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— Original Articles —

Status of antimicrobial use among dentists in Japan

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SUMMARY

Although excess antimicrobials prescribed by medical doctors and dentists can lead to antimicrobial resistance in normal flora, few studies have explored their actual use among dentists in Japanese communities. We investigated a representative sample of dentists working in various community clinics throughout Japan in order to determine the actual use of antimicrobials in urban dental clinics. A questionnaire regarding antimicrobial use was sent to 500 randomly selected dentists in 500 dental clinics in communities throughout Japan. Among the 252 respondents (50.4% response rate), 31 (12.3%) and 169 (66.7%) administered antimicrobials before and after dental procedures, respectively, regardless of patient background or type of procedure, whereas 51 (20.2%) decided time and indication of antimicrobial administration depending on patient background. A total of 227 respondents (90.0%) prescribed antimicrobials for 3-4 days. The most commonly administered antimicrobial was third-generation cephalosporins in 129 respondents (51.2%), followed by first-generation cephalosporins in 34 (13.5%), penicillins in 30 (11.9%), macrolides in 29 (11.5%) and new quinolones in 14 (5.6%). Indications of prophylactic use of antimicrobials tended to exceed the guidelines to prevent infective endocarditis and to be used longer than their recommendations. Collaboration between dental and medical fields and information campaigns for appropriate antimicrobial use in dental clinics should be accelerated.

INTRODUCTION

As in general medical practice, antimicrobials are commonly administered in dentistry for prophylaxis or treatment of infectious diseases. Antimicrobial agents are most commonly administered in dentistry for preventing infective endocarditis or minimally invasive treatment-related local infection and for treating periodontal diseases. With the emergence of antimicrobial resistance in medical fields, the importance of proper antimicrobial use in the community has been widely recognized. However, until recently, no nationwide studies have evaluated this parameter in Japanese dental clinics. According to an institutional evaluation by the Japanese Ministry of Health, Labour and Welfare[1)], there are 68,500 dental clinics throughout Japan as of December 2012, a number that far exceeds the number of dental university hospitals. To determine the actual use of antimicrobials in urban dental clinics, we investigated a representative sample of dentists working in various community

clinics throughout Japan.

MATERIALS AND METHODS

Five hundred dentists working in 500 urban clinics were randomly selected from among all dental clinics in Japan. The number of subjects selected in each prefecture was proportional to the population of the respective prefecture. A questionnaire was sent to 1 dentist per clinic. The questionnaire included the following items: 1) number of practice years after graduation; 2) the number of dentists working in a clinic; 3) indications for antimicrobial administration; 4) timing of antimicrobial administration; 5) duration of administration; and 6) most commonly prescribed antimicrobial. Responses were returned via postcards and participation was rewarded with a 1,000-yen gift certificate. Questionnaires returned within the 5 months from August 1 to December 31, 2011 were used for evaluation. This study was approved by the Juntendo Hospital Ethics Committee (Number: 2011029).

RESULTS

Table 1 shows the background data for the 252 dentists (50.4% response rate) who returned the questionnaire. Most respondents worked in small clinics of no more than a few dentists. Figure 1 shows the findings regarding the actual antimicrobials prescribed. A total of 115 respondents (45.6%) reported that they prescribed prophylactic antimicrobials for all procedures, including tooth extraction, whereas 136 (54.0%) reported that they were prescribed for patients with specific conditions.

Of these, 104 responders provided detailed comments on indications for antimicrobials. Forty-nine respondents cited prophylactic administration, of whom 7 specified patients with valve or congenital heart disease, 13 specified patients with diabetes or other immunosuppressed diseases who needed invasive procedures and were thought to be at high risk of local infection, 19 specified patients who underwent difficult extraction and 10 respondents reported administration for prevention of local infection after invasive implantation procedures. In contrast, 55 respondents reported that they limited antimicrobial use to treatment of periodontal infection.

Regarding the timing of oral antimicrobial administration, 31 (12.3%) reported antimicrobial administration before any dental procedures and 169 (67.1%) reported their use after dental procedures, regardless of patient background or type of procedure, whereas 51 (20.2%) reported that the timing of antimicrobial

Table 1. Background data for respondents

Area	Number	%
Hokkaido	9	3.6
Tohoku	18	7.1
Kanto	86	34.1
Chubu	45	17.9
Kinki	40	15.9
Chugoku	14	5.6
Shikoku	8	3.2
Kyushu	32	12.7
Total	252	
Number of practicing dentists in clinic	Number	%
1- 2	223	88.5
3- 5	25	9.9
6-10	4	1.6
Total	252	
Number of years after graduation in practice	Number	%
1-10	11	4.4
11-20	49	19.4
21-30	100	39.7
31-40	69	27.4
41-50	17	6.7
>51	6	2.4
Total	252	

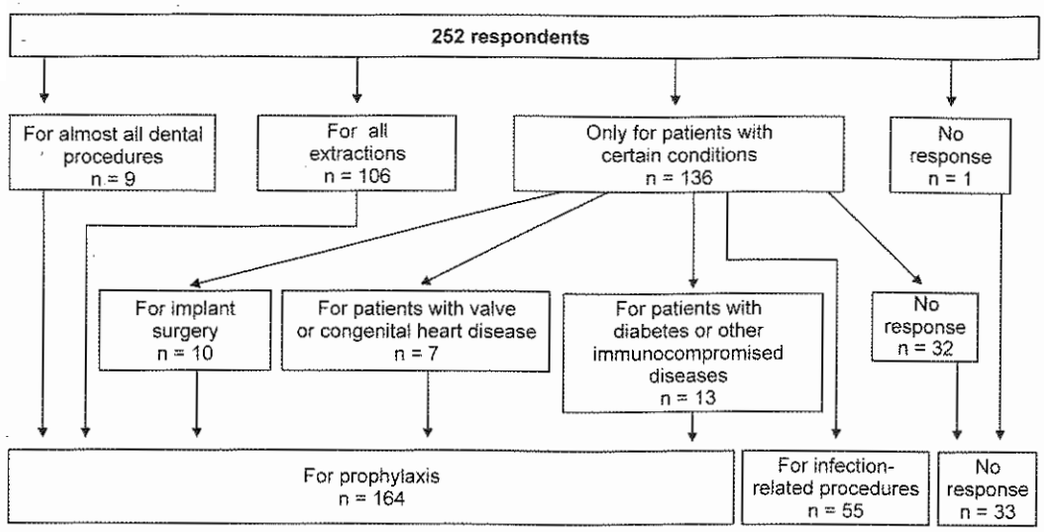

Fig. 1. Administration of antimicrobial agents. Among 500 dentists, there were 252 respondents (50.4%). One-hundred fifty-one respondents (45.6%) reported that they prescribed prophylactic antimicrobials for all procedures, whereas 136 (54.0%) reported that they were prescribed for patients with specific conditions.

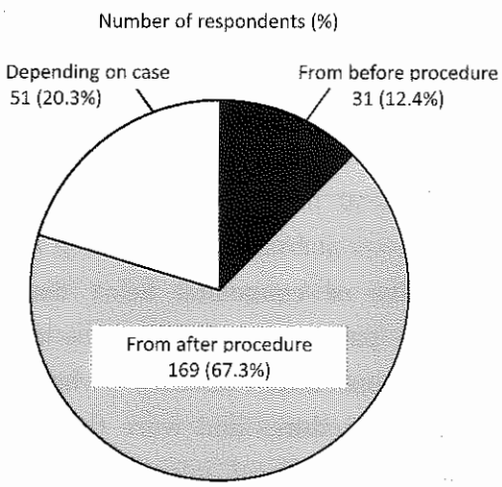

Fig. 2. Timing of antimicrobial administration. One hundred and sixty eight respondents (67%) replied that they usually administrated prophylactic antimicrobials after procedures.

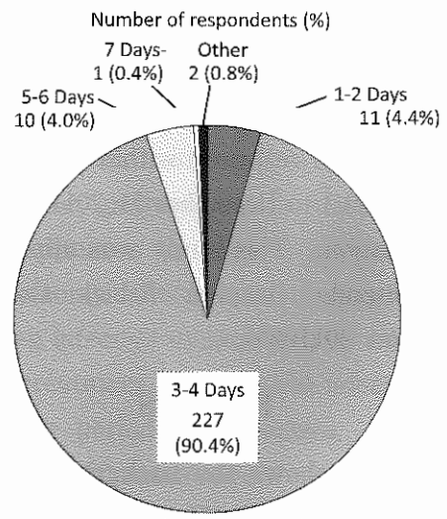

Fig. 3. Duration of antimicrobial administration. The prolonged usage of prophylactic antimicrobials for 3 to 4 days was most commonly preferred.

administration depended on particular cases (Figure 2). Among those who reported administration depending on the case, 9 specified administration before implant surgery and 16 specified patients with diabetes and/or valve disease before any procedures.

With regard to the duration of antimicrobial administration, most respondents (90.0%) reported 3 to 4 days (Figure 3). With regard to the types of antimicrobials most frequently administered, 30 respondents (11.9%) reported penicillin, 34 (13.5%) reported first-generation cephalosporins, 9 (3.6%) reported second-generation cephalosporins, 129 (51.2%) reported third-generation cephalosporins, 29 (11.5%) reported macrolides, and 14 (5.6%) reported new quinolones, while 2 (0.8%) gave no response (Figure 4). Among the 30 who

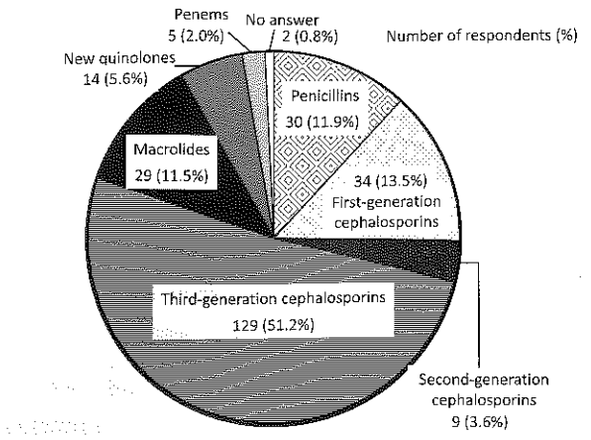

Fig. 4. Most frequently administered antimicrobial agents. Third-generation cephalosporins were the most preferred by Japanese dentists working in clinics.

reported commonly prescribing penicillin, none reported prescribing penicillin combined with a β-lactamase inhibitor.

DISCUSSION

This nationwide survey of actual antimicrobial administration by 252 dentists working at Japanese community dental clinics found that the use of antimicrobials for prophylaxis or treatment of periodontal infection exceeded the indications, regardless of patients' underlying condition. In particular, the percentage of dentists who reported administering antimicrobials for prophylaxis before a procedure was found to be relatively low, while prophylactic use for 3 to 4 days was the most common, which is longer than recommended. The percentage of dentists who preferred oral third - generation cephalosporins for both prophylaxis and treatment of periodontal infection treatment was relatively high.

Among the study participants, 65.1% reported commonly prescribing antimicrobials for prophylaxis, thus suggesting that a large percentage of dentists recognize the seriousness of infectious diseases after dental procedures. A potential problem is that 45.7% reported prescribing antimicrobials for all tooth extraction procedures, regardless of patient condition, thus suggesting that antimicrobials are often used outside of their indications. Guidelines on prophylactic use of antimicrobials have been established for infective endocarditis. The revised Endocarditis Prophylaxis Guidelines issued by the American Heart Association (AHA) in 2007 and the revised Guidelines for Infective Endocarditis Prevention and Treatment issued by the Japanese Circulation Society (JCS) in 2008 are shown in Table 2[2)3)]. In its 2007 revision, AHA recommended prophylactic administration of antimicrobials for a smaller number of conditions than it had recommended in the 1997 guidelines. In its 2008 revision, JCS recommended prophylactic administration to Class II patients in addition to Class I patients, whom the 2007 AHA guidelines defined as the highest risk group. Although there are some differences between the two guidelines, prophylactic use of antimicrobials is necessary for limited patients prior to all dental procedures, including manipulation of gingival tissue and penetration of root apex of tooth and oral mucosa. In contrast, these guidelines emphasize that patients who do not undergo the specified procedures or are not members of the specified groups of patients should not use antimicrobials prophylactically.

For prevention of infective endocarditis, both the AHA and JCS guidelines recommend oral antimicrobials should be taken 1 hour before initiation of a procedure (30 minutes if administration is intravenous), preferably in the form of single-dose oral administration of 2 g of amoxicillin (AMPC)[2)3)]. In this study, 67.1% of respondents reported prescribing antimicrobials after a procedure and only 12.3%

Table 2. Guidelines for Prevention of Infective Endocarditis of the American Heart Association (2007) and the Japanese Circulation Society (2008)

Targets for prophylaxis during odontogenic procedures (AHA[1] 2007 guidelines)
Cardiac conditions associated with the highest risk of adverse outcome from endocarditis for which prophylaxis with dental procedures is reasonable 1. Prosthetic cardiac valve or prosthetic material used for cardiac valve repair 2. Previous infective endocarditis 3. Congenital heart disease (CHD): Except for the conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of CHD • Unrepaired cyanotic CHD, including palliative shunts and conduits • Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first6months after the procedure (Prophylaxis is reasonable because endothelialization of prosthetic material occurs within 6 months after the procedure.) • Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization) 4. Cardiac transplantation recipients who develop cardiac valvulopathy
Targets for prophylaxis during dental surgery (JCS[2] 2008 guidelines)
Class I
Patients with high risk of serious infective endocarditis that need prophylaxis • Patients with artificial valve replacement, including biological valves and allograft valves • Patients with previous history of infectious endocarditis • Complex cyanotic congenital heart diseases (single ventricle, complete transposition of great arteries, and tetralogy of Fallot) • Patients undergoing shunting of cardiovascular system and pulmonary circulation system
Class II a
Patients with high risk of infective endocarditis who will benefit from prophylaxis • All types of congenital heart disease • Acquired valve diseases • Obstructive cardiomyopathy • Mitral valve prolapse associated with valve regurgitation
Class II b
Patients with possible risk of infective endocarditis (in whom, though not proven, possible benefit of prophylaxis administration cannot be excluded) • Patients with artificial pacemaker or implantable cardioverter-defibrillator • Patients with long-term central venous catheters
Footnotes: [1]American Heart Association, [2]The Japanese Circulation Society.

reported prophylactic administration before a procedure. Due to the possibility of infection in the surgical area and procedure-related transient bacteremia, administration of oral antimicrobials several hours after a procedure cannot prevent infective endocarditis. While Shigi et al. reported that the rate of awareness of proper antimicrobial administration before a procedure for prevention of infective endocarditis is 74.2% among Japanese dentists[4], more than half of the respondents in the present study reported prescribing third-generation cephalosporins most frequently among all antimicrobials, indicating a discrepancy between actual practice and current guidelines.

Currently for odontogenic infections, there are no international guidelines for administration of antimicrobial agents, even though there is an original guideline in Japan[5]. However, the most important therapy for odontogenic infections includes several surgical procedures, such as drainage and removal of necrotic tissue ; thus, antimicrobial treatment is

merely a helpful tool. Systemic antimicrobial administration is indicated for certain types of patients, including patients with low immunity, such as patients with HIV or severe diabetes, as well as patients with acute necrotic gingivitis or osteomyelitis. Patients with fever, lymph node swelling, spread of infection to surrounding tissues and invasion of bone cortex are also candidates for systemic antimicrobial administration.

Selection of antimicrobials should be based on estimation of the causative bacteria, but reliable statistical data regarding causative bacteria in odontogenic infection are very limited. Numerous anaerobic or microaerobic bacteria, such as *Porphyromonas gingivalis*, *Tannerella forsythensis*, *Treponema denticola*, *Fusobacterium nucleatum* and *Prevotella intermedia*, *Aggregatibacter actinomycetemcomitans* and *Streptococcus anginosus* group, have been reported as causative agents of odontogenic infection[6)-8)]. In reviews of oral antimicrobial use, several forms of penicillin with a β-lactamase inhibitor, such as amoxicillin-clavulanate (AMPC/CV) and AMPC (or penicillin V) in combination with metronidazole (AMPC + metronidazole), are considered standard agents for oral bacterial flora[9)10)].

In this study, 51.2% of the respondents specified third-generation cephalosporins as their first-choice antimicrobial. Third-generation cephalosporins have a broader spectrum and higher microbial activity against gram-negative bacilli when compared to penicillin and first-generation cephalosporins. However, the antimicrobial activity of third-generation cephalosporins against anaerobic bacteria is relatively low, and several studies of their susceptibility found that they provided no greater microbial activity against the bacteria responsible for odontogenic infection than did penicillin[11)-14)]. In addition, the low bioavailability of oral third-generation cephalosporins could not achieve their effective concentration in the blood. Thus, administration of oral third-generation cephalosporins as a first-choice agent in prophylactic administration and treatment of periodontal infection is not reasonable.

Oral third-generation cephalosporins are widely prescribed in both dentistry and medicine. In a previous nationwide evaluation of 17 private dental university hospitals, approximately 60% of respondents reported administering third-generation cephalosporins, a percentage similar to that reported in the present study[15)]. In the 2010 Guidelines for Antimicrobial Treatment in Patients with Periodontal Diseases, the Japanese Society of Periodontal Diseases recommends administration of penicillin and third-generation cephalosporins for prophylactic administration after tooth extractions and surgical dental procedures[5)]. With one study finding that general practitioners administer antimicrobials to 60% of patients diagnosed with acute upper-respiratory infection in Japan, 46% of them were oral third-generation cephalosporins[16)]. Broad-spectrum oral third-generation cephalosporins are widely prescribed in Japan, and there is concern regarding the development of resistance in bacteria unrelated to active infection. One molecular epidemiological analysis of *Streptococcus pneumonia* in Japan found that selective pressure on bacterial flora due to oral cephalosporin administration has resulted in increased antimicrobial resistance in *Streptococcus pneumoniae*[17)]. These findings indicate that administration of oral third-generation cephalosporins should be restricted as much as possible, in both medicine and dentistry.

In the treatment of periodontal infection, the susceptibility of both bacteria and biofilm to an agent is an important consideration. In this study, 11.5% of respondents reported macrolides as their first choice of agent for treating periodontal infection. Although one study reported the usefulness of azithromycin against the biofilm in treating chronic periodontitis[18], another study found that macrolides exert limited antimicrobial activity against anaerobic bacteria[14]. Moreover, another study observed that 90% of a patient's oral bacterial flora developed resistance toward macrolides after 1 week of azithromycin administration[19]. Considering the possibility of bacterial resistance, a cautious policy should be taken when administering antimicrobials to treat acute periodontal infection.

This study had several limitations. The items in the questionnaire regarding antimicrobial administration did not clearly differentiate between administration for prophylaxis and treatment of periodontal infection. The authors re-classified all replies based on the detailed comments, which raised concerns that the replies might not have accurately reflected the purpose of administration. We also had to ask dentists about their awareness of taking past medical history before dental procedures in order to understand the risk factors for complications. The response rate to the questionnaire was so low that the actual antimicrobial use by non-responders was unclear, and the responders may have had a relatively high level of understanding of infectious diseases. These factors make it difficult to estimate the practice of all dentists in Japan, and whether inappropriate prophylaxis actually raised the percentage of infective endocarditis could not be analyzed in this study.

Conclusion

This survey found the use of antimicrobials for prophylaxis or treatment of periodontal infection exceeded indications. The importance of administering antimicrobials for prophylaxis before a procedure was not widely recognized, while use of oral third-generation cephalosporins for both prophylaxis and treatment of periodontal infection treatment was relatively frequent, even though oral third-generation cephalosporins have problems with regard to activity against anaerobes and development of resistant bacterial flora. Collaboration between dental and medical fields should be accelerated in order to ensure the correct application of prophylactic use of antimicrobials and appropriate antimicrobial choice for treatment of periodontal infections.

ACKNOWLEDGEMENTS

We are grateful to all of the dentists who responded to our questionnaire. This study was supported by a Grant-in-Aid (S1201013) from the MEXT (Ministry of Education, Culture, Sports, Science and Technology)-Supported Program for the Strategic Research Foundation at Private Universities, 2012-2017.

CONFLICTS OF INTEREST

None

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