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ESKAPE Pathogens in Oral and Maxillofacial Infections

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Purpose: Most cases of oral and maxillofacial infections are usually easily treated by proper diagnosis, elimination of causative factors, and antibiotic therapy. However, the emergence and the increase of multidrug-resistant bacteria make treatment challenging. "ESKAPE" pathogens are the most common opportunistic organisms in nosocomial infections and have resistant to commonly used antibiotics. There are many medical reviews of ESKAPE pathogens, but few in dentistry. This study focuses on oral and maxillofacial infection especially with ESKAPE pathogens. The purpose of this study is to prepare feasible data about tracing and treatment of infection related to pathogens that may be beneficial to clinicians.

Methods: A total of 154 patients with oral and maxillofacial infections were reviewed by analyzing retrospectively hospitalized data in the Department of Oral and Maxillofacial surgery, Chosun University Hospital, Korea, past 5 years from January 2014 to December 2018. Based on the medical records and microbiological tests, the results were divided into two groups: infections with ESKAPE pathogens and other bacteria.

Results: A total of 22 species were isolated from 154 patients. The proportion of ESKAPE pathogens among all bacterial isolates collected from infected patients was 39.6%. Causative factors, especially in post-operative infection, showed a statistically significant correlation to ESKAPE infections (29 cases). And average of treatment period in ESKAPE group was longer than non-ESKAPE groups. Overall, *Klebsiella pneumoniae* (60.7%) was the most frequently isolated ESKAPE pathogen. And high antibiotic resistance rates had been detected in the ESKAPE during the five-year period.

Conclusions: Infections with ESKAPE pathogens are now a problem that can no longer be overlooked in Dentistry. Based on results of this study, ESKAPE pathogens were highly associated with post-operative or opportunistic infections. Clinicians should be careful about these antibiotic resistant pathogens and use appropriate antibiotics to patients while having dental treatments.

Key Words: *Acinetobacter baumannii*; *Klebsiella pneumoniae*; *Pseudomonas aeruginosa*; *Staphylococcus aureus*

INTRODUCTION

Oral and maxillofacial infections are usually caused by normal oral bacteria and can be easily treated with appropriate diagnosis, removal of causative factors, and antibiotic therapy [1,2]. Due to continued research and the development of antibiotics, the incidence of infections in the oral and maxillofacial area has decreased. However, such infections are still responsible for an array of diseases in the dentistry field. Severe infections are still a challenge; they can lead to osteomyelitis, fascial space abscesses, and bacteremia, which in turn may result in life-threatening complications [3-5]. Dental infections are almost always multibacterial and occur with a mixture of aerobic, facultative

anaerobic, and anaerobic bacteria such as the *Streptococcus* species, *Peptostreptococcus* species, *Prevotella* species, and *Fusobacterium* species [2,6-8].

The emergence of multidrug-resistant bacteria leads to the treatment failure of various infectious diseases and is one of the most serious medical and social problems in modern society [9]. Particularly problematic, representative multidrug-resistant bacteria are the ESKAPE pathogens, which received their name due to the fact that they 'escape' the effects of antibiotics [10-12]. ESKAPE pathogens include *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and the *Enterobacter* species. ESKAPE pathogens, together with Gram-negative strain, are one of the most common causes of nosocomial infections, making effective antibiotic treatment difficult and therefore adversely affecting the treatment of severely infected patients [13-15].

A number of studies investigating world-wide trends of infection by ESKAPE and their treatment have been recently published [13,16-18]. The emergence of resistant bacteria that are difficult to eradicate with conventional treatments has led to an increased morbidity and mortality, as well as an increased treatment-derived economic burden. Consequently, the selection of an effective treatment strategy has become an important issue in the field. ESKAPE pathogens are the main cause of pneumonia, urinary tract infections, and abdominal cavity infections; therefore, both domestic and international studies have investigated these strains in the context of such diseases. However, systematic studies and reports on oral and maxillofacial infections caused by ESKAPE are insufficient. The main empiric antibiotics used for the treatment of the oral and maxillofacial area are amoxicillin-clavulanic acid, metronidazole, and erythromycin. However, the resistance to amoxicillin in dental infections is between 9 to 54%, and the number of antibiotic-resistant bacteria has been shown to be gradually increasing [7,19-22].

Currently, infections such as osteomyelitis and abscess occur very frequently in the dental field. However, there are almost no case reports and retrospective study of infection by the ESKAPE strains.

In addition, it was a very difficult problem to detect bacteria from patients with no pus.

And for patient who do not have been healed well even after taking amoxacillin, which is often used in dentistry, we scrape the infected tissue and culture the bacteria instead of pus culture to detect ESKAPE bacteria.

The authors have already submitted and published some case reports of ESKAPE strains in South Korea, and intend to submit them to this academic journal by proceeding with retrospective study based on various experiences.

This study classified and characterized infected patients who visited the Department of Oral and Maxillofacial Surgery at Chosun University Dental Hospital between January 2014 and December 2018 according to the causative agent of infection. In particular, as an analysis of infection by and treatment of multidrug-antibiotic-resistant bacteria termed "ESKAPE", this study was intended to act as a reference for the diagnosis of causative bacteria other than normal resident bacteria, establishment of treatment plans, and judgment of prognosis in future oral and maxillofacial infections.

MATERIALS AND METHODS

1. Subjects

This study was conducted with the approval of the Institutional Review Board (IRB) of the Chosun University Dental Hospital (no. CUDHIRB 1902 009) and the written informed consent was waived by the board. A total of 467 patients visited Chosun University Dental Hospital from January 2014 to December 2018 due to oral and maxillofacial infections. Among them, 154 patients whose bacteria were isolated through a microbial culture test were included in the study.

2. Methods

The survey was conducted based on the medical records and microbiological test results of 154 subjects. According to the isolated bacteria, patients were divided into an ESKAPE group, where ESKAPE pathogens were identified as the causative agent, or a non-ESKAPE group, when the causative agent was the other bacteria. Statistical analysis was performed, with particular focus on the ESKAPE group.

Bacterial samples were collected using a sterile cotton swab (Transystem 108C; Copan Diagnostics Inc., Murrieta,

CA, USA) at the site of infection and then used for the microbial culture test.

In the antibiotic susceptibility test, ampicillin, oxacillin, benzylpenicillin, and piperacillin were used as penicillin antibiotics, and amoxicillin-clavulanic acid, ampicillin-sulbactam, ticarcillin-clavulanic acid, and piperacillin-tazobactam were used as antibiotics containing β-lactam inhibitors. Cephalosporin-based cefazoline, cefuroxime, cefoxitin, ceftazidime, cefotaxime, and cefepime, carbapenem-based doripenem, ertapenem, imipenem, and meropenem, aminoglycoside-based antibiotics including amikacin and gentamicin, quinolone-based ciprofloxacin and levofloxacin, glycopeptide-based teicoplanin and vancomycin, macrolide-based erythromycin, lincosamide based clindamycin, and tetracycline-based minocycline and tetracycline were used. In addition, trimethoprim-sulfamethoxazole, mupirocin, rifampin, colistin, and fusidic acid were also used as other antibiotic classes.

3. Statistical Analyses

Statistical analyses were performed using SPSS 20.0 (IBM Corp., Armonk, NY, USA). Frequencies and percentages were calculated for each item, and a chi-square test was performed for categorical variables. A binary logistic regression analysis was performed to calculate the corrected cross ratio for each item. The significance level was set a $p<0.05$.

RESULTS

1. Frequency of Occurrence According to Sex and Age

Among the 154 patients, the male to female ratio was 1.52:1, and the average age was 58.5 years. Both the ESKAPE (59.0%, n=36) and non-ESKAPE (61.3%, n=57) groups had a higher percentage of men, and the average age was higher in the ESKAPE group (62.2 years) than in the non-ESKAPE group (58.1 years). However, there were no significant differences in sex (p=0.778) and age (p=0.152) between the groups.

2. Frequency of Occurrence According to Systemic Disease

Systemic medical history was confirmed in 87 of 154 patients (56.5%). In the ESKAPE group, 35 patients (57.4%) had systemic disease, while in the non-ESKAPE group, 52 (55.9%) had systemic disease. The number of patients with hypertension was 64 (41.6%), followed by diabetes (26.0%, n=40), and osteoporosis (16.9%, n=26). In addition, 22 patients (14.2%) had heart, liver, kidney, cranial neurological, and blood-related diseases. There were 44 patients with two or more diseases, accounting for 28.6% of the total patients. Statistical analyses of the frequency of infection by ESKAPE and non-ESKAPE according to the existence of systemic disease or disease type, revealed no significant differences (p=0.070).

3. Frequency of Occurrence According to Cause of Infection

A total of 101 patients (65.6%) had dental infections, thus accounting for the majority of the study population. Of them, 58 patients (37.7%) had odontogenic infections of endodontic origin, such as dental caries and apical abscess, and 43 (27.9%) had infections of periodontal origin. The second most common causes were infections after open surgery, including medication-related osteo-necrosis of the jaw, teeth extraction, cyst enucleation, and open reduction surgery, which were found in 43 patients. Meanwhile, 6 patients (3.9%) developed infections after non-open surgery such as periodontal or endodontic treatment, and 4 (2.6%) developed infections due to local irritation factors such as dentures (Fig. 1).

The incidence of infection according to causative factor was significantly different between the two groups (p=0.010), with the proportion of cases being higher in the non-ESKAPE group in all items other than postoperative infection. Among the 49 patients with postoperative infection, 29 patients (59.2%) were infected with ESKAPE, with a statistically significant difference between the two groups.

4. Frequency of Occurrence According to Infection Site

The infection site was classified as either maxilla or mandible, and the incidence was investigated by subdividing them into anterior, premolar, and molar areas. Most infections of the maxillary anterior and premolar were at the inoculation stage or showed localized swelling, while fascial space abscess and osteomyelitis were more common in

posterior and mandibular areas.

When considering the total number of infection cases at each site, infections were more common in the mandible (60.7% in the ESKAPE group and 72% in the non-ESKAPE group), and in the posterior region (62.3% in the ESKAPE and 68.8% in the non-ESKAPE). However, the difference in incidence according to site between the two groups was not statistically significant (p=0.682).

5. Treatment Progress and Hospitalization

Treatment duration was calculated as the period of time from the date of admission to the Chosun University Dental Hospital due to symptoms of infection up until the end of the follow-up test or start of the recovery phase. For patients with osteomyelitis due to infection, the start of the recovery stage was set as the time at which bone destruction stopped and new bone formation was observed, while in patients with abscess discharge, it was set at the time at which the fistula was blocked.

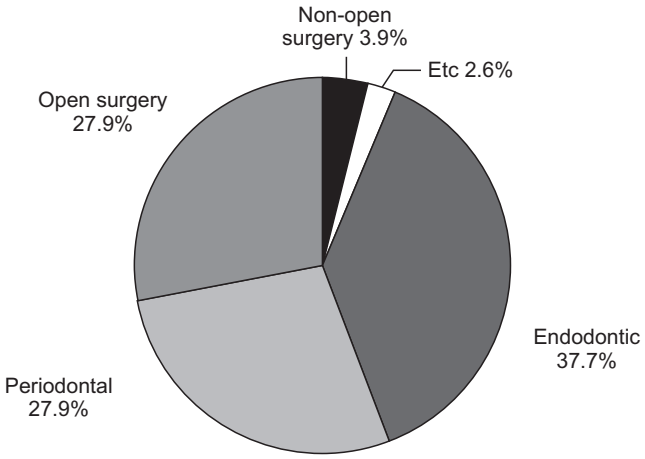

Fig. 1. Distribution of infection sources. The most frequent causative factor was odontogenic infection with periodontal or endodontic origin (101 cases, 65.6%), followed by post-operative infection caused by open surgery or other non-open intra-oral treatment (49 cases, 31.8%).

Among the 154 patients, treatment duration ranged from 1 week up until 12 months, with 10 patients being lost to follow-up. After excluding two patients who had incomplete follow-up, the ESKAPE group had an average treatment period of 2.15 months, which was significantly longer than the non-ESKAPE group (p=0.001; Table 1). However, there was no significant difference between the two groups in terms of hospitalization (p=0.068). A total of 22 and 21 patients in the ESKAPE and non-ESKAPE group received inpatient treatment, respectively.

6. Microbial Culture Test Result

A total of 22 bacteria were identified in 154 patients, of which *Streptococcus* species was detected in 79 patients, accounting for 51.3% of the total cases. And a total of 42 patients were infected by two or more bacteria. The number of isolated of the bacterial species and the number analyzed are outlined in Table 2.

In the ESKAPE group, *K. pneumoniae* was the most common bacteria (n=37), followed by *S. aureus* (n=15),

Table 1. Distribution of treatment period

Treatment period	All patients (n=154)	ESKAPE (n=61)	Non-ESKAPE (n=93)
1 wk	58 (37.7)	16 (26.2)	42 (45.1)
2 wk	30 (19.5)	5 (8.2)	25 (26.9)
3 wk	4 (2.6)	3 (4.9)	1 (1.1)
1 mo	13 (8.4)	7 (11.5)	6 (6.4)
2 mo	9 (5.8)	8 (13.1)	1 (1.1)
3 mo	9 (5.8)	8 (13.1)	1 (1.1)
4 mo	10 (6.5)	5 (8.2)	5 (5.4)
5-11 mo	10 (6.5)	6 (9.8)	4 (4.3)
12 mo	1 (0.7)	1 (1.7)	0 (0)
Follow up loss	10 (6.5)	2 (3.3)	8 (8.6)
Average (mo)*	1.44	2.15	0.95

ESKAPE, *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species.
Values are presented as number (%).
*p=0.001; logistic regression test.

Table 2. Causative pathogens isolated from oral and maxillofacial infections

Group	Organism	Number of patients
Aerobic		
Gram (+) cocci		
Gram (+) rods		
Gram (–) cocci	*Acinetobacter baumannii*	1
Gram (–) rods	*Neisseria sicca*	2
	Pseudomonas aeruginosa	2
Facultative anaerobic		
Gram (+) cocci	*Staphylococcus aureus*	15
	Staphylococcus capitis	1
	Staphylococcus epidermidis	1
	Streptococcus species	79
Gram (+) rods	*Actinomyces naeslundii*	1
Gram (–) cocci		
Gram (–) rods	*Citrobacter freundii*	2
	Eikenella corrodens	1
	Enterobacter aerogenes	3
	Enterobacter cloacae	8
	Escherichia coli	2
	Klebsiella oxytoca	5
	Klebsiella pneumoniae	37
	Morganella morganii	1
	Serratia marcescens	4
Anaerobic		
Gram (+) cocci	*Granulicatella adiacens*	1
	Granulicatella elegans	1
	Kocuria rosea	1
Gram (+) rods	*Propionibacterium acnes*	1
Gram (–) cocci		
Gram (–) rods	*Prevotella melaninogenica*	1
Fungus	*Candida albicans*	3

Enterobacter spp. (n=11), *P. aeruginosa* (n=2), and *A. baumannii* (n=1). *E. faecium* was not detected. Cases of two or more causative ESKAPE occurring together were observed as follows: *S. aureus* and *Enterobacter* species in 2 patients, and *K. pneumoniae* and *A. baumannii*, *K. pneumoniae* and *P. aeruginosa*, and *K. pneumoniae* and *Enterobacter* spp. in 1 patient each.

The total number of patients with infections in which bacteria were detected rose during the 5 years between 2014 and 2018, increasing from 3 cases in 2014, to 27 in 2015, 33 in 2016, 34 in 2017 and finally 57 in 2018. The number of cases in the ESKAPE group also showed an upward trend (Fig. 2).

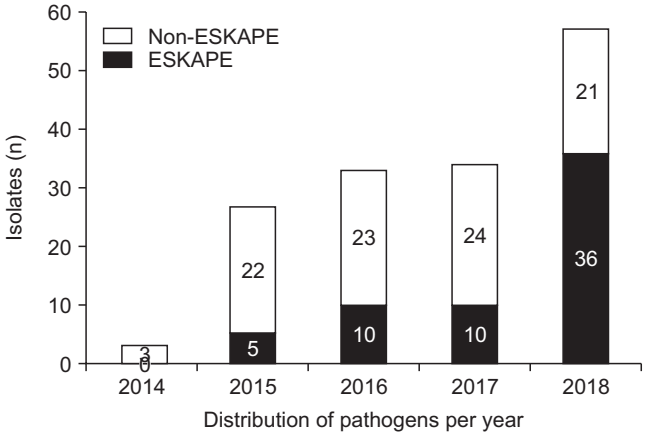

Fig. 2. Trends in the number of ESKAPE pathogens isolated between 2014 and 2018. The total number of oral and maxillofacial infections increased between 2014 and 2018, with the number of ESKAPE pathogens dramatically increasing from 0 to 36. ESKAPE, *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter* species.

7. Antibiotic Sensitivity Test Results

At Chosun University Dental Hospital, amoxicillin-clavulanic acid was first used as an oral or intravenous antibiotic. Based on the antibiotic susceptibility test, the ESKAPE group showed resistance to the primary antibiotic in 14 cases (3 for *K. pneumoniae* and 11 for *Enterobacter* spp.), and 8 cases in the non-ESKAPE (2 cases each for *Serratia marcescens*, *Citrobacter freundii*, and *Klebsiella oxytoca*, and one each for *Morganella morganii* and *Escherichiacoli*). With the exception of 9 patients, all the remaining patients showed an improvement in symptoms after treatment and first-line antibiotics. Even though resistance was shown as a result, antibiotics were not changed in patients whose symptoms were relieved by the initial treatment. However, after consultation with the infectious diseases department, the antibiotics of the patients whose symptoms did not improve were changed. Eight out of nine patients in question belonged to the ESKAPE. The patient in the non-ESKAPE who required an antibiotic change had an *S. marcescens* and *Staphylococcus epidermidis* infection.

Table 3 summarizes the results of the antibiotic susceptibility tests for ESKAPE strains at Chosun University Hospital. Penicillin resistance was observed in 90.7% of *K. pneumoniae* and 100% of *Enterobacter* spp. ($p<0.05$). *K. pneumoniae* were significantly sensitive to antibiotics

Table 3. Antibiotic susceptibility of isolated microorganisms

Antibiotic	*Staphylococcus aureus*		*Klebsiella pneumoniae*		*Acinetobacter baumannii*		*Pseudomonas aeruginosa*		*Enterobacter* spp.	
	S	R	S	R	S	R	S	R	S	R
β-lactam										
Penicillin*	11 (78.6)	3 (21.4)	4 (9.3)	39 (90.7)	1 (100.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	11 (100.0)
Cephalosporin*	-	-	184 (93.9)	12 (6.1)	2 (66.7)	1 (33.3)	4 (100.0)	0 (0.0)	30 (54.5)	25 (45.5)
Monobactam	-	-	36 (92.3)	3 (7.7)	0 (0.0)	1 (100.0)	2 (100.0)	0 (0.0)	10 (90.9)	1 (9.1)
Carbapenem	-	-	82 (100.0)	0 (0.0)	2 (100.0)	0 (0.0)	6 (100.0)	0 (0.0)	22 (100.0)	0 (0.0)
+β-lactam inhibitor*	-	-	80 (96.4)	3 (3.6)	2 (100.0)	0 (0.0)	2 (100.0)	0 (0.0)	10 (45.5)	12 (54.4)
Non β-lactam										
Aminoglycoside	12 (85.7)	2 (14.3)	74 (91.4)	7 (8.6)	0 (0.0)	1 (100.0)	6 (100.0)	0 (0.0)	21 (95.5)	1 (4.5)
Quinolone*	5 (71.4)	2 (28.6)	41 (97.6)	1 (2.4)	0 (0.0)	1 (100.0)	4 (100.0)	0 (0.0)	10 (90.9)	1 (9.1)
Glycopeptide	14 (100.0)	0 (0.0)	-	-	-	-	-	-	-	-
Macrolide	12 (92.3)	1 (7.7)	-	-	-	-	-	-	-	-
Lincosamide	7 (100.0)	0 (0.0)	-	-	-	-	-	-	-	-
Tetracycline	14 (100.0)	0 (0.0)	42 (100.0)	0 (0.0)	2 (100.0)	0 (0.0)	-	-	11 (100.0)	0 (0.0)
Trimethoprim-Sulfamethoxazole	5 (71.4)	2 (28.6)	38 (97.4)	1 (2.6)	1 (100.0)	0 (0.0)	-	-	11 (100.0)	0 (0.0)
Others	37 (90.2)	4 (9.8)	2 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	2 (100.0)	0 (0.0)	-	-

S, sensitive; R, resistant.
Values are presented as number (%).
*p-value<0.05 is statistically significant; Pearson's chi-squared test.

containing cephalosporin and β-lactam inhibitor, and *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, and *Enterobacter* spp. were significantly sensitive to quinolone-based antibiotics ($p<0.05$). However, other antibiotics included in the test did not show significant results.

DISCUSSION

Antibiotic resistance is a serious issue that threatens the health, economic, and social welfare of individuals worldwide [23]. In particular, ESKAPE pathogens have a wide range of antibiotic resistance mechanisms including inactivation of antibiotics, modification of the point of action, inhibition of cell membrane function, release of antibiotics, and mechanical defense, thus increasing the risk and severity of infection by these bacteria [10,13]. The widespread resistance to existing antibiotics requires the development of new antibiotics and treatment methods. This study was conducted to evaluate the risk of infection by antibiotic-resistant bacteria, especially ESKAPE in the oral and maxillofacial area, and antibiotics that can be used during such infection.

According to previous studies, *Streptococcus viridans*, Gram-positive cocci, and *S. viridans* were detected in 51.4% [24], 57.7% [25], and 41.37% [1] of patients with oral and maxillofacial infection, respectively. The *Streptococcus* species accounted for 51.3% of cases in our study, which is in line with the results of previous studies. In a total of 154 infected patients, obtained from the 5-year study period, ESKAPE strains were found in 61 patients (39.6%). These results indicate that ESKAPE pathogens are non-negligible sources of infection in the oral and maxillofacial area.

The results obtained from the survey showed a similar trend to that of previous studies [24-32]. Although no significant value was found between the two groups in the case, the ESKAPE group showed a distribution at a relatively higher age than the non-ESKAPE. This result is supported by the fact that the frequency of opportunistic infection is high in the elderly and that ESKAPE bacteria are one of the causative agents of such infections.

Regarding the cause of infection, and in line with previous studies, dental infection was the highest causative factor [32-35]. Compared with other causes of infection, higher

proportion of postoperative infections in the ESKAPE than in the non-ESKAPE indicate that various treatments in the oral cavity provide an opportunity for bacteria other than resident bacteria, such as ESKAPE, to penetrate into the oral cavity and increase the frequency of infection. These results also support the fact that ESKAPE pathogens are one of the causative agents of nosocomial and opportunistic infections and remind us that more attention should be paid to infection during dental procedures.

ESKAPE infection is associated with a prolonged treatment period and a high mortality rate [36-39]. In addition to ESKAPE, Gram-negative bacteria accounted for a large proportion of the antibiotic-resistant bacteria [40]. The β-lactamase activity of Gram-negative anaerobic bacillus is not considered a virulence factor by itself, but interferes with the effect of penicillin, which is the most widely used antibiotics in dentistry. To effectively treat these bacterial infections early diagnosis is key [41]. The quick identification of the causative agent and the selection of appropriate antibiotics is essential [38,42-44].

Results from this study confirmed that the susceptibility of *S. aureus* to non-β-lactam antibiotics was higher than that to β-lactam antibiotics. In line with this, recent studies have reported the prevalence of methicillin-resistant *S. aureus* (MRSA) is increasing [45]. MRSA cannot be excluded in *S. aureus* infections, and for MRSA, vancomycin can be used depending on the results.

According to previous studies, *K. pneumoniae* has a 56% to 75% resistance rate to cephalosporin, and a high sensitivity to piperacillin and amikacin [45-47]. And *Enterobacter* spp. showed relatively high resistance to penicillin-, clindamycin-, and fluoroquinolone-based antibiotics, and the resistance rate increased with time. Meanwhile, a high susceptibility to carbapenem, piperacillin-tazobactam, and amikacin has been reported. In this study, *K. pneumoniae* and *Enterobacter* spp. showed very high resistance to penicillin. When an infection occurs, microbial testing is essential, and appropriate antibiotics should be considered based on the results of the antibiotic susceptibility test so that the infection does not persist and lead to serious complications.

P. aeruginosa was susceptible to antibiotics such as amikacin, tobramycin, piperacillin-tazobactam, meropenem, and colistin in previous study, but this study showed 100% sensitivity to all antibiotics [17]. *A. baumannii*, however, was 100% resistant to monobactam-based aztreonam and aminoglycoside- and quinolone-based antibiotics. It is important to note that, in this study, *A. baumannii* and *P. aeruginosa* were identified in only one and two cases, respectively, resulting in poor reliability. In the study by Jones et al. [48] *A. baumannii* showed sensitivity to only colistin and tetracycline. According to Jellison et al. [49] and Oliveira et al. [50], sulbactam and β-lactamase inhibitors were effective.

Although many overseas studies have identified antibiotics that can be effectively used against various infectious bacteria and antibiotic-resistant bacteria, it is difficult to apply the results of overseas studies domestically due to environmental, genetic, and social differences. Further, the number of domestic studies on this issue is insufficient. It may be difficult to apply the results of the relatively well-studied urinary tract, blood, respiratory tract, and limb infections to the oral and maxillofacial area.

Oral and maxillofacial infections can spread quickly through the fascia and cause severe infections. Severe cases of infection can cause serious and fatal complications such as life-threatening necrotizing fasciitis, mediastinitis, cavernous sinus thrombosis, brain abscess, and so on. Indeed, if diagnosis and treatment are not performed early, the mortality rate is reported to be as high as 20% to 50% [25]. Based on this, there is a need for various fields to extend treatment periods and reduce the incidence of serious complications. Comprehensive and active efforts to support medical personnel, medical institutions, health organizations, and health care policy departments are necessary. In addition, when looking at the high postoperative infection rate of ESKAPE, active efforts for the control of infections in hospital are essential. This is of particular importance in the field of dental care, where the spread of infection is easy due to aerosols, and postoperative infection and opportunistic infection should be noted.

A significant strength of this work is the fact that it is the first study focusing on ESKAPE in the oral and maxillofacial area in Korea. Our results will provide key information for future research aiming to understand the real-life extent of infections by unknown antibiotic resistant strains, including ESKAPE, and establishing countermeasures.

However, there are some limitations to this study. First, because the study was conducted based on data obtained from medical records and microbial test results, the results did not include a review of the degree of infection, clinical symptoms, treatments performed other than antibiotic therapy, and radiological data for each patient. Second, given that the study was conducted on patients who visited a university hospital, it is possible that the resistance rate of antibiotics was overestimated. Third, various antibiotics were not consistently applied to the detected strains during the antibiotic susceptibility test, which was conducted in the hospital's microbiological laboratory. This makes it difficult to analyze and compare various antibiotic resistance rates for each bacterium. Thus, future studies should aim to apply the same antibiotics to compare several strains. Lastly, the main limitation of this study is that it includes a small number of subjects in a single institution, thus leading to the possibility of selection bias. Further, the generalizability of the results to the overall Korean population is limited. To increase the reliability of the results, future studies aiming to obtain more extensive and long-term results by including a larger number of subjects are essential. In addition, further research and continuous follow-up will be needed to establish information on additional resistant bacteria, prevent infection, select appropriate antibiotics, and establish treatment plans.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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