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심한 근관 감염에서의 항생제 선택

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ABSTRACT

Antimicrobial choice of severe endodontic infection

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Objectives : The purpose of our study was to evaluate penicillin as a still drug of choice for severe endodontic infection, by analyzing the antimicrobial susceptibilities from endodontic infections with swelling to figure out appropriate antibiotics as empirical treatment.
Materials and methods : This study involved 18 patients who attended for emergency treatment because of facial or periapical swelling associated with root canal infections. Identification and antimicrobial susceptibility test of each pathogen were performed by Vitek2 Systems (bioMérieux, Marcy l'Etoile, France).
Results : The most frequent bacteria was *Streptococcus spp*.(77%), and the resistance against penicillin was 35% in overall patients, followed by clindamycin and erythromycin (17%), which was much higher than previous studies.
Conclusions : In our study, the higher resistance made penicillin alone not to be chosen as the first antibiotic drug for severe endodontic infections. Combinations with other drug, penicillin with wider spectrum of activity, or changing to other antibiotics was considered while remembering the increased risk of resistant microorganism.

Key words : penicillin, antimicrobial, endodontic, infection, susceptibility

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Ⅰ. Introduction

Cause of periradicular periodontitis is microbiologic and proper antimicrobial treatment is needed as an adjunctive treatment of acute endodontic infection[1]. Endodontic infections are polymicrobial with several predominant bacteria cultured from each infection[2]. The ideal choice of antibiotics is determined by antimicrobial susceptibility test after culturing the purulent pathogens. Unfortunately, it takes several days to weeks to get the test result and find out the proper antibiotics which are susceptible for the bacteria of the infection[3]. As a result, the choice of antibiotics is prone to depend on previously published test or previous clinical success, however, resistance to antibiotics is commonly appearing and changing, and there is a concern that bacteria have increased their resistance to the currently using antibiotics[4, 5]. Accordingly updated data for antibiotic therapy and periodic, accurate antimicrobial susceptibility test result is needed[6].

Penicillin has been used as a drug of choice for acute dental infection for a long time, and it has also shown desirable effect against many of the facultative and strict anaerobes commonly found in polymicrobial endodontic infections[4, 6, 7].

Nowadays, reports have shown that some bacterial species (especially gram-negative anaerobes) have become resistant to penicillin[7~10]. The prevalence of penicillin resistance for bacteria commonly found in endodontic infections and acute dental abscesses has been reported to be approximately 5 to 20%[8, 10, 11], which may evoke questionable efficacy of penicillin on dental infections[12].

The purpose of our study was to evaluate penicillin as a still drug of choice for endodontic infection, by analyzing the antimicrobial susceptibilities of culturable bacterial species isolated from acute periapical abscesses to figure out what else could be used before antimicrobial susceptibility test result as empirical antibiotics.

Ⅱ. Materials and methods

1) Patient Selection

Approval for this retrospective analysis was obtained from institutional review board of the Dongsan Medical Center(IRB File No. 2014-04-042-001). This study involved samples and chart reviews collected from patients who attended the Department of Dentistry, Dongsan Medical Center, Keimyung University for emergency treatment because of facial or periapical swelling associated with root canal infections during March, 2012 to December, 2013. 18 patients were selected. Report of gingival or facial swelling, tenderness to percussion and nonvital pulp

in the examined tooth existed in all patients. All patients had a periapical radiolucency varies in diameter, and they were diagnosed as acute periapical abscess. The age of patients ranged from 16~78 years, with an average age of 55 years. The patients selected had not received antibiotic therapy recently due to the acute periapical abscess.

2) Sampling and Culture of Pathogens

The clinical samples were aseptically aspirated with a needle from each abscess or swabbed during incision procedure after proper disinfection. The samples were immediately transported to the laboratory and processed under aerobic and anaerobic conditions.

For aerobic culture, samples were spread on Blood agar and MacConkey agar plate for overnight incubation in the chamber with 37℃ , 5% CO_2 .

For anaerobic culture, samples were inoculated on Brucella agar and pheynyleth anol agar plate for 48 hours in anaerobic jar with an atmosphere of 85% N_2, 10% H_2, and 5% CO_2.

The characteristics of cultured colonies were observed and identified with Gram (G) stain and other biochemical tests: catalase test and oxidase test for gram-positive pathogens, and triple sugar test for gram-negative pathogens.

3) Identification and Antimicrobial Susceptibility Test

Vitek2 Systems(bioMérieux, Marcy l' Etoile, France), which uses advanced colorimetry to identify pathogens and to test antimicrobial susceptibility, processed the pathogens with various biochemical tests with various detection cards.

Each pathogens were identified by Vitek2 Systems with GPI card for gram-positive bacteria, GNI card for gram-negative bacteria, ANI card for strict anaerobes.

The antimicrobial susceptibilities were also processed with AST cards by Vitek2 Systems and determined as susceptible (S), intermediate susceptible (I), resistant (R), for 9 antimicrobial drugs: penicillin, cefotaxime, ceftriaxone, clindamycin, erythromycin, levofloxacin, linezolid, tetracycline and vancomycin.

Ⅲ. Results

From 18 acute periapical abscess patients, facultative anaerobes were predominant, that was 17 of 18 patients. The most dominant pathogen was *Streptococcus spp.* (77%), followed by *Staphylococcus spp.* The age, gender, clinical features, dominant pathogens and antimicrobial susceptibilities are shown in Table 1 and Figure 1,2. Because the *Bacillus species* could not be measured its antimicrobial susceptibility by Vitek 2 Systems, it was ruled out when calculating the antimicrobial susceptibility.

Table 1. Dominant pathogens and antimicrobial susceptibilities of 18 patients with related clinical features (RCT: root canal treatment, CM: clindamycin, EM: erythromycin, TC: tetracycline)

Age	Sex	Lesion	Dominant pathogens	Resistance
64	F	#13 apical lesion, necrosis	*Klebsiella pneumoniae*	penicillin
61	M	#47 apical lesion, previous RCT	*Streptococcus anginosus*	none
72	M	#16 apical lesion, necrosis,	*Bacillus species*	---
68	M	#46 apical lesion, caries	*Staphylococcus hemolytic*	penicillin
41	F	#46 apical lesion, necrosis	*Streptococcus alpha hemolytic*	CM
78	M	#36 apical lesion, previous RCT	*Staphylococcus warneri*	none
78	F	#35 apical lesion, caries	*Streptococcus alpha hemolytic*	none
50	M	#34 apical lesion, caries	*Streptococcus oralis*	CM,EM
76	F	#13 apical lesion, necrosis	*Streptococcus alpha hemolytic*	CM
40	M	#16 apical lesion, previous RCT	*Streptococcus mitis*	none
48	M	#15 pulp necrosis, flare up	*Streptococcus mitis*	EM,TC
55	M	#24 apical lesion, necrosis	*Streptococcus alpha hemolytic*	none
43	M	#46 apical leision, necrosis	*Streptococcus parasanguis*	penicillin
16	M	#31 apical lesion ,necrosis	*Streptococcus alpha hemolytic*	penicillin,cefotaxim
52	M	#44 apical lesion, necrosis,	*Streptococcus parasanguis*	penicillin
51	M	#22 apical lesion, previous RCT	*Streptococcus oralis*	none
41	M	#26 apical lesion, necrosis	*Streptococcus salivarius*	penicillin, EM
59	M	#26 apical lesion, previous RCT	*Streptococcus alpha hemolytic*	none

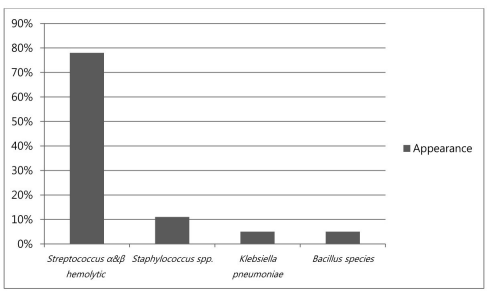

Figure 1. The overall appearance rates of dominant pathogens expressed as a percentage

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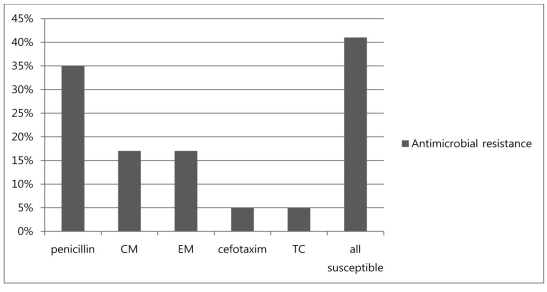

Figure 2. The overall resistance rates against antibiotics expressed as a percentage.

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35% of resistance to penicillin, which was higher than ever reported, was shown in overall patients followed by clindamycin and erythromycin(17%)[9~11]. 41% of patients did not show any resistance to the tested antibiotics.

Ⅳ. Discussion

The antibiotic prescription should be adjunctive to proper clinical treatment. Antibiotics are used when signs and symptoms are associated with systemic involvement, and for patients with progressive infections or immunodeficiency[4]. When selecting certain antibiotics, it should be recognized that endodontic infections are ecosystems of bacteria, therefore if a certain antibiotic has effect on some bacteria, it may affect other bacteria as well indirectly[13].

This study showed that pathogens isolated from acute endodontic abscesses have a predominance of facultative anaerobic bacteria. Facultative anaerobes were found in 17 of 18 patients and only 1 strict anaerobe, *Bacillus species*, was found in this study.

Brook et al[11] evaluated 39 patients with periapical abscesses and the predominant isolates were *Bacteroides species, Streptococcus species* and anaerobic cocci. There was also a predominance of facultative oral *Streptococci* in early infections(less than 3 days of symptoms) with a later predominance of obligate anaerobes in the study by Lewis et al[14]. These findings supported the predominance of facultative streptococci strains in overall patients of this study.

Resistance to penicillin is usually by three ways. There are barriers to bacterial cell wall penetration, inhibition to bind to the penicillin-binding proteins, and β-lactamase production. β-lactam antibiotics, like penicillin, are still considered to be the drug of choice for endodonic infections[15]. The prevalence of penicillin resistance in oral infections, however, has been reported as 5% to 20%[9~11]. Lewis et al[10] reported the resistance to penicillin V in acute suppurative infection of oral cavity as 23%, whereas only 5% resistance to amoxicillin /clavulanic acid.

In our study, the prevalence of penicillin resistance was found out to be 35%, followed by clindamycin and erythromycin. This means penicillin alone may not likely to be chosen as the first antibiotic drug due to its high resistance for pathogens of endodontic infections. Moreover, the resistance against erythromycin and clindamycin which used to be prescribed to patients who are allergic to penicillin is observed. This is noticed in studies involving other populations[16, 17].

Combinations with other drug, such as metronidazole which is effective against anaerobes , broad spectrum penicillin, such as amoxicillin/clavulanate: Augmentin®,

changing to other antibiotics, such as 3rd generation cephalosporin: Meiact® may be considered while remembering the increased risk of resistant organisms[4, 16, 18~20].

Clindamycin is a powerful antibiotic drug against both strict and facultative anaerobes[12, 18]. It is often recommended for serious odontogenic infections when penicillin is contraindicated or for patients with renal dysfunction without reducing of its dose. Baumgartner and Xia[4] reported 96% of bacteria in their study were susceptible to clindamycin, and Khemaleelakul et al[1] reported clindamycin had efficacy against 89% of the tested bacteria. Whereas, in our study, 83% of tested bacteria were susceptible to clindamycin and erythromycin ,which was lower than previous studies. The reduced relative efficacy of clindamycin, the drug of choice for patients allergic to penicillin or renal insufficiency patients is consistent with some precious studies[10, 17, 20]. Hence, the single use of clindamycin as an alternative drug in penicillin-allergic patients or renal insufficiency patients has to be carefully considered.

Antibiotic therapy for patients with systemic signs and symptoms, progressive infections, or patients who are immunocompromised was supported by previous studies[7, 21], however, if patients received proper endodontic treatment, there was no significant difference in pain and swelling between a placebo and penicillin prescription[21]. Thus, the use of antibiotics to prevent posttreatment infections in healthy patients was not recommanded[18, 22]. The risk and benefit of antibiotics to the patient must be considered with the possibility of bacterial resistance to antibiotics, adverse reactions and drug allergies[4]. The increasing resistance to antimicrobial drugs is a concern, and patients are acquiring new or present pathogens that developed resistance. Thus, periodic studies on the antimicrobial susceptibility should be delineated to guide dental therapy in patients with severe endodontic infection or in need of systemic antibiotics.

In our study, the higher resistance made penicillin alone not to be chosen as the first antibiotic drug for severe endodontic infections. Combinations with other drug, penicillin with broad spectrum of activity, or changing to other antibiotics might be considered. More treatment outcome studies with larger patient databases should be performed in future researches in this area. An important goal of this study was the choice of effective antimicrobial drugs and endodontic treatment strategies for people with severe endodontic infection or failure of appropriate drainage.

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