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Abstract

Objective. The aim of this study is to obtain helpful information for an effective antimicrobial therapy against orofacial odontogenic infections; such information would be obtained from recent bacteriologic features and antimicrobial susceptibility data.

Study design. The bacteriology and antimicrobial susceptibility of major pathogens in 163 patients with orofacial odontogenic infections to seven antibiotics was examined.

Results. Mixed infection of strict anaerobes with facultative anaerobes (especially viridans streptococci) was observed most often in dentoalveolar infections, periodontitis, and pericoronitis. Penicillin (penicillin G) was effective against almost all pathogens, although it did not work well against ß-lactamase-positive *Prevotella*. Cefmetazole was effective against all test pathogens. Erythromycin was ineffective against viridans streptococci and most *Fusobacterium*. Clindamycin exerted a strong antimicrobial activity on anaerobes. Minocycline was effective against almost all of the test pathogens. The antimicrobial activity of levofloxacin against viridans streptococci was not strong.

Conclusions. An antibiotic that possesses antimicrobial activity against both viridans streptococci and oral anaerobes should be suitable for treatment of dentoalveolar infection, periodontitis, and pericoronitis. Penicillin remains effective as an antimicrobial against most major pathogens in orofacial odontogenic infections. Cefmetazole, clindamycin, and minocycline may be effective against most pathogens, including penicillin-unsusceptible bacteria.

Although numerous patients suffer from orofacial odontogenic infections, many of these infections can be managed without the use of antibiotics, e.g., by tooth extraction, endodontic therapy, and surgical treatment, including drainage.[1-6] However, when an acute bacterial infection has progressed or antimicrobial therapy might be of benefit to patients, antibiotics are prescribed.[1-6] When antibiotics are prescribed for the treatment of orofacial odontogenic infections, clinicians should choose them on a case-specific basis, and the choice should be based on several factors, e.g., laboratory data, patient's health, age, allergies, drug absorption and distribution ability, and plasma levels.[1-6] Penetration and metabolism of the drug, type or location of the infection, previous use of antibiotics, and cost are other factors to be considered.[1-6] The laboratory data regarding bacteriology and antimicrobial susceptibility is crucial information for the clinician considering the administration of the antimicrobial therapy.[3,6,7-9] However, it may take several days or even longer to obtain such data. Hence, antibiotics may be chosen empirically. ß-Lactam antibiotics, especially penicillins, have traditionally been recommended as a first-line antibiotic because they work well against most causative bacteria and because penicillins have a low incidence of side effects.[1-6] Furthermore, such medicines are relatively inexpensive.[3,6] Some studies have suggested that the antimicrobial activity of penicillins has decreased against the causative bacteria related to orofacial odontogenic infections, such as streptococci and oral anaerobes.[1,4-6] However, the debate continues over whether penicillins remain adequate as the first-line antibiotics of choice.[1-7] Alternative regimens of antimicrobial therapy have been proposed for patients with penicillin allergies, or in cases in which penicillin therapy has failed.[2-6] In addition, the properties of each antibiotic therapy should be considered based on up-to-date information about domestic antimicrobial susceptibility.

In the present study, the bacteriological features of orofacial odontogenic infections and the antimicrobial susceptibility of pathogens recently isolated at our hospital were determined. Based on the data, we estimated the antimicrobial effectiveness of each antibiotic as regards the treatment of orofacial odontogenic infections.

MATERIALS AND METHODS

Patients

The case histories of a total of 163 patients with obstructed abscesses caused by orofacial odontogenic infections were investigated. The patients were treated at our hospital between April 1991 and March 1997. Patients who required intensive medical care (e.g., cases with diabetes mellitus, rheumatoid arthritis, respiratory tract infections, leukaemia) were excluded. The following orofacial odontogenic infections were studied: dentoalveolar infections (128 cases), periodontitis (24 cases), and pericoronitis (11 cases). Before pus collection, at our hospital, other hospitals, or private practices, ninety-one patients had received antibiotics (ß-lactam antibiotics) during the course of the infection.

All subjects in this study gave their informed consent to participate.

Bacteriologic examination

To identify causative agents, pus specimens were sampled. The specimens were collected from the abscesses with an 18-gauge needle. The specimens were placed in anaerobic transport devices (Seed Tube; Eiken, Tokyo, Japan) and were immediately transported to the laboratory.

When the specimens reached the laboratory, bacteriologic examination was performed immediately as follows: a portion of each specimen was incubated on

Brucella HK agar (Kyokuto, Tokyo, Japan) with 5% sheep blood in an atmosphere of 5% CO_2, 10% H_2, and 85% N_2 at 37°C for 78 h. At the same time, a portion of the specimen was also incubated on Brucella HK agars with 5% sheep blood in an aerobic atmosphere and in an atmosphere of 10% CO_2, 20% H_2, and 70% N_2 at 37°C for 48 h. Incubation continued for at least seven days, even in the absence of bacterial growth. Aerobic and micro-aerophilic bacteria were identified using conventional methods.[10,11] Anaerobic bacteria were identified using Rap ID ANA II (Innovative Diagnostic System, Norcross, GA). In addition to the test, gas liquid chromatography was performed when needed to identify the bacteria.[11,12] After the bacteriologic examination, bacterial strains were stored in 10% skim milk (Becton-Dickinson, Cockeysville, MD) at –80°C until the susceptibility test could be performed.

Susceptibility test

Antibiotics were obtained from their manufacturers as laboratory powders; each antibiotic was of a defined potency: penicillin G (Banyu, Tokyo, Japan), cefazolin (Fujisawa, Osaka, Japan), cefmetazole (Sankyo, Tokyo, Japan), erythromycin (Shionogi, Osaka, Japan), clindamycin (Pharmacia & Upjohn, North Peapack, NJ), minocycline (Takeda, Osaka, Japan), and levofloxacin (Dai-ichi, Tokyo, Japan).

All minimum inhibitory concentrations (MICs) were determined by the agar dilution method recommended by the National Committee for Clinical Laboratory Standards (NCCLS).[7,8] The MICs of streptococci were determined using Mueller-Hinton agar (Becton Dickinson) with 5% sheep blood in an atmosphere of 10% CO_2, 20% H_2, and 70% N_2 at 37°C for 24 h.[7] A reference strain of *Streptococcus pneumoniae* ATCC 49619 was used as the control in each test.[7] The

MICs of anaerobes were determined using Brucella HK agar with 5% sheep blood in an atmosphere of 5% CO_2, 10% H_2, and 85% N_2 at 37°C for 48 h.[8] Reference strains of *Bacteroides fragilis* ATCC 25285 and *Bacteroides thetaiotaomicron* ATCC 29741 were used as controls in each test.[8] In the present study, the susceptibility breakpoints against viridans streptococci and anaerobes were determined by NCCLS criteria.[7-9] Since the breakpoints of cefazolin, minocycline, and levofloxacin against anaerobes have not been determined by the NCCLS, we determined them based on the breakpoints of other similar antibiotics, i.e., those which resemble them in structure and pharmacokinetics. The breakpoints against viridans streptococci were as follows: penicillin G, ≤0.12μg/ml; cefazolin, ≤8μg/ml; cefmetazole, ≤8μg/ml; erythromycin and clindamycin, ≤0.25μg/ml; minocycline, ≤2μg/ml; levofloxacin, ≤2μg/ml. The breakpoints against strict anaerobes were as follow: penicillin G, ≤0.5μg/ml; cefazolin, ≤8μg/ml; cefmetazole, ≤16μg/ml; clindamycin, ≤2μg/ml; minocycline, ≤4μg/ml; levofloxacin, ≤2μg/ml. As the breakpoint of erythromycin against strict anaerobes has not been determined by the NCCLS, it was determined for the present study to be ≤4μg/ml, according to a report by Spangler *et al*.[13]

ß-Lactamase test

Nitrocefin disks (Cefinase disk; Becton Dickinson) were inoculated as described above with a small portion of growth from the Brucella blood agar plates and the disks were observed for a change in colour from yellow to red.[6,14] *Bacteroides fragilis* ATCC 25285 was included as a positive control.[14]

Correlation of antimicrobial activity of penicillin G with that of other antibiotics

The strains of each pathogen were divided into two groups. When the strain did

not grow at the breakpoint concentration of penicillin G, the strain was defined as penicillin G-susceptible (PS). In contrast, when the strain grew at the breakpoint concentration, the strain was defined as penicillin G-unsusceptible (PU). The MIC values and the susceptibility rates of PS strains against antibiotics were compared with those of PU strains.

Statistical analysis

Statistical comparisons of the susceptibility rates and incidence of ß-lactamase-producing bacteria were performed by X^2 test.

RESULTS

Bacterial examination

A total of 664 strains were isolated from the test cases. Viridans streptococci, *Peptostreptococcus*, *Gemella*, pigmented and nonpigmented *Prevotella*, *Porphyromonas*, and *Fusobacterium* were predominant (Table I). Fundamentally, there was no difference in the bacteriologic data as regards the type of infection (dentoalveolar infections, periodontitis, and pericoronitis) and in presence or absence of past administration of antibiotics (data not shown). Antimicrobial susceptibilities were determined in viridans streptococci, *Peptostreptococcus*, pigmented and nonpigmented *Prevotella*, *Porphyromonas*, and *Fusobacterium*.

Relation between the isolation flora and type of the infection

Most of the dentoalveolar infections, periodontitis, and pericoronitis were mixed infections involving a number of bacterial species (Table II). Average numbers of isolated strains per abscess of dentoalveolar infections, periodontitis, and

pericoronitis were 4.1 (range 1-10), 4.3 (range 2-7), and 3.7 (range 2-6), respectively. Anaerobes were isolated from 90.6% to 100% in the three types of infection. Most of the facultative anaerobes isolated from the three types of infection were viridans streptococci. Isolation flora in all three types of infection were similar to one another, although aerobes and facultative anaerobes were found more frequently in the dentoalveolar infections than in cases of periodontitis and pericoronitis (Table II). More than half of each odontogenic infection had mixed flora including both strict anaerobes and facultative anaerobes; this was especially the case with viridans streptococci.

Susceptibility to penicillin G

Viridans streptococci showed a susceptibility rate of 77% and 0.25μg/ml of MIC_{90} value to penicillin G, suggesting that penicillin G would work well to eradicate viridans streptococci (Table III). *Peptostreptococcus*, *Porphyromonas,* and *Fusobacterium* showed 86%, 100%, and 89% susceptibility rates, respectively, and their MIC_{90} values were low. Although 72% of pigmented and 82% of nonpigmented *Prevotella* were susceptible to penicillin G, their MIC_{90} values were very high (≥16μg/ml). Eighty-five percent (22 of 26) of the PU strains of pigmented *Prevotella* were ß-lactamase positive, whereas 0% (0 of 67) of the PS strains were ß-lactamase positive; these results were significant ($P< .0001$). In nonpigmented *Prevotella*, all PU strains produced ß-lactamase, but none of the PS strains produced it ($P< .0001$).

Correlation of the susceptibility to penicillin G with that to the other antibiotics

Cefazolin worked well against viridans streptococci, *Peptostreptococcus,*

Porphyromonas, and *Fusobacterium* (Table IV). However, PU strains of pigmented and nonpigmented *Prevotella* showed greater MIC_{50} and MIC_{90} values, and significantly smaller susceptibility rates than did the PS strains ($P < .0001$)(Table IV). All cefazolin-unsusceptible strains (MIC, ≥16µg/ml) of pigmented and nonpigmented *Prevotella* produced ß-lactamase. Cefmetazole was also effective against viridans streptococci, *Peptostreptococcus, Porphyromonas*, and *Fusobacterium* (Table V). Moreover, cefmetazole worked well against both PS and PU strains of pigmented and nonpigmented *Prevotella* (Table V).

Only 55% of the PS viridans streptococci were susceptible to erythromycin. Surprisingly, PU viridans streptococci was not susceptible to erythromycin at all, and this susceptibility rate was significantly lower than that of the PS strains ($P < .0005$)(Table VI). The MIC_{50} and MIC_{90} values of PS and PU strains of *Fusobacterium* were very high. Erythromycin was effective against only 29% and 0% of PS and PU *Fusobacterium*, respectively.

In viridans streptococci, clindamycin was effective against 54% of the PS strains and 0% of the PU strains, respectively (Table VII). However, the MIC_{90} values of clindamycin against both strains were the same, namely, 0.5µg/ml. Clindamycin showed a quite strong antimicrobial activity against all strict anaerobes tested. In particular, clindamycin worked very well against pigmented and nonpigmented *Prevotella*, regardless of their susceptibilities to penicillin G (Table VII).

Although the antimicrobial activity of minocycline against the PU strains of pigmented *Prevotella* was decreased, minocycline was effective against most of the bacteria tested (Table VIII).

Only 56% of PS viridans streptococci were susceptible to levofloxacin (Table IX), and the PU viridans streptococci showed significantly smaller susceptible rate (25%)

than PS strains ($P < .005$). Levofloxacin was effective against strict anaerobes, although its antimicrobial activity against *Fusobacterium* was weaker than when in contact with other bacteria.

DISCUSSION

Many investigators have demonstrated that viridans streptococci, *Peptostreptococcus*, *Prevotella*, *Porphyromonas*, and *Fusobacterium* are frequently isolated from orofacial odontogenic infections.[1-6,15,16] Our bacteriologic data was in good agreement with that of these previous studies. The present study was analyzed with respect to isolation flora and type of infection. Most of patients had mixed infections, regardless of the type of infection that had initially been diagnosed (Table II). The average number of isolates per abscess was approximately four strains, which was a finding in agreement with those of other reports.[15,16] Only small differences in the isolated flora were observed among these types of infections (Table II). Strict anaerobes were found in almost of all of the patients, and these were often accompanied with facultative anaerobes, especially streptococci, regardless of the type of infection. It has been reported that a combination of anaerobic gram-positive cocci and anaerobic gram-negative rods were found frequently in dental root canal infections.[17,18] In the present study, the combination of strict anaerobic gram-positive cocci and strict anaerobic gram-negative rods was also found somewhat frequently in all types of infection examined. The present study suggests that the combination may be associated with all kinds of odontogenic infections. Further study of individual pathogens in various bacterial combinations is required to elucidate the role of these pathogens in the occurrence and prognosis of odontogenic infection.

Determination of the respective breakpoints may be important to analyze susceptibility data and to estimate antimicrobial effectiveness.[7-9] In general, breakpoints are determined based on data concerning the clinical outcome, the pharmacology of the agents, e.g., tissue and serum concentrations, degree of protein-binding, distribution of susceptibility of bacteria to agents, etc.[7] However, the specific breakpoints against pathogens in odontogenic infections have not been established. When antibiotics are administered, concentrations of antibiotics in oral and maxillofacial regions are much smaller than those found in serum samples.[19-21] In addition, the respective concentrations of antibiotic vary according to oral and maxillofacial regions; concentrations at the mandibular bone are lower than those in the dental alveolar serum, dental follicle, and gingiva.[19-21] Thus, it may be difficult to determine the special breakpoints for orofacial odontogenic infections. In the present study, the susceptibility breakpoints were determined by NCCLS criteria,[7-9] which are widely used in various bacterial studies. However, NCCLS breakpoints might be too strict for some of test antibiotics because the breakpoints are below the typical serum or tissue concentrations of the antibiotics. The bacterial strains that were determined to be unsusceptible to certain antibiotics according to the present criteria might actually be clinically susceptible to those antibiotics, as they may be affected by other factors, such as infection site or dosage.

The effectiveness of penicillins against viridans streptococci and ß-lactamase-producing anaerobic gram-negative rods has been previously debated in the literatures.[1-6,22] In the present study, the growth of 90% of viridans streptococci was inhibited at 0.25μg/ml penicillin G despite a susceptibility rate of 77% (Table III), indicating that penicillins remain reasonably effective against viridans streptococci. Seventy-two percent and 82% of pigmented and nonpigmented *Prevotella* were

susceptible to penicillin G at the tested concentrations, respectively, and their MIC_{90} values were high (≥16μg/ml). Notably, PU strains of pigmented and nonpigmented *Prevotella* were shown to produce ß-lactamase more frequently than did PS strains ($P< .0001$), indicating that the resistance of *Prevotella* against penicillin G is correlated with ß-lactamase production. It is important that, despite this resistance, more than 70% of pigmented and nonpigmented *Prevotella* were susceptible to penicillin G at the tested concentrations.

Cephalosporins should generally not be prescribed for patients who have immediate hypersensitivity reactions to penicillin, because some of these patients may also be allergic to several other ß-lactam antibiotics.[23] On the other hand, the cephalosporins are bactericidal and have few side effects; some of them have broader antimicrobial spectra and show stronger bactericidal activity against the pathogens specific to orofacial odontogenic infections.[23] In the present study, cefazolin and cefmetazole were shown to exert a great antimicrobial activity against the viridans streptococci, *Peptostreptococcus*, *Porphyromonas*, and *Fusobacterium* (Tables IV and V). Interestingly, the PU strains of pigmented and nonpigmented *Prevotella*, compared with the PS strains, were more resistant to cefazolin ($P< .0001$). In contrast, cefmetazole was active against all test bacteria. Cefazolin belongs to the first-generation cephalosporins, and is vulnerable to ß-lactamase,[23] while the stability of cefmetazole in response to ß-lactamase has been confirmed.[23,24] ß-Lactamase-stable cephalosporins, including cefmetazole, are effective against infections. However, these antibiotics are expensive.[6] In addition, some of these cephalosporins, including cefmetazole, are intravenously administered antibiotics.[23] The high cost or the inconvenience of intravenous administration of antibiotics may preclude wide use against odontogenic infections.

Erythromycin and clindamycin have been prescribed to patients who are allergic to penicillin.[1-6] However, it has been noted that erythromycin is not effective against *Fusobacterium*.[5,25] Our findings confirmed the poor antimicrobial activity of erythromycin against *Fusobacterium* (Table VI). Furthermore, erythromycin was not effective against viridans streptococci. In particular, erythromycin showed only weak antimicrobial activity against the PU strains. It has been demonstrated that *Streptococcus* and *Fusobacterium* are more frequently isolated from severe odontogenic infections than from milder infections.[26] The results of the present study suggest that erythromycin may be effective against mild or moderate infections in people with penicillin allergies, but it may not be suitable in cases of more severe infection. In addition, even in cases in which penicillin therapy fails, erythromycin may not be recommended.

Clindamycin is a powerful antibiotic against strict anaerobes including ß-lactamase-producing bacteria.[1-5,27] Our findings confirmed that clindamycin is a powerful agent against strict anaerobes, particularly against pigmented and nonpigmented *Prevotella* (Table VII). In the present study, the susceptibility rates of viridans streptococci to clindamycin, according to the breakpoint determined by NCCLS,[7] were low. However, growth of most viridans streptococci (both the PS and the PU strains) was inhibited by 0.5μg/ml clindamycin. Clindamycin produces high alveolar concentrations,[3] and bactericidal activity is achieved clinically with the usual recommended dose.[2] In addition, clindamycin might increase host defence potential,[28-30] and inhibit ß-lactamase production.[31] Thus, clindamycin would be effective in the treatment of infections. However, because of its propensity to cause antibiotic-associated colitis, it has not been widely used in more routine cases of mild to moderate infections.[1,3] We recommend clindamycin for the treatment of severe

infections, or in cases in which penicillin therapy has failed.

Many studies have indicated widespread resistance to tetracyclines.[1,3] In the present study, although the antimicrobial activity against the PU pigmented *Prevotella* was slightly decreased, minocycline was effective against all test bacteria (Table VIII). Although minocycline is bacteriostatic, it exerts greater antimicrobial activity against strict anaerobic bacteria than that of tetracycline or other parent compounds.[3,32] In cases in which infection is mild or moderate, minocycline may be effective, especially for patients allergic to penicillin or in cases of penicillin therapy failure. However, when minocycline is prescribed, an attention should be paid to its adverse effects, e.g., gastrointestinal upset, photosensitivity, tooth discoloration.[2,3]

The present study demonstrated that less than 60% of viridans streptococci were susceptible to levofloxacin (Table IX), a fluoroquinolone, which was not as effective against strict anaerobic bacteria as the other test antibiotics. In addition, fluoroquinolones are less cost-effective than the other antibiotics. Thus, the present results do not suggest that fluoroquinolones be used for the treatment of such infections.

In conclusion, viridans streptococci, anaerobic gram-positive cocci, and anaerobic gram-negative rods were isolated frequently from orofacial odontogenic infections. Mixed infection of strict anaerobes with facultative anaerobes, especially viridans streptococci, was predominant in odontogenic infections regardless of the type of infection. When orofacial odontogenic infections are treated with antibiotics, an antimicrobial spectrum against both viridans streptococci and oral strict anaerobes may be required. Penicillin still possesses powerful antimicrobial activity against major pathogens in orofacial odontogenic infections. However, ß-lactamase-producing bacteria may be resistant to penicillin. The susceptibility

results suggest that cefazolin may not have more advantages than penicillin, but cefmetazole may be more effective against infection than penicillin because cefmetazole possesses strong antimicrobial activity against ß-lactamase-producing bacteria. Moreover, clindamycin may be effective in the treatment of orofacial odontogenic infections. Minocycline also demonstrated good antimicrobial activity. However, the findings of the present study indicate that erythromycin and levofloxacin are of questionable benefit in the treatment of severe orofacial odontogenic infections.

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Table I. Organisms isolated from orofacial odontogenic infections

Aerobes	*Number of isolates*	*Anaerobes*	*Number of isolates*
Viridans streptococci	139	*Peptostreptococcus*	105
Staphylococcus	9	Pigmented *Prevotella*	93
Corynebacterium	9	*Fusobacterium*	90
Campylobacter	9	Nonpigmented *Prevotella*	56
Neisseria	8	*Gemella*	36
Actinomyces	7	*Porphyromonas*	35
Lactobacillus	6	*Bacteroides*	14
Enterobactor	3	*Eubacterium*	9
Heamophilus	3	*Veillonella*	8
Pseudomonas	2	*Propionibacterium*	2
Micrococcus	1	Unidentified anaerobic gram-positive coccus	1
Enterococcus	1	Unidentified anaerobic gram-positive rods	6
Klebsiella	1		
Branhamella	1		
Unidentified aeobic gram-negative rods	1	Unidentified anaerobic gram-negative rods	9
Total	200	Total	464

Table II. Relation between the isolated flora and type of odontogenic infections.

Isolated flora	*Number of cases (Proportion, %)*		
	Dentoalveolar Infection (n=128)	*Periodontitis (n=24)*	*Pericoronitis (n=11)*
Single bacterial species			
Strict anaerobe	2 (1.6)	0	0
Facultative anaerobe	4 (3.1)	0	0
Aerobe	0	0	0
Plural bacterial species			
Strict anaerobes alone	31 (24.2)	5 (20.8)	3 (27.3)
AGPC & AGNR *	24(18.8)	3(12.5)	3(27.3)
AGNR *	3 (2.3)	1 (4.2)	0
AGPC *	4 (3.1)	1 (4.2)	0
Strict anaerobes & Facultative anaerobes	75 (58.6)	16 (66.7)	6 (54.5)
AGPC & AGNR & Facultative anaerobes *	41(32.0)	8(33.3)	4(36.4)
AGNR & Facultative anaerobes	24(18.8)	4(16.7)	1 (9.1)
AGPC & Facultative anaerobes	5 (3.9)	3(12.5)	1 (9.1)
AO & Facultative anaerobes	5 (3.9)	1 (4.2)	0
Strict anaerobes & Aerobes	1 (0.8)	0	1 (9.1)
Strict anaerobes & Facultative anaerobes & Aerobes	7 (5.5)	2 (8.3)	1 (9.1)
Facultative anaerobes alone	5 (3.9)	1 (4.2)	0
Facultative anaerobes & Aerobes	3 (2.3)	0	0
Aerobes alone	0	0	0

AGPC, Strict anaerobic gram-positive cocci; AGNR, Strict anaerobic gram-negative rods; AO, strict anaerobes other than AGPC and AGNR.
*A few cases contained AO.

Organisms isolated from orofacial odontogenic infections

Aerobes	*Number of isolates*		*Anaerobes*	*Number of isolates*	
	*Antibiotics (-)** (72 cases)	*Antibiotics (+)†* (91 cases)		*Antibiotics (-)** (72 cases)	*Antibiotics (+) †* (91 cases)
Viridans streptococci	69	70	*Peptostreptococcus*	43	62
Staphylococcus	3	6	*Gemella*	16	20
Micrococcus	0	1	*Eubacterium*	7	2
Enterococcus	0	1	*Propionibacterium*	1	1
Corynebacterium	7	2	Pigmented *Prevotella*	32	60
Lactobacillus	3	3	Nonpigmented *Prevotella*	23	32
Actinomyces	4	3	*Porphyromonas*	18	16
Neisseria	3	5	*Fusobacterium*	38	50
Pseudomonas	0	2	*Bacteroides*	3	10
Enterobactor	0	3	*Veillonella*	3	5
Klebsiella	0	1	Unidentified anaerobic gram-positive coccus	0	1
Branhamella	0	1			
Heamophilus	2	1	Unidentified anaerobic gram-positive bacilli	4	1
Campylobacter	4	5			
Unidentified aeobic gram-negative bacillus	1	0	Unidentified anaerobic gram-negative bacilli	3	6
Average number of isolates	1.3	1.1		2.7	2.9

* Patients who had not received any antibiotics before specimen collection.
† Patients who had received antibiotics before specimen collection.

Table III. Antimicrobial susceptibility to penicillin G

Pathogen	*MIC(μg/ml)**			*Susceptibility rate (%)†*
	Range	*50%*	*90%*	
Viridans streptococci	≤0.015 - 0.5	0.12	0.25	77
Peptostreptococcus	≤0.015 - 4	≤0.015	2	86
Pigmented *Prevotella*	≤0.015 - 64	≤0.015	32	72
Nonpigmented *Prevotella*	≤0.015 - 64	≤0.015	16	82
Porphyromonas	≤0.015 - 0.5	0.03	0.12	100
Fusobacterium	≤0.015 - 2	0.03	1	89

*50% and 90%, MIC_{50} and MIC_{90}, respectively.

†The breakpoints of penicillin G against viridans streptococci and anaerobes are 0.12 μg/ml and 0.5 μg/ml, respectively.

Table IV. Antimicrobial susceptibility to cefazolin

Pathogen	*Type of strain**	*Number of strain*	*MIC(μg/ml) †*			*Susceptibility rate (%)‡*	
			Range	*50%*	*90%*		
Viridans streptococci	PS	107	≤0.015 - 4	0.25	2	100	
	PU	32	2 - 4	2	4	100	
Peptostreptococcus	PS	90	≤0.015 - 2	0.06	1	100	
	PU	15	≤0.015 - 8	0.03	8	100	
Pigmented *Prevotella*	PS	67	≤0.015 - 0.5	0.03	0.12	100	
	PU	26	≤0.015 - 64	2	32	73	§
Nonpigmented *Prevotella*	PS	46	≤0.015 - 4	0.06	1	100	
	PU	10	4 - 64	16	64	30	§
Porphyromonas	PS	35	≤0.015 - 2	0.25	2	100	
Fusobacterium	PS	80	≤0.015 - 8	0.12	1	100	
	PU	10	0.06 - 0.5	0.06	0.06	100	

* PS, penicillin G susceptible-strains; PU, penicillin G unsusceptible-strains. All test *Porphyromonas* strains were susceptible to penicillin G.

† 50% and 90% indicate MIC_{50} and MIC_{90}, respectively.

‡ The breakpoints of cefazolin against viridans streptococci and anaerobes are 8 μg/ml.

§ $P < .0001$. Statistically significant difference from that of PS strains.

Table V. Antimicrobial susceptibility to cefmetazole

Pathogen	*Type of strain**	*Number of strain*	*MIC(μg/ml) †*			*Susceptibility rate (%)‡*
			Range	*50%*	*90%*	
Viridans streptococci	PS	107	≤0.015 - 8	1	8	100
	PU	32	4 - 8	8	8	100
Peptostreptococcus	PS	90	≤0.015 - 4	0.12	1	100
	PU	15	≤0.015 - 16	0.25	16	100
Pigmented *Prevotella*	PS	67	≤0.015 - 0.5	≤0.015	0.5	100
	PU	26	0.03 - 8	0.5	2	100
Nonpigmented *Prevotella*	PS	46	≤0.015 - 64	0.06	8	96
	PU	10	0.03 - 8	4	4	100
Porphyromonas	PS	35	≤0.015 - 1	0.12	0.25	100
Fusobacterium	PS	80	≤0.015 - 16	0.5	4	100
	PU	10	0.5 - 8	0.5	8	100

*,† See Table IV.

‡The breakpoints of cefmetazole against viridans streptococci and anaerobes are 8 μg/ml and 16 μg/ml, respectively.

Table VI. Antimicrobial susceptibility to erythromycin

Pathogen	*Type of strain**	*Number of strain*	*MIC(μg/ml) †*			*Susceptibility rate (%)‡*	
			Range	*50%*	*90%*		
Viridans streptococci	PS	107	≤0.015 - 8	0.25	1	55	
	PU	32	0.5 - 64	0.5	2	0	§
Peptostreptococcus	PS	90	≤0.015 - 64	1	8	89	
	PU	15	≤0.015 - 64	0.5	64	80	
Pigmented *Prevotella*	PS	67	≤0.015 - 1	0.12	1	100	
	PU	26	0.06 - 64	0.5	32	77	§
Nonpigmented *Prevotella*	PS	46	≤0.015 - 64	0.5	32	89	
	PU	10	0.03 - 64	0.06	32	80	
Porphyromonas	PS	35	≤0.015 - 64	≤0.015	0.25	94	
Fusobacterium	PS	80	0.03 - 64	8	64	29	
	PU	10	8 - 64	8	64	0	

*,† See Table IV.

‡ The breakpoints of erythromycin against viridans streptococci and anaerobes are 0.25 μg/ml and 4 μg/ml, respectively.

§ $P < .0005$. Statistically significant difference from that of PS strains.

Table VII. Antimicrobial susceptibility to clindamycin

Pathogen	*Type of strain**	*Number of strain*	*MIC(μg/ml) †*			*Susceptibility rate (%)‡*
			Range	*50%*	*90%*	
Viridans streptococci	PS	107	≤0.015 - 1	0.25	0.5	54
	PU	32	0.5 - 8	0.5	0.5	0 §
Peptostreptococcus	PS	90	≤0.015 - 1	0.12	0.5	100
	PU	15	≤0.015 - 2	0.03	2	100
Pigmented *Prevotella*	PS	67	≤0.015 - 0.03	≤0.015	≤0.015	100
	PU	26	≤0.015 - 0.12	0.03	0.06	100
Nonpigmented *Prevotella*	PS	46	≤0.015 - 2	≤0.015	0.25	100
	PU	10	≤0.015 - 0.12	≤0.015	0.06	100
Porphyromonas	PS	35	≤0.015 - 0.06	≤0.015	0.03	100
Fusobacterium	PS	80	≤0.015 - 0.25	0.06	0.12	100
	PU	10	0.06 - 0.12	0.12	0.12	100

*,† See Table IV.

‡ The breakpoints of clindamycin against viridans streptococci and anaerobes are 0.25 μg/ml and 2 μg/ml, respectively.

§ $P < .0001$. Statistically significant difference from that of PS strains.

Table VIII. Antimicrobial susceptibility to minocycline

Pathogen	*Type of strain**	*Number of strain*	*MIC(μg/ml) †*			*Susceptibility rate (%)‡*
			Range	*50%*	*90%*	
Viridans streptococci	PS	107	≤0.015 - 2	0.25	0.5	100
	PU	32	≤0.015 - 64	0.5	2	94
Peptostreptococcus	PS	90	≤0.015 - 4	0.12	2	100
	PU	15	≤0.015 - 4	0.06	4	100
Pigmented *Prevotella*	PS	67	≤0.015 - 8	0.03	0.12	94
	PU	26	0.12 - 16	2	8	81
Nonpigmented *Prevotella*	PS	46	≤0.015 - 2	0.03	0.5	100
	PU	10	0.03 - 2	0.03	2	100
Porphyromonas	PS	35	≤0.015 - 8	≤0.015	2	97
Fusobacterium	PS	80	≤0.015 - 4	0.06	1	100
	PU	10	0.03 - 2	0.03	2	100

*,† See Table IV.

‡The breakpoints of minocycline against viridans streptococci and anaerobes are 2 μg/ml and 4 μg/ml, respectively.

Table IX. Antimicrobial susceptibility to levofloxacin

Pathogen	*Type of strain**	*Number of strain*	*MIC(μg/ml) †*			*Susceptibility rate (%)‡*
			Range	*50%*	*90%*	
Viridans streptococci	PS	107	≤0.015 - 64	2	8	56
	PU	32	1 - 16	4	8	25 §
Peptostreptococcus	PS	90	≤0.015 - 8	0.5	1	99
	PU	15	≤0.015 - 8	0.06	8	87
Pigmented *Prevotella*	PS	67	≤0.015 - 8	0.25	4	90
	PU	26	0.25 - 32	1	4	77
Nonpigmented *Prevotella*	PS	46	≤0.015 - 32	0.5	1	91
	PU	10	0.25 - 32	2	4	80
Porphyromonas	PS	35	≤0.015 - 16	0.25	1	91
Fusobacterium	PS	80	≤0.015 - 4	1	4	76
	PU	10	0.5 - 4	0.5	4	70

*,† See Table IV.

‡ The breakpoints of levofloxacin against viridans streptococci and anaerobes are 2 μg/ml.

§ $P < .005$. Statistically significant difference from that of PS strains.