Past administration of β-lactam antibiotics and increase in the emergence of β-lactamase-producing bacteria in patients with orofacial odontogenic infections.

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The past administration of ß-lactam antibiotics increases the emergence of ß-lactamase-producing bacteria in patients with orofacial odontogenic infections

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ABSTRACT

Objectives. The purpose of this study was to determine the current status of ß-lactamase-producing bacteria in orofacial odontogenic infections.

Study design. Microbiological data from pus specimens of 111 cases with orofacial odontogenic infections were analyzed in relation to the past administration of ß-lactams in the enrolled infections.

Results. ß-lactamase-producing bacteria were isolated more frequently from the ß-lactam-administered group (38.5%) than from the ß-lactam-nonadministered group (10.9%) ($P < .005$), and they were isolated more frequently as the duration of administration increased. The predominant bacteria isolated included *Prevotella*, the most frequent isolate, viridans streptococci, *Peptostreptococcus*, and *Fusobacterium*, and 7.1% of total isolates produced ß-lactamase. Penicillin and cefazolin worked well with ß-lactamase-nonproducing *Prevotella*, but were remarkably affected by ß-lactamase-producing *Prevotella*. Cefmetazole, sulbactam/cefoperazone, and imipenem worked well against both kinds of *Prevotella*.

Conclusions. ß-lactams are still suitable for the first antimicrobial therapy in the treatment of the infections. However, since past ß-lactam administration increases the emergence of ß-lactamase-producing bacteria, ß-lactamase-stable antibiotics should be prescribed to patients with unresolved infections who have received ß-lactams.

For the treatment of orofacial odontogenic infections, the ß-lactam antibiotics are recommended because they work well against the specific bacterial causative agents of orofacial odontogenic infections with a very low incidence of adverse effects.[1-6] Additionally, treatment with ß-lactam antibiotics is cost-effective. A problem with antimicrobial therapy with ß-lactams is the increasing rates of ß-lactam resistance, which lead to treatment failures.[3-6] ß-lactam resistance is considered to be closely correlated with the emergence of ß-lactamase producing bacteria.[3-9] There have been many reviews of orofacial odontogenic infections stressing the importance of ß-lactamase-producing bacteria in ß-lactam resistance.[3-6] Surprisingly, however, very little data regarding the occurrence of ß-lactamase-producing bacteria in orofacial odontogenic infections, on which the reviews should be based, is available. Most of the examinations of ß-lactamase-producing bacteria have been limited to a few bacterial species or to periodontal disease.[10-14] We therefore determined that data regarding the current status of the occurrence of ß-lactamase-producing bacteria in orofacial odontogenic infections were required.

Purulent orofacial odontogenic infections can be managed by tooth extraction, endodontic therapy, and surgical treatment, including drainage, without the use of antibiotics.[1,3-5] However, when acute bacterial infection has progressed, or when antimicrobial therapy might benefit patients, antibiotics are prescribed. In Japan, when acute odontogenic infections except pulpitis and gingivitis simplex are diagnosed or strongly suspected, almost all oral surgeons prescribe antibiotics in the course of the treatment to ensure the efficacy of treatment, or to minimize the risk of infection progression.

In Japan, oral surgeons in large hospitals and medical centers are often referred the patients with unsolved infections from other oral surgeons or doctors. The oral surgeons should take into account the past administration of antibiotics for orofacial odontogenic infections. To effectively administer antimicrobial therapy for patients, microbiological data from an individual pus specimen must be obtained. Generally, however, it takes several days or longer to obtain the necessary data, and we therefore frequently start empiric antimicrobial therapy. For this reason, it is necessary to establish a principle regimen of empiric antimicrobial therapy for orofacial odontogenic infections, including cases treated with antibiotics in the past.

To address these issues, we investigated the relationships between the past administration of ß-lactam antibiotics, the emergence of ß-lactamase-producing pathogens, and the antimicrobial susceptibility of the isolates from pus specimens of orofacial odontogenic infections. Our results show that *Prevotella* has the highest incidence of ß-lactamase production in frequent isolates, and that the past administration of ß-lactam antibiotics increases the isolation of ß-lactamase-producing bacteria. Furthermore, based on the results, we discuss a regimen of antimicrobial chemotherapy for the effective treatment of orofacial odontogenic infections.

MATERIAL AND METHODS

Patients

The case histories of a total of 111 patients with obstructed abscesses caused by orofacial odontogenic infections were investigated. All patients were treated at our hospital during the 48 months between January 1993 and December 1996.

Patients who required serious medical care (e.g., cases with diabetes mellitus, rheumatoid arthritis, respiratory tract infections, leukemia) were excluded. The types of infection observed were dentoalveolar infections, 95 cases; periodontitis, 8 cases; and pericoronitis, 8 cases.

The subjects were classified into two groups: the ß-lactam (+) group and the ß-lactam (-) group. The former had received ß-lactam antibiotics for the treatment of orofacial odontogenic infections prior to the pus collection for this study. The administration of ß-lactams had occurred once in the course of the infection within 8 days prior to the pus collection. The patients had received only ß-lactam antibiotics during the course of their infections and had not been administered any additional antibiotics within the previous 3 months. A total of 65 cases belonged to the ß-lactam (+) group. The types of infection included were dentoalveolar infections, 56 cases; periodontitis, five cases; and pericoronitis, four cases. The average age of this group was 40.3 years (range 7-77 years). ß-lactam antibiotics were prescribed to 47 patients in our hospital, and to 18 patients at other hospitals and private practices. The ß-lactam antibiotics administered to the patients were oral-penicillin, four cases; intravenous-penicillin, two cases; oral-first-generation cephalosporin, six cases; intravenous-first-generation cephalosporin, one case; intravenous-second-generation cephalosporin, 21 cases; oral-third-generation cephalosporin, 27 cases; intravenous-third-generation cephalosporin, two cases; and carbapenem, two cases. The appropriateness of the use of antibiotics, including the dose and duration, was confirmed by the authors. The other group was the ß-lactam (-) group, who had not received any antibiotics within 3 months prior to the pus collection for this study. Forty-six cases belonged to the ß-lactam (-) group.

The average age was 48.7 years (range 18-85 years). The types of infection included were dentoalveolar infections, 39 cases; periodontitis, three cases; pericoronitis, four cases. Information regarding the past and physical histories of the patients were obtained by interview and from the medial records of our hospital, if they existed. When patients were treated for orofacial odontogenic infections by doctors other than the authors, we interviewed the doctors regarding the patient histories.

This study was performed based on the permission of all patients who participated.

Bacterial quantitative examination

The pus specimens were collected from the abscesses by aspiration with an 18-gauge needle. The specimens were placed in anaerobic transport devices (Seed Tube; Eiken, Tokyo, Japan) and immediately transported to the laboratory. The specimens were 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, the same specimens were aerobically incubated on Brucella HK agar with 5% sheep blood, and on the same agar in an atmosphere of 10% CO_2, 20% H_2, and 70% N_2 at 37°C for 48 h. Even when no bacteria growth was observed, incubation was continued for at least 7 days. Anaerobic bacteria were identified using Rap ID ANA Ⅱ (Innovative Diagnostic System, Norcross, GA). In addition to this test, gas liquid chromatography was performed as needed to identify bacteria.[15] Aerobic and micro-aerophilic bacteria were identified using conventional methods.[16] Bacterial strains were stored in 10% skim milk (Difco, Detroit, MA) at -80°C.

ß-lactamase test

Nitrocefin disks (Cefinase disk; BBL Microbiology Systems, Cockeysville, MD) were inoculated with a small portion of growth from the Brucella blood agar plates described above and observed for a change in color from yellow to red.[17]

Susceptibility test

Antibiotics were obtained from their manufacturers as laboratory powders, each of a defined potency: penicillin G (Banyu, Tokyo, Japan), ampicillin (Meiji, Tokyo, Japan), cefazolin (Fujisawa, Tokyo, Japan), cefmetazole (Sankyo, Tokyo, Japan), sulbactam/cefoperazone (Pfizer, Tokyo, Japan), and imipenem (Banyu). All minimum inhibitory concentrations (MICs) were determined by the agar dilution method recommended by the National Committee for Clinical Laboratory standards[18]; the MICs of anaerobes were determined using the 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. The susceptibility breakpoints were determined on the basis of the propositions of the National Committee for Clinical Laboratory standards[18]; the breakpoints used were 2.0 µg/ml for penicillin G and ampicillin, 8.0 µg/ml for cefazolin, 16.0 µg/ml for cefmetazole and sulbactam/cefoperazone, and 4.0 µg/ml for imipenem.

Statistical analysis

Statistical comparisons of the incidence of ß-lactamase-producing bacteria and susceptibility rate in the susceptibility test were performed by a χ^2 test.

RESULTS

ß-lactamase-producing bacteria were isolated in 25 of 65 cases (38.5%) in the ß-lactam (+) group, while in only five of 46 cases (10.9%) in the ß-lactam (-) group. The incidence of the isolation of ß-lactamase-positive bacteria in the ß-lactam (+) group was significantly higher than in the ß-lactam (-) group ($P < .005$) (Table I). Furthermore, we found a correlation between the incidence of the isolation of ß-lactamase-producing bacteria and the duration of the past administration of ß-lactams (Table I). The incidence of isolation of ß-lactamase-producing bacteria was low in the patients who had received ß-lactam for 1 or 2 days. However, as the administration duration increased, ß-lactamase-producing bacteria were isolated more frequently. It is interesting that both patients who received ß-lactam for 8 days had ß-lactamase-producing bacteria.

A total of 449 strains of bacteria were isolated from the 111 cases (Table II). Out of a total of 449 isolates, 32 (7.1%) were ß-lactamase-positive strains. Twenty-nine of 266 isolates (10.9%) and three of 183 isolates (1.6%) were ß-lactamase-producing bacteria in the ß-lactam (+) and in the ß-lactam (-) groups, respectively. This difference was significant ($P < .001$). A distinct difference in the variety of bacterial species isolated between the ß-lactam (+) and ß-lactam (-) groups was not observed. *Prevotella*, viridans streptococci, *Peptostreptococcus*, and *Fusobacterium* were isolated frequently (Table II). In the isolated organisms, ß-lactamase-producing strains were detected in *Enterobacter*, *Klebsiella*, *Prevotella*, *Porphyromonas*, and *Bacteroides*, but no strains of the other species produced ß-lactamase. All isolates of *Enterobacter* and *Klebsiella* produced ß-lactamase, but these species were rarely isolated. The pigmented

Prevotella (*P. intermedia*, *P. melaninogenica*, and *P. loescheii*) and nonpigmented *Prevotella* (*P. oralis*, *P. oris*, and *P. buccae*) were isolated frequently, and a significant number of these isolates produced ß-lactamase: 27.3% (18 of 66) of pigmented *Prevotella* strains and 16.7% (7 of 42) of nonpigmented *Prevotella* strains were ß-lactamase positive. ß-lactamase-producing strains of pigmented *Prevotella*, nonpigmented *Prevotella*, and *Bacteroides* were often found in the ß-lactam (+) group. In particular, ß-lactamase-producing strains of *P. intermedia* were isolated more frequently from the ß-lactam (+) group than from the ß-lactam (-) group with a significance of $P < .05$.

ß-lactamase-producing bacteria were detected in two of four cases receiving oral-penicillin, in one of two cases received intravenous-penicillin, in four of six cases receiving oral-first-generation cephalosporin, in one of one cases receiving intravenous-first generation cephalosporins, in five of 21 cases receiving intravenous-second generation cephalosporin, in 11 of 27 cases receiving oral third-generation cephalosporin, in zero of two cases receiving intravenous-third generation cephalosporin, and in one of two cases receiving intravenous carbapenem.

Since *Prevotella* was isolated frequently and showed a high incidence of ß-lactamase production (Table II), the antimicrobial susceptibility of *Prevotella* to several ß-lactam antibiotics was determined (Table III). In both pigmented *Prevotella* and nonpigmented *Prevotella*, the MIC (MIC_{50} and MIC_{90}) values of penicillin G, ampicillin, and cefazolin of ß-lactamase-producing strains were distinctly greater than those of the nonproducing strains. In addition, the susceptibility rates of ß-lactamase-producing strains in pigmented and

nonpigmented *Prevotella* were significantly smaller than those of the nonproducing strains ($P < .03$). The MIC values of cefmetazole and sulbactam/cefoperazone of the ß-lactamase-producing strains in pigmented *Prevotella* were also higher than those of the non ß-lactamase-producing strains, but all strains were susceptible to cefmetazole and sulbactam/cefoperazone. In nonpigmented *Prevotella*, there were little differences in the MIC values of cefmetazole and sulbactam/cefoperazone between ß-lactamase-producing and nonproducing strains, and all strains were susceptible to them. Imipenem had quite low MIC values and high susceptibility rates against both pigmented and nonpigmented *Prevotella*, but there were no strict differences in MIC values or susceptibility rates between ß-lactamase-producing strains and nonproducing strains of both pigmented and nonpigmented *Prevotella*.

DISCUSSION

In Japan, the use of antibiotics in oral surgery is strictly regulated by the Ministry of Health and Welfare of Japan via the national health insurance.[19] The costs of exceeded dose and incorrect selection of antibiotics are billed to the hospitals employing the oral surgeons who prescribed them, or to the surgeons themselves if they are owners of clinics. Thus, to our knowledge, remarkably inappropriate use of antibiotics for the treatment of orofacial odontogenic infections is rare in Japan, although there would be differences concerning the management of antibiotic therapy between nations.

Three modes of resistance to ß-lactam antibiotics have been proposed regarding pathogens of the orofacial odontogenic infection: ß-lactamase production, barriers to target sites, and penicillin-binding proteins.[7,20] ß-lactamase

production would protect not only ß-lactamase-producing bacteria but also the nonproducing bacteria from ß-lactam antibiotics[21-23]: because orofacial odontogenic infections are polymicrobial,[2,4-6,24] the emergence of ß-lactamase-producing bacteria may protect the nonproducing bacteria from the ß-lactam antibiotics. It is well known that staphylococcal organisms and some gram-negative bacilli can produce ß-lactamase.[25-28] In the present study, ß-lactamase was detected in aerobic and strictly anaerobic gram-negative bacilli, while none of the *Staphylococcus* isolated produced this enzyme. The incidence of ß-lactamase-producing anaerobic gram-negative bacilli has been reported in several studies.[10-12,17] ß-lactamase is detected in 26% to 100% of pigmented *Prevotella* involving *P. intermedia*, *P. melaninogenica*, *P. loescheii*,[10,17] 37.5% to 77.1% of nonpigmented *Prevotella*,[10,12] 13% to 23.5% of *F. nucleatum*,[11,12,17] and 33.3% of *P. gingivalis*.[12] In the present study, 27.3% of pigmented *Prevotella*, 16.7% of nonpigmented *Prevotella*, 0% of *Fusobacterium,* and only one strain of *Porphyromonas* produced ß-lactamase. The incidence of ß-lactamase-producing bacteria observed in this study was lower than that of previous studies.

ß-lactamase-producing bacteria resist antimicrobial chemotherapy with penicillins.[3-7,22] In addition, ß-lactamase produced by *P. melaninogenica* and *P. oralis* have been shown to be more active against penicillins than against cephalosporins.[7] Cefazolin is a first- generation cephalosporin.[29] In general, the first-generation cephalosporins are affected by ß-lactamase more strongly than the second- or third- generation agents. Cefmetazole is stable with ß-lactamase and active against anaerobic bacteria.[30,31] Sulbactam/cefoperazone is a member of the cephalosporin family made by combining cefoperazone and

sulbactam, a ß-lactamase inhibitor.[32] Adding sulbactam to ß-lactam antibiotics has been shown to increase antibacterial activity against ß-lactamase-producing bacteria.[7,32-34] Imipenem has an unusually broad spectrum, a high potency, a stability to ß-lactamase, and no cross-resistance with other ß-lactam agents.[34-36] It is interesting that the activity of test penicillins and cefazolin against ß-lactamase-producing *Prevotella* was decreased remarkably in the present study, while these antibiotics inhibited the growth of the ß-lactamase-nonproducing *Prevotella*. In contrast, cefmetazole and sulbactam/cefoperazone were active against both ß-lactamase-producing and nonproducing *Prevotella*. Moreover, imipenem greatly inhibited the growth of ß-lactamase-producing *Prevotella*.

In penicillin therapy, the relationship between exposure to penicillin and the emergence of ß-lactamase-producing bacteria has been discussed.[13,14,37] Brook et al [37], Heimdahl et al [13], and Kinder et al [14] have noted that the use of penicillin is associated with the emergence of ß-lactamase-producing bacteria, while the work of Lewis et al [22] dose not support this conclusion. In the present study, although cephalosporins were administered more frequently than penicillins, ß-lactamase-producing bacteria were found more frequently in the ß-lactam (+) group than in the ß-lactam (-) group. Especially in *Prevotella*, which was the most frequent isolate, ß-lactamase-producing strains were found more frequently in the ß-lactam (+) group than in the ß-lactam (-) group. This suggests that past antimicrobial therapy with ß-lactam antibiotics for an unresolving infection increases the incidence of ß-lactamase-producing bacteria in abscesses of odontogenic infections.

We found an interesting correlation between the incidence of ß-lactamase-producing bacteria and the duration of ß-lactam administration in the past

treatment in orofacial odontogenic infections. When the duration was 1 or 2 days, few ß-lactamase-producing bacteria emerged. However, when patients received ß-lactam antibiotics for 3 days or more, 50% or more of the cases acquired ß-lactamase-producing bacteria. In Japan, the daily doses of ß-lactams usually used for adult orofacial odontogenic infections are regulated by Health and Welfare of Japan. For example, the doses for an adult (with 60 kg weight) are as follows: oral-ampicillin, 1 g; intravenous-ampicillin, 2 g; cephalexin, 750 mg; cefazolin, 1 g; cefmetazole, 2 g; cefpodoxime, 200 mg; cefdinir, 300 mg.[19] All patients in the ß-lactam (+) group received the appropriate doses. A clear correlation between the incidence of ß-lactamase-producing bacteria and the type of antibiotics or route of administration was not found. Further studies to evaluate the relations between the incidence of ß-lactamase-producing bacteria and the type of antibiotics, dosage, or route of administration may be required based on both the patient population and the microbiological population. However, the present study suggests that if patients with orofacial odontogenic infections have already received ß-lactam antibiotics for 3 days or more, regardless of the type of antibiotic or the route of administration, we should assume that ß-lactamase-producing bacteria are present in the lesion and are associated with infection progression.

Based on this study, we propose a principle for developing a regimen to treat orofacial odontogenic infections empirically. If the patients have not received ß-lactam antibiotics in the course of the infections, or even if they have received ß-lactam antibiotics with an appropriate dose for a duration of 1 day or 2 days, penicillins and primitive cephalosporins are suitable to prescribe, since in this instance there is only a small possibility of the occurrence of ß-lactamase-

producing bacteria, and these antibiotics are considered to be effective. In contrast, if the patients already received antimicrobial therapy with ß-lactams in the course of the infections for a duration of 3 days or more, it should be assumed that ß-lactamase-producing bacteria may occur or be present in the unsolving lesion. In such cases, ß-lactamase-stable ß-lactams or non-ß-lactam antibiotics such as clindamycin and macrolide may be effective.[1-6,38,39] In this case, we recommend the primary use of ß-lactamase-stable ß-lactams, since they have great effectiveness against pathogens of the infection, especially *Prevotella*, *Porphyromonas*, and *Fusobacterium*,[33,34] and the occurrence of side effects is lower than with other antibiotics. In addition, cost should be taken into account. Many of these ß-lactamase-stable antibiotics are more expensive than penicillins and primitive cephalosporins.[5,40] For example, in Japan, the costs of cefmetazole, sulbactam/cefoperazone, and imipenem are two to five times as high as the cost of penicillins or primitive cephalosporins. Moreover, to prevent increasing the incidence of resistance to these ß-lactamase-stable agents, they should not be abused. Therefore, we do not agree with the practice of prescribing ß-lactamase-stable antibiotics to all patients without consideration. Not only *Prevotella* but also viridans streptococci, *Peptostreptococcus*, and *Fusobacterium* have been shown to be frequent isolates in orofacial odontogenic infections.[2,4,24,41] The resistance mechanisms of viridans streptococci and *Peptostreptococcus* against ß-lactams are rather to alter membrane permeability or to alter target sites (the mutation of penicillin-binding proteins) than to induce ß-lactamase production.[42,43] However, the regimen proposed here would be effective against these bacteria, including *Fusobacterium*, based on the susceptibility data of other studies[12,44-46] and our unpublished data. Our

department now employs this regimen, and satisfactory results are being obtained (unpublished data).

The results of this study and the regimen proposed here may be helpful in devising a more effective treatment for orofacial odontogenic infections.

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Table I. Correlation between the incidence of ß-lactamase-producing bacteria and the ß-lactam-administered duration in past antimicrobial treatment

*Group**	*Duration (days)*	*Incidence*[†]
ß-lactum (-)	No administration	5/46 (10.9)
ß-lactum (+)	1	0/ 7
	2	2/14 (14.3)
	3	15/30 (50.0)
	4	2/ 4 (50.0)
	5	2/ 4 (50.0)
	6	2/ 4 (50.0)
	7	0/ 0
	8	2/ 2 (100)

*See the text regarding this grouping.

[†]No. of cases from which ß-lactamase -producing bacteria were isolated / No. of total cases (percents).

Table II. Incidence of ß-lactamase-producing bacteria from patients with orofacial odontogenic infections

Aerobes	*Incidence **		*Anaerobes*	*Incidence **	
	ß-lactam (+) group †	*ß-lactam (-) group* ‡		*ß-lactam (+) Group* †	*ß-lactam (-) group* ‡
Viridans streptococci	0/49	0/38	*Peptostreptococcus*	0/44	0/29
Staphylococcus	0/ 2	0/ 1	*Gemella*	0/16	0/ 9
Micrococcus	0/ 1	0/ 0	*Eubacterium*	0/ 1	0/ 5
Corynebacterium	0/ 1	0/ 3	Pigmented *Prevotella*	17/47 (36.2)	1/19 (5.3)
Lactobacillus	0/ 3	0/ 2	*P. intermedia*	12/30 (40.0) §	1/14 (7.1)
Actinomyces	0/ 1	0/ 3	*P. melaninogenica*	4/ 7 (57.1)	0/ 2
Neissesria	0/ 1	0/ 1	*P. loescheii*	1/10 (10.0)	0/ 3
Klebsiella	1/ 1 (100)	0 / 0	Nonpigmented *Prevotella*	6/24 (25.0)	1/18 (5.6)
Enterobacter	2/ 2 (100)	0/ 0	*P. oralis*	4/ 9 (44.4)	1/ 7 (14.3)
Campyrobacter	0/ 3	0/ 3	*P. oris*	1/ 6 (16.7)	0/ 3
Unidentified aerobes	0/ 4	0/ 3	*P. buccae*	1/ 9 (11.1)	0/ 8
			Porphyromonas gingivalis	0/10	0/12
			P. endodontalis	0/ 1	1/ 3 (33.3)
			Fusabacterium nucleatum	0/33	0/21
			F. necrophorum	0/ 5	0/ 5
			Bacteroides	3/ 9 (33.3)	0/ 2
			Veillonella	0/ 2	0/ 1
			Unidentified anaerobes	0/ 6	0/ 5
Total	3/ 68 (4.4)	0/ 54	Total	26/ 198 (13.1) §	3/ 129 (2.3)

*No. of ß-lactamase-producing isolates / No. of total isolates (percents).

†,‡ See the text regarding this grouping.

§ Statistically significant at $P < .05$.

Table III. Antimicrobial susceptibility of *Prevotella* against ß-lactam antibiotics

	ß-lactamase-producing strains			*ß-lactamase-nonporducing strains*		
	MIC (µg/ml)		*Susceptibility*	*MIC (µg/ml)*		*Susceptibility*
	50%	*90%*	*rate(%)*	*50%*	*90%*	*rate(%)*
Pigmented *Prevotella*						
Penicillin G	4.0	32.0	33.3 *	≤0.015	2.0	87.5
Ampicillin	0.5	64.0	61.1 *	0.06	0.5	93.8
Cefazolin	2.0	16.0	83.3 *	≤0.015	0.5	100
Cefmetazole	0.5	2.0	100	≤0.015	1.0	100
Sulbactam/ cefoperazone	1.0	8.0	100	≤0.015	1.0	100
Imipenem	≤0.015	0.06	100	≤0.015	0.06	100
Non-pigmented *Prevotella*						
Penicillin G	16.0	32.0	0.0 *	0.06	0.5	100
Ampicillin	16.0	32.0	0.0 *	0.1	2.0	82.9
Cefazolin	16.0	64.0	28.6 *	0.1	1.0	100
Cefmetazole	4.0	4.0	100	0.2	8.0	100
Sulbactam/ cefoperazone	2.0	2.0	100	0.5	8.0	100
Imipenem	≤0.015	0.06	100	0.06	0.2	100

In pigmented *Prevotella*, 18 ß-lactamase-producing strains and 48 ß-lactamase nonproducing strains were tested. In nonpigmented *Prevotella*, seven ß-lactamase-producing strains and 35 ß-lactamase-nonproducing strains were tested.

* $P < .03$ vs. ß-lactamase-nonproducing strains.