaerobic Streptococcus spp.); 2 HACEK group isolates (2 Eikenella spp. [2 E. corrodens isolates]); and 10 other bacteria (4 Actinomycyes spp. [2 A. odontolyticus isolates and 2 Actinomyces spp.]; 4 Corynebacterium spp., and 2 Lactobacillus spp.).

$^d$ The isolates recovered from the oxacillin group comprised 42 Streptococcus spp. (facultative anaerobes; 42 viridans group streptococci [18 S. mitis group isolates, 6 S. anginosus group isolates, 10 S. salivarius group isolates, and 8 S. mutans group isolates]); 6 coagulase-negative staphylococci (2 coagulase-negative staphylococci [the results were not sufficiently conclusive to ascribe the isolates to any coagulase-negative staphylococcal species] and 4 S. epidermidis isolates); 2 Neisseria spp. (2 N. cinerea isolates); 6 obligate anaerobic bacteria (2 Peptostreptococcus spp., 2 Fusobacterium spp., and 2 Eubacterium spp.); and 6 other bacteria (2 Actinomyces spp., 2 Lactobacillus spp., and 2 nonfermenting gram-negative bacilli).

Baseline and 30 s, 15 min, and 1 h after completion of the dental extractions; the percentage of positive blood cultures; and the frequency of polymicrobial blood cultures between the different study groups. The Mann-Whitney U statistic was used to compare the MICs of AMX, CLI, and MXF for all strains isolated in the baseline and 30 s, 15 min, and 1 h after completion of the dental extractions; the percentage of positive blood cultures between the control group and the AMX group (29 and 0.5). Statistically significant differences were also observed in the proportion of polymicrobial blood cultures between the control group and the AMX group (29 and 0.5).

RESULTS

Characteristics of study group. The study group was made up of 221 patients, including 126 (57%) males and 95 (43%) females, with a mean age of 24.9 ± 5.7 years (age range, 18 to 57 years). With regard to the oral health scale, 46 patients (21%) belonged to grades 0 and 1, 84 (38%) to grade 2, and 91 (41%) to grade 3. The median number of teeth extracted per patient was 4 (interquartile range, 6). No significant differences were found between the different study groups with regard to age, sex, oral health grade, or number of teeth extracted (Table 1).

Prevalence of bacteremia. At the baseline, the percentages of positive blood cultures detected were 9.4% in the control group, 5% in the AMX group, 12.5% in the CLI group, and 7.5% in the MXF group.

The prevalence of bacteremia at 30 s after completion of the final dental extraction was 96.2% in the control group. In comparison with the control group, this percentage was significantly lower in the AMX group (46.4%; P < 0.001) and in the MXF group (56.9%; P < 0.001) but not in the CLI group (85.1%; P < 0.1). The administration of AMX and MXF showed efficacies significantly superior to those achieved in the patients administered CLI (P < 0.001 and P ≤ 0.001, respectively) (Fig. 1).

The prevalence of bacteremia at 15 min after the completion of the final dental extraction was 64.2% in the control group. In comparison with the control group, this percentage was significantly lower in the AMX group (10.7%; P < 0.001) and in the MXF group (24.1%; P < 0.001) but not in the CLI group (70.4%; P < 0.6). The administration of AMX and MXF showed efficacies significantly superior to those achieved in the patients administered CLI (P < 0.001 and P < 0.001, respectively) (Fig. 1).

The prevalence of bacteremia at 1 h after completion of the final dental extraction was 20% in the control group. In comparison with the control group, this percentage was significantly lower in the AMX group (3.7%; P ≤ 0.01) and in the MXF group (7.1%; P < 0.05), whereas it reached 22.2% in the CLI group (P < 0.9). The administration of AMX and MXF showed efficacies significantly superior to those achieved in the patients administered CLI (P < 0.001 and P < 0.005, respectively) (Fig. 1).

Characteristics and identification of bacterial isolates. Statistically significant differences were observed in the percentages of positive blood cultures between the control group and the AMX and MXF groups (47.8 versus 17.5 and 25.5%, respectively; P < 0.001) but not the CLI group (47.8% and 50%, respectively; P < 0.5). Statistically significant differences were also observed in the proportion of polymicrobial blood cultures between the control group and the AMX group (29 and 0.5).
The bacteria that were the most frequently isolated from all the study groups were the anaerobic bacteria (facultative and obligate anaerobes); the percentages of facultative anaerobes varied between 66.7% in the AMX group and 83.9% in the MXF group; the percentages of obligate anaerobes varied between 9.8% in the control group and 22.2% in the AMX group. Gram-positive cocci were the most frequently observed bacteria in all the study groups; the lowest prevalence occurred in the AMX group (29%), and the highest occurred in the MXF group (80.6%). The highest percentage of gram-negative bacilli was observed in the AMX group (27.8% versus 6.4% to 8.8% in the other groups).

The most frequent bacterial genus in the positive blood cultures in the control group was *Streptococcus* (63.1%, particularly the viridans group), followed by the genera *Staphylococcus* (11.3%) and *Neisseria* (7.5%). In the AMX group, the most frequent bacterial isolates were viridans group streptococci (44.4%), all of which belonged to the *S. mitis* group, followed by obligate anaerobes, such as *Peptostreptococcus* spp. (11.1%) and *Prevotella* spp. (11.1%). In the CLI group, the most frequent bacterial genus was *Streptococcus* (58.5%), particularly the viridans group, followed by the genera *Neisseria* (14.8%) and *Prevotella* (5.9%). In the MXF group, the most frequent isolates were viridans group streptococci (67.7%), followed by *Staphylococcus* spp. (9.7%) and obligately anaerobic bacteria (9.7%). The genera, groups, and, where indicated, species of bacteria identified in all the study groups are shown in Table 2.

Antimicrobial sensitivities of bacteria isolated in postextraction blood cultures. The profiles of sensitivity to the beta-lactams (PEN, AMP, AMX), EM, CLI, and MXF were studied for 177 bacterial strains derived from the positive postextraction blood cultures (62 isolates from the control group, 24 from the AMX group, 66 from the CLI group, and 25 from the MXF group). The MIC\(_{90}\) of PEN for the isolates was 2 mg/liter, and the MIC\(_{90}\)s of AMP and AMX were 1 mg/liter. The MIC\(_{90}\)s of EM and CLI were ≥256 mg/liter. The MIC\(_{90}\) of MXF for the isolates was 0.19 mg/liter. Figure 2 shows the percentage of cumulative MICs of AMX, CLI, and MXF for all strains isolated from the different study groups. The MIC\(_{90}\) of AMX for the isolates from the control group and the AMX group were 0.75 mg/liter and 4 mg/liter, respectively, with this difference being statistically significant (P < 0.005). The MIC\(_{90}\) of CLI for the isolates from the control group and the CLI group were ≥256 mg/liter. The MIC\(_{90}\)s of MXF for the isolates from the control group and the MXF group were 0.125 mg/liter and 0.380 mg/liter, respectively. Table 3 shows the MICs and the antimicrobial sensitivity profiles of the *Streptococcus* spp. (133 isolates), obligate anaerobic bacteria (20 isolates), and other bacteria (24 isolates) isolated in the postextraction blood cultures, irrespective of the study group from which they were
isolated bacteria in postextraction blood cultures (36, 46), in
group. Viridans group streptococci are the most frequently
cases of polymicrobial bacteremia were observed in the AMX
received a prophylactic dose of PEN; in the present series, no
polymicrobial BDE was less frequent when the patient had
prevalence and duration of BDE.

In the present series, AMX prophylaxis also significantly reduced the
positive blood cultures for the controls, respectively. In the
final dental extraction were negative (0% versus 16% and 14%
from the AMX group at 30 and 45 min after completion of the
under general anesthesia, as all the cultures of blood collected
that AMX prophylaxis also reduced the duration of BDE in a
respectively.

The qualitative interpretation of the MICs was not performed due to the low number of microorganisms of some of the bacterial genera identified and the lack of specific CLSI criteria for some of these isolates.

The CLSI criteria were applied to perform the qualitative interpretation (29, 30).

<table>
<thead>
<tr>
<th>Bacteria and antibiotic</th>
<th>MIC (mg/liter)</th>
<th>% of isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>0.032</td>
<td>0.5</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>0.064</td>
<td>0.5</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>0.064</td>
<td>0.5</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0.125</td>
<td>≥256</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.064</td>
<td>≥256</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>0.064</td>
<td>0.19</td>
</tr>
<tr>
<td>Obligate anaerobic bacteria</td>
<td>0.5</td>
<td>32</td>
</tr>
<tr>
<td>Penicillin</td>
<td>0.125</td>
<td>≥256</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>0.38</td>
<td>≥256</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>3</td>
<td>≥26</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.064</td>
<td>≥256</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>0.064</td>
<td>0.19</td>
</tr>
<tr>
<td>Other bacteria</td>
<td>0.064</td>
<td>0.19</td>
</tr>
</tbody>
</table>

recovered. Only 1.5%, 0.8%, and 0.8% of the *Streptococcus*
spp. were highly resistant to PEN, AMP, and AMX, respectively; 45.9% and 22.6% of the *Streptococcus* spp. showed high levels of resistance to EM and CLI, respectively; and 45% of the obligate anaerobes were highly resistant to PEN, 30% were highly resistant to AMP, 35% were highly resistant to AMX, and 20% were highly resistant to CLI. The MIC₉₀ of MXF of *Streptococcus* spp., obligate anaerobic bacteria, and other bacteria were 0.19 mg/liter, 0.19 mg/liter, and 0.5 mg/liter, respectively.

**DISCUSSION**

The efficacy of AMX for the prevention of bacteremia after
dental manipulations has been demonstrated both in children
and in adults (25, 41, 49). Recently, Lockhart et al. (25) found
that AMX prophylaxis also reduced the duration of BDE in a
group of children undergoing dental treatment while they were
under general anesthesia, as all the cultures of blood collected
from the AMX group at 30 and 45 min after completion of the
final dental extraction were negative (0% versus 16% and 14%
positive blood cultures for the controls, respectively). In the
present series, AMX prophylaxis also significantly reduced the
prevalence and duration of BDE.

Baltch et al. (3) and Josefsson et al. (21) demonstrated that
polymicrobial BDE was less frequent when the patient had
received a prophylactic dose of PEN; in the present series, no
cases of polymicrobial bacteremia were observed in the AMX
group. Viridans group streptococci are the most frequently
isolated bacteria in postextraction blood cultures (36, 46), in
agreement with the results obtained in previous studies (5).

AMX prophylaxis showed a “selective effect” on *Streptococcus*
spp., with a marked reduction in their prevalence in the posi-
tive postextraction blood cultures in our series, in which all the
streptococci in the AMX group belonged to the *S. mitis* group.

Since 1990, due to the high prevalence of undesirable gas-
trointestinal effects caused by EM, the expert committees of
BE recommend the administration of CLI as the prophylactic alternative in PEN-allergic patients “at risk” of BE before certain dental manipulations (10, 42). Aitken et al. (1) sug-
gested that CLI was more effective than EM in reducing the
prevalence of BDE of streptococcal etiology; but other au-
tors, such as Hall et al. (19), did not detect significant differ-
ences between the two AP regimens. In the literature we have
only found one report, published by Göker and Güvener (17)
in 1992, which compared the prevalence of positive blood
cultures after extraction of the third molar from patients re-
ceiving CLI prophylaxis and from patients in a control group;
the frequencies of BDE in both groups were similar. In the
present series, CLI prophylaxis did not reduce the prevalence
or the duration of BDE.

In some current protocols for BE prophylaxis, the adminis-
tration of macrolide antibiotics such as azithromycin and clari-
thromycin has been proposed as the second choice for PEN-
allergic patients “at risk” of BE before certain dental manipulations (10, 42). The CLSI (30) has
stated, “In *Streptococcus* spp., the profiles of resistance to
azithromycin, clarithromycin and dirithromycin may be pre-
dicted based on the activity of EM.” In view of the low level of
activity of EM against the bacteria isolated in the postextrac-

**TABLE 3. MIC₅₀s, MIC₉₀s, MIC ranges, and profiles of sensitivities to beta-lactams, erythromycin, clindamycin, and moxifloxacin for the bacteria isolated in the postextraction blood cultures**

<table>
<thead>
<tr>
<th>Bacteria and antibiotic</th>
<th>MIC (mg/liter)</th>
<th>% of isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus</em> spp. (n = 133 isolates)</td>
<td>0.032</td>
<td>0.5</td>
</tr>
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<td>Penicillin</td>
<td>0.064</td>
<td>0.5</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>0.064</td>
<td>0.5</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0.125</td>
<td>≥256</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.064</td>
<td>≥256</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>0.064</td>
<td>0.19</td>
</tr>
</tbody>
</table>

* = A total of 177 isolates were tested. Abbreviations: S, sensitive; IR, intermediate resistance; HR, high-level resistance; NA, not applicable.

b The CLSI criteria were applied to perform the qualitative interpretation (29, 30).

c The qualitative interpretation of the MICs was not performed due to the low number of microorganisms of some of the bacterial genera identified and the lack of specific CLSI criteria for some of these isolates.
tion blood cultures in the present series, the efficacy of azithromycin in the prevention of BDE could be questioned.

MXF has shown good in vitro activity against both oral streptococci (macrolide-sensitive or -resistant) and anaerobic pathogens (23, 27, 43, 47). Recently, we have found in a series of BDE that all the streptococci isolated showed a low MIC to MXF (47). Furthermore, the properties of MXF are favorable both pharmacokinetically (high bioavailability, long half-life, and good tissue penetration) and pharmacodynamically (MXF is bactericidal at concentrations two- to fourfold higher than the MIC) (26). The most common drug-related adverse effects involve the gastrointestinal tract and the central nervous system and were usually transient and mild in severity (4). Its lack of significant drug interactions in target groups makes it an option in diabetic patients and elderly individuals, as well as in those with renal dysfunction or with mild to moderate hepatic impairment (4). MXF appears to be tolerated by patients with hypersensitivity reactions to beta-lactam antibiotics (7). Although all these arguments would justify clinical trials with this antibiotic, to our knowledge no studies in which the effect of MXF on the prevention of bacteremia following dental manipulations has been investigated have been published to date. In the present series, the administration of a single oral dose of 400 mg of MXF leads to a significant reduction in the prevalence and duration of BDE.

The effect of AP in the bloodstream in the first minutes after the onset of a bacteremic episode has been questioned, since the time of exposure of the bacteria to the antibiotic is probably insufficient for the antibiotic to act (16, 19). In view of this, some authors (1, 6) have suggested that the success of AP in the prevention of postdental manipulation bacteremia could be attributed to the local effect of the drug on the bacteria in the oral cavity, before these invade the bloodstream. In accordance with the findings of other authors (25, 35), in our study, the administration of the antibiotic was performed 1 to 2 h before anesthesia induction, signifying that at least 2 h passed in the majority of patients before the dental extractions were started; this is the minimum estimated time for MXF to cause its bactericidal effect in oral bacteria in the dental alveolar crevicular fluid and saliva (11). Given the concentrations reached by AMX and MXF in saliva, gingival crevicular fluid, capillary blood, and alveolar bone after the administration of therapeutic doses (2, 15, 28, 44), 90% of the bacteria in the present series would be sensitive to the activities of AMX and MXF. However, in our series, the MIC\textsubscript{90} of CLI was much higher than the concentrations reached by this antibiotic in the dental alveolar serum (8), and this could justify the lack of efficacy of CLI in the prevention of BDE.

The cumulative MICs of AMX in the AMX group were higher than that in the control group (MIC\textsubscript{90}, fivefold higher). This could be conditioned by the “selective effect” on some bacterial genera shown by AMX prophylaxis. However, when only \textit{Streptococcus} spp. were evaluated, the cumulative MIC in the AMX group was also higher than that in the control group (MIC\textsubscript{90}, fourfold higher). This suggests that AMX prophylaxis has another “selective effect” on some bacterial strains based on MICs. No “selective effects” were detected after CLI or MXF prophylaxis.

Despite the local effect of AP, it has been suggested that the total elimination of the bacteria from the gingival sulcus by means of antibiotic administration is impossible (13), probably due to the polymicrobial nature of the gingival flora and the ability of the microorganisms to form biofilms. As a consequence, in the present series, the AP did not avoid the occurrence of some positive blood cultures in the first 15 min following dental manipulations in the majority of the papers published to date (25, 41). MXF may have a complementary action in later stages, based on the low MICs for the bacteria isolated from the positive postextraction blood cultures, its long half-life, and its ability to reduce the densities of the biofilms formed by the viridans group streptococci isolated from patients with BE and patients with sepsis (33).

In conclusion, in our setting, AMX continues to be the antibiotic of choice for the prevention of BDE in patients who are “at risk” of BE and who are not allergic to PEN. In contrast, we would question the use of prophylaxis with CLI for the prevention of BDE in patients “at risk” of BE with allergy or intolerance to PEN. MXF might represent a safe prophylactic alternative for the prevention of BDE when beta-lactams are contraindicated, although appropriate use is essential if this group of agents is to remain clinically useful.

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REFERENCES


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