Comparison of sensitivity of bacteria isolated in odontogenic infections to ceftriaxone and amoxicillin-clavulanate

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Abstract

Background: Odontogenic infections is a cause of mortality and morbidity in maxillofacial patients. This is largely due to resistance of organisms to antibiotics prescribed.

Objectives: To isolate organisms involved in odontogenic infections and compare the sensitivity of the organisms to Ceftriaxone and Amoxicillin-Clavulanate.

Methods: The causative organisms and antibiotic sensitivity were determined by the following steps: Aspiration of pus done with needle, sample of pus or exudate collected using sterile swab if aspiration was unsuccessful and specimen were placed in transport media (thioglycolatebroth) and sent immediately to microbiology laboratory for culture of organisms and antibiotic sensitivity.

Results: Out of a total 55 samples taken for bacteriology, 42 (76.4%) yielded positive culture for bacteria. A total number of 21 bacteria species were identified from the positive cultures. Overall, 52% of isolated organisms were sensitive to amoxicillin-clavulanate, 70% were sensitive to Ceftriaxone while 24% were resistant to both antibiotics (Table 3). Ceftriaxone was statistically significantly more potent in inhibiting bacteria growth than amoxicillin-clavulanate (P =0.009).

Keywords: Sensitivity of bacteria, odontogenic infections, ceftriaxone, amoxicillin-clavulanate

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Introduction

Odontogenic orofacial infections are pathologic states of the head and neck resulting from pathogenic organisms whose primary source is the tooth and/or tooth supporting structures.

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Odontogenic infections have the potential to spread extremely rapidly from localised infections to cause airway embarrassment, requiring prompt and aggressive medical and surgical intervention. In their most severe forms, odontogenic infections can result into acute airway obstruction, multiple organ failure and ultimately death of the patient.[1,2] The clinical spectrum of odontogenic orofacial infections includes dento-alveolar abscess, infections of one or more spaces, Ludwig's angina and necrotising fasciitis.[1,2,3]

Odontogenic infections arise either from pulp necrosis most commonly from dental caries, or trauma or pericoronal infections.[4] In all instances, they are of oral microbial origin. Depending on the type, quantity and virulence

of the micro-organisms, they may spread into the maxilla or mandible and then into the surrounding face, jaws or neck.

Complications of odontogenic orofacial infections include descending mediastinitis, septic shock, upper airway obstruction, jugular vein thrombosis, venous septic embolus, carotid artery pseudoaneurysm or rupture, pleural empyema, pericarditis and disseminated intravascular coagulopathy.[5,6,7] These conditions are life threatening and increase the mortality rate to about 50% especially in cases of descending mediastinitis.

The organisms involved in odontogenic orofacial infections are mixed consisting of both aerobes and anaerobes which in most cases reflect the oral microflora.[8] Facultative aerobes involved include *Streptococcus* group- *viridans, milleri*; *Staphylococcus aureus* while anaerobes include *Prevotella*, *fusobacterium*, *Porphyromonas* and *Actinomyces*.[9] Other organisms not common to oral microflora involved in odontogenic infections include *Klebsiella pneumoniae*, *Neisseria gonorrhoea*, *Proteus sp*, *Pseudomonas aeroginosa* etc.[8]

Most common aerobic isolate is *Streptococcus viridans*[9,10] but Lee et al[11] reported a higher isolation of *Klebsiella pneumoniae* in deep space infections. Many of these organisms are sensitive to penicillin, clindamycin and cephalosporins.[12] Though, there has been increasing resistance to the beta-lactam antibiotics especially from Beta-lactamase producing *Staph. aureus*, *Klebsiella sp*, *Eikenella corrodens*, *Proteus sp* and *Pseudomonas sp*,[8,12] resistance to newer drugs such as imipenem and 4th generation cephalosporins are rare.

In most reports the drug of choice for odontogenic infections is parenteral penicillin.[13] Even for serious fascial space infections, including Ludwig's angina, penicillin is preferred.[5,7,14] Large doses of up to 20 million units daily for intravenous penicillin may be required for serious infections.[15] It should be noted that Kuriyama et al[13] in the year 2000 found an increased rate of resistance to beta-lactam antibiotics in subjects with odontogenic infection who had received such antibiotics prior to sampling. This study provides clinical evidence of increased resistance among bacteria cultured from odontogenic infections.[16] They recommended beta-lactamase stable antibiotics in patients with unresolved infections that have previously received beta-lactam antibiotics. The beta-lactamase stable antibiotics include amoxicillin-clavulanate combination (augmentin), amoxicillin-sulbactam combination (unasyn) and the beta-lactamase resistant penicillins including imipenem cilastin and meropenem.[17,18]

Due to increased resistance of bacteria to Penicillin, the use of beta-lactamase stable antibiotics and 3rd and 4th generation cephalosporins has increased. This study compared the sensitivity of bacteria isolated in odontogenic infections to either amoxicillin-clavulanate or Ceftriaxone (3rd generation cepholosporin). Since antibiotic therapy is a vital part of management of odontogenic infections, this will guide in providing adequate empirical antibiotics. This will reduce mortality and morbidity associated with odontogenic infections. The null hypothesis is that there is no difference in sensitivity of bacteria isolated in odontogenic infections to amoxicillin-clavulanate and ceftriaxone.

Materials and methods

Study setting

The study was carried out in the Department of Oral and Maxillofacial Surgery of Lagos University Teaching Hospital (LUTH) in Surulere, Lagos, Nigeria.

Inclusion criteria were

1. Patients with bacterial infections of odontogenic origin including dentoalveolar abscess.
2. Patients with deep fascial space spreading infections.
3. Patients with infection causing localisation of pus in the head and neck.

Exclusion criteria were

1. Patients with non-bacterial infections like viral and fungal infection. This was done by clinical assessment.
2. Patients with non-odontogenic infections from surgical wounds and upper respiratory tract infection
3. Patients with dental caries and periodontitis without dentoalveolar abscess
4. Patients with infected cysts or neoplasms
5. Patients with cervicofacial abscess of unknown cause
6. Patients who refused consent

Causative organisms and antibiotic sensitivity

The causative organisms and antibiotic sensitivity were determined by the following steps:

1. Aspiration of pus done with needle
2. Sample of pus or exudate collected using sterile swab if aspiration was unsuccessful.

3. Specimen were placed in transport media (thioglycolate broth) and sent immediately to microbiology laboratory for culture of organisms and antibiotic sensitivity. Time between sample collection and transport to laboratory was less than 5 minutes and culture was done immediately.

In the laboratory the primary culture was done on blood agar (aerobic incubation), (blood agar base (oxoid) + 5% sheep blood), chocolate agar in CO_2 and anaerobic blood agar (Fastidious anaerobe agar + 5% sheep blood). A metronidazole and gentamicin disc was placed in the first quadrant of all anaerobic plates. All isolates on the blood agar and chocolate agar were Gram stained after 24 hours of growth in air and CO_2 respectively while isolates from the anaerobic blood agar were Gram stained after 48 hours. All Gram negative bacilli were identified using the API 20E. All Gram positive cocci were tested for catalase production. The haemolytic reactions of all catalase-negative organisms was determined and their ability to grow in the presence of 6.5% NaCl. Catalase positive organisms were tested for coagulase production and resistance to Novobiocin as well as their ability to grow on mannitol salt agar. Characterization of the anaerobes was done by AP120A according to manufacturers' instructions. For anaerobic culture, an anaerobic jar (Oxoid) with the gas processing kit that provided an atmosphere of 80% N2, 10% H_2 and 10% CO_2 was used.

Antibiotic sensitivity testing was done by the disk diffusion method. The test medium was iso-sensitest agar supplemented with whole blood for streptococci and lysed blood with vitamin K for anaerobes. Commercially available antibiotic disks (ceftriaxone and augmentin) were used and interpretation of inhibition zone was in accordance with Clinical and Laboratory Standard Institute (CLSI).

Data management and analysis

Data was analysed using SPSS for windows (version 20.0; SPSS mc, Chicago. IL, USA) statistical software package; and presented in descriptive and tabular forms. Frequency distribution and cross tabulations to examine relationships between variables were done. The Fisher's exact test was used to compare differences in antibiotic sensitivity between ceftriaxone and amoxicillin-clavulanate.

Results

A total of 55 subjects who presented with odontogenic orofacial space infections at the Lagos University Teaching Hospital (LUTH) between January 2014 and April 2015 and who met the inclusion criteria participated in the study.

Demographics

There were 30 males (54.5%) and 25 females (45.5%) with a male-to-female ratio of 1.2:1. The median age was 39 years (range, 8 months – 94 years). Subjects in the 4th decade of life (31-40 years) had the highest incidence, followed by those in 3rd decade of life. (Table 1)

Table 1: Frequency of occurrence of odontogenic orofacial infections in different age groups

Age groups	Frequency (%)
0-10	2 (3.6)
11-20	5 (9.1)
21-30	10 (18.2)
31-40	11 (20)
41-50	9 (16.4)
51-60	6 (10.9)
61-70	8 (14.5)
>70	4 (7.3)
TOTAL	**55 (100)**

Odontogenic orofacial space infections

Out of the 55 cases seen, majority (71%) presented with abscess, followed by Ludwig's angina (12.7%) and necrotising fasciitis. Dentoalveolar abscess was the most commonly seen abscess followed by abscesses involving the orofacial potential spaces (Table 2). Cases of cellulitis were limited to submandibular and sub-mental spaces, while necrotising fasciitis involved sub-mandibular, submental and other spaces. The most common potential spaces involved were submandibular space, followed by sub-mental space and buccal space. Sub-mandibular space had the highest prevalence with a frequency of 18 (28%) followed by sub-mental space 12 (19%) while least was temporal space 3 (5%).

Out of a total 55 samples taken for bacteriology, forty-two (76.4%) yielded positive culture for bacteria. A total number of 21 bacteria species were identified from the positive cultures. Gram negative aerobes 25 (50%) were the most common bacteria isolated followed by Gram positive aerobes 17 (34%) and the least isolated were anaerobes 8 (16%). (Table 2) Most of the organisms were isolated from abscesses 29 (58%). The most commonly isolated organism was the *Staphylococcus aureus* 11(22%) followed by *Proteus mirabilis* 8 (16%). (Table 2)

Isolated bacteria in abscess, cellulitis, Ludwig's angina and necrotising fasciitis:

Abscess: A total of 29 bacteria were isolated and the most isolated organism was *Staphylococcus aureus* 8 (27.6%) followed by *Proteus mirabilis* 6 (20.7%). The most isolated anaerobe in abscess was *Prevotella intermedia* (Table 2).

Cellulitis: A total of 4 bacteria were isolated. The most common was the gram positive aerobes with the *Staphylococcus aureus* 2 (50%) the most prevalent. The other organisms isolated were alpha hemolytic *Streptococci* and *Eikenella corrodens*. No gram-negative bacteria were isolated (Table 2).

Table 2: Bacteria isolated in odontogenic orofacial infections

Bacteria Isolated	Abscess	Cellulitis	NF	Ludwig	Total	%
GRAM POSITIVE AEROBES						
Alpha haemolytic Streptococci	1	1	0	0	2	4
Coagulase negative Staphylococcus	3	0	0	0	3	6
Staphylococcus aureus	8	2	0	1	11	22
Enterococcus faecalis	0	0	0	1	1	2
Total number of gram +veaerobes					**17**	
	0	0	0	1	1	2
GRAM NEGATIVE AEROBES	1	0	0	0	1	2
Acinetobacter baumanii	0	0	1	0	1	2
Burkholderia cepacia	1	0	0	0	1	2
Chryseomonas luteola	1	0	1	1	3	6
Enterobacter aerogenes	1	0	0	0	1	2
Escherichia coli	1	0	0	0	1	2
Enterobacter cloacae	0	0	2	1	3	6
Enterobacter sakazakii	0	0	0	2	2	4
Klebsiella pneumoniae	6	0	0	2	8	16
Pseudomonas aeruginosa	0	0	1	0	1	2
Proteus mirabilis	1	0	0	0	1	2
Pseudomonas putida	1	0	0	0	1	2
Providentia stuartii					**25**	
Proteus vulgaris						
Total number of gram –ve aerobes	1	1	0	0	2	4
ANAEROBES	0	0	2	0	2	4
Eikenella corrodens	1	0	1	0	2	4
Peptostreptococcus anaerebius	2	0	0	0	2	4
Prevotella denticola					**8**	
Prevotella intermedia	**29**	**4**	**8**	**9**	**50**	**100**
Total anaerobes						
Total number of bacteria						

Necrotizing fasciitis: A total of 8 bacteria were isolated. Gram negative aerobes were the most isolated with the *Klebsiella pneumonia* and *Peptostreptococcus anaerebius* the most common Gram negative organisms. No gram positive aerobe was isolated.

Ludwig's angina: A total of 9 bacteria were isolated. The most prevalent organism was gram negative aerobe 7 (77.7%) with *Pseudomonas aeroginosa* and *Proteus mirabilis* 2 (22.2%) being the most isolated.

Antibiotic sensitivity

Overall, 52% of isolated organisms were sensitive to amoxicillin-clavulanate, 70% were sensitive to ceftriaxone while 24% were resistant to both antibiotics (Table 3). Ceftriaxone was statistically significantly more potent in inhibiting bacteria growth than amoxicillin-clavulanate (P =0.009). Both antibiotics were quite efficacious against organisms isolated in abscess but ceftriaxone was more potent in organisms isolated in cellulitis, necrotizing fasciitis and Ludwig's angina. No organism isolated in necrotizing fasciitis was sensitive to amoxicillin-clavulanate. Resistance to both antibiotics was more common in organisms isolated in necrotizing fasciitis (62.5%), but no organism isolated in cellulitis was resistance to both antibiotics.

Table 3: Antibiotic sensitivity of organisms isolated in abscess, cellulitis, necrotising fasciitis and Ludwig's angina to amoxicillin-clavulanate and ceftriaxone. Fisher's exact test was the statistical test used

	Abscess	Cellulitis	NF	Ludwig	**Total**	Percentage of Tn	*P*-value
Amox-clav (N_1)	22 (76%)	2(50%) 3(75%)	0(0%) 3(37.5%)	2(22%) 4(44%)	**26** **35**	52% 70%	0.009
Ceftriaxone (N_2)	25 (86%)	0(0%)	5(62.5%)	4(44%)	**12**	24%	
Resistant to both (N_3)	3 (10%)						

Tn =Total number of bacteria isolated (50)
N_1 = number of bacteria sensitive to amoxicillin-clavulanate (Amox-clav)
N_2 = number of bacteria sensitive to ceftriaxone
N_3 = number of bacteria resistant to both antibiotics

Discussion

Bacteria involved in odontogenic orofacial space infections are generally reported to be of mixed aerobic-anaerobic infection.[19,20] Eighty-four per cent of organisms isolated in this study were aerobes while 16% were anaerobes. This is in contrast with studies carried out on bacteriology of odontogenic infections in Nigeria by Ndukwe et al[21] and Osazuwa et al[22] who indicated that anaerobes are the most predominant organisms in orofacial infections and gram positive aerobes had minimal role to play. This may be because they considered both odontogenic and non-odontogenic infections unlike this study where only odontogenic infections were considered. In agreement with their studies, the present study found *Prevotella sp* as the the most common anaerobe. Some reports recorded that *Prevotella sp* are normal commensals of the oral cavity, thus reporting *Bacteroides* and *Fusobacterium spp*. as the most common anaerobic organisms causing odontogenic infections.[20,23]

In the present study, the most prevalent bacteria isolated were *Staphylococcus aureus* in agreement with a study by Gerd et al.[24] Though some authors believe this is because of skin contamination,[3] it is generally accepted as a pathogen in orofacial infections.[24,25] Sanchez et al[9] however, reported a high culture of *Streptococcus sp* isolated and this may be due to the large number of cellulitis considered in the study. They also reported like this study that the most prevalent anaerobic organism isolated was *Prevotella sp*.

Bacteriology of necrotizing fasciitis has been mostly reported to be polymicrobial with *Peptostreptococcus sp* as most isolated anaerobe[21] which is similar to the result of this study. *Klebsiella pnuemoniae* was the most isolated aerobe isolated in subjects with necrotizing fasciitis who were also noted to present with a high percentage of diabetics in this study supporting the report of Lee et al[8] that high *Klebsiella pneumoniae* isolate in odontogenic infections is due to elevated blood sugar in diabetics.

The first choice of empirical antibiotic in many reports on antibiotics management of odontogenic orofacial infections are beta lactam penicillins[5,7] though Kuriyama et al[13] reported a high resistance of bacteria to beta lactam penicillins in patients who had received antibiotics prior to sampling. Flynn et al[26] reported that only 46% of bacteria isolates were sensitivity to penicillin; the result of which is similar to what was obtained in the present study. In contrast, Lee et al[8] reported that 85% of bacteria isolates in their study were sensitive to penicillin. The percentage of organisms sensitive to amoxicillin-clavulanate especially in cases of necrotizing fasciitis and Ludwig's angina was low supporting the view of Kuriyama et al13and Flynn et al[26]. This may be explained by the fact that most subjects who presented at our clinic with severe space infections were referred from other centres who had prescribed medications during early phase of the infection. Due to inadequate or inappropriate dosage and incomplete treatment, there is tendency to develop resistance to the antibiotics used and to similar antibiotics.[26]
In the present study, bacteria isolate in severe odontogenic orofacial infections were significantly more sensitive to ceftriaxone than amoxicillin-clavulanate which may indicate that ceftriaxone is a better choice as an empirical antibiotic for severe odontogenic infections. Empirical antibiotics should be changed if there is no improvement in 48 hours, progression of infection or organisms involved have been shown to be resistant to the antibiotic.[13,16]

Conclusion

Odontogenic infection is a mixed microbial infection which can be fatal if not properly managed. The choice of empirical antibiotic is paramount in management of odontogenic infection. Organisms involved in severe odontogenic infections are more resistant to amoxicillin-clavulanate than to ceftriaxone according to our findings. Thus, ceftriaxone should be considered as an empirical antibiotic for severe odontogenic infections.

Conflict of interest

None declared.

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