Systematic Review and Meta-Analysis

Medicine

OPEN

Antimicrobial resistance in odontogenic infections

A protocol for systematic review

María Verónica Cuevas-Gonzalez, PhD[a], Gabriela Anaid Mungarro-Cornejo, DDS[b], León Francisco Espinosa-Cristóbal, PhD[b], Alejandro Donohue-Cornejo, PhD[b], Karla Lizette Tovar Carrillo, PhD[b], Rosa Alicia Saucedo Acuña, PhD[b], Alma Graciela García Calderón, MEd[b], Dalia Abril Guzmán Gastelum, MS[b], Graciela Zambrano-Galván, PhD[c], Juan Carlos Cuevas-Gonzalez, PhD[b,*]

Abstract

Background: It is estimated that up to 90% of head and neck infections have an odontogenic origin, which are considered among the most common in the oral cavity and maxillofacial region. Bacterial resistance has been 1 of the main problems related to the treatment of this type of infection in recent years. The frequency of this resistance is increasing, which is mainly due to patient self-medication and the mutations that bacteria present. Therefore, the objective of this study is to analyze the antimicrobial resistance of antibiotics commonly administered for the treatment of odontogenic infections.

Method: To carry out the study, PubMed, ScienceDirect, and Scopus databases were reviewed using the keywords "odontogenic infection", "pharmacological treatment", and "microbial resistance. Studies whose main objective was the pharmacological treatment of odontogenic infections were selected. Exclusions were review-type studies, systematic reviews, or in vitro or animal model studies. For the analysis of risk of bias, the Checklist for Analytical Cross-Sectional Studies of the Joanna Briggs Institute was used. The search and analysis of the studies was carried out by 2 researchers independently.

Results: A total of 13 studies were included in this review. The mean age was 39.6 years; the location of the infection in the study subjects was in the submandibular and vestibular spaces; there were periodontal, periapical, and dentoalveolar lesions; the main microorganisms identified were *Streptococcus, Staphylococcus, Prevotella, Peptostreptococcus, Clostridium*, and *Klebsiella*; and finally, the main microorganisms identified for bacterial resistance were penicillin, clindamycin and amoxicillin.

Conclusion: The health professional is obliged to update their knowledge to avoid such antibiotic resistance and thus provide better patient care.

Keywords: a systematic review, antimicrobial resistance, odontogenic infections

1. Introduction

It is estimated that up to 90% of head and neck infections are of odontogenic origin and are among the most common in the oral cavity and maxillofacial region.[1] Development begins either in the tooth or 1 of its supporting structures due to caries, periodontal disease, unsuccessful endodontic treatments, and/or pericoronitis. Odontogenic infections can stay localized or spread to adjacent tissues and even to distant regions.[2] When this happens, the patient may experience complications including osteomyelitis, sepsis, and mediastinitis.[3]

This type of infection commonly responds favorably to outpatient management; however, when treatment is not successful, the condition can become severely complicated, even compromising the patient's life and making hospital care essential.[4] Even though most cases can be treated in a simple way, it has been estimated that the mortality rate ranges from 10% to 40%.[3] Among the factors that increase the probability of complications are patient self-medication, inadequate clinical management of antibiotics, and bacterial resistance[5]; the latter is of great importance since it currently represents a severe public health problem. Resistance to antimicrobial therapy worryingly affects the efficacy of antibiotics and leads to increased rates of morbidity and mortality associated with this type of infection.[6]

The treatment of these infections requires extensive knowledge on the part of the health professional to determine the appropriate pharmacological scheme. Many of these patients go to the dentist, which makes it essential for the practitioner to stay up to date on the use of antibiotics to make

The authors have no consent to disclose.

The authors have no funding and conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

The authors have no ethical statement to disclose.

[a] Faculty of Health Sciences Valle de las Palmas, Autonomous University of Baja California, Baja CA, México, [b] Juarez City, Chihuahua, Mexico, [c] Research Division, Faculty of Medicine, Juarez University of the State of Durango, Mexico.

** Correspondence: Juan Carlos Cuevas-Gonzalez, Institute of Biomedical Sciences, Autonomous University of Ciudad Juarez, Av. Benjamín Franklin no. 4650, Zona Pronaf Condominio LA Plata, 32310 Cd Juárez, Chihuahua, Mexico (e-mail: cuevas_gonzalez@hotmail.com).*

How to cite this article: Cuevas-Gonzalez MV, Mungarro-Cornejo GA, Espinosa-Cristóbal LF, Donohue-Cornejo A, Tovar Carrillo KL, Saucedo Acuña RA, García Calderón AG, Guzmán Gastelum DA, Zambrano-Galván G, Cuevas-Gonzalez JC. Antimicrobial resistance in odontogenic infections: A protocol for systematic review. Medicine 2022;101:50(e31345).

Received: 7 March 2022 / Received in final form: 21 September 2022 / Accepted: 22 September 2022

http://dx.doi.org/10.1097/MD.0000000000031345

appropriate decisions.[7] Therefore, the objective of this study is to analyze the antimicrobial resistance of antibiotics commonly administered for the treatment of odontogenic infections. To carry out the study, three databases were analyzed: PubMed, ScienceDirect, and Scopus to identify studies that included the pharmacological treatments used in odontogenic infections and their effects. This study was based on the PRISMA criteria.

2. Materials and Methods

2.1. Research question

What is the response to antibiotic treatment in adult subjects with odontogenic infections?

2.2. Registration protocol

The study was registered in PROSPERO No. CRD42021265241.

2.3. Selection criteria

Inclusion criteria were:

- Clinical case studies, case series, retrospective studies.
- Studies whose main objective was the treatment of odontogenic infections.
- Studies whose methodology explicitly mentioned the antibiotic treatment administered to patients.

Exclusion criteria were:

- Studies that were reviews or systematic reviews.

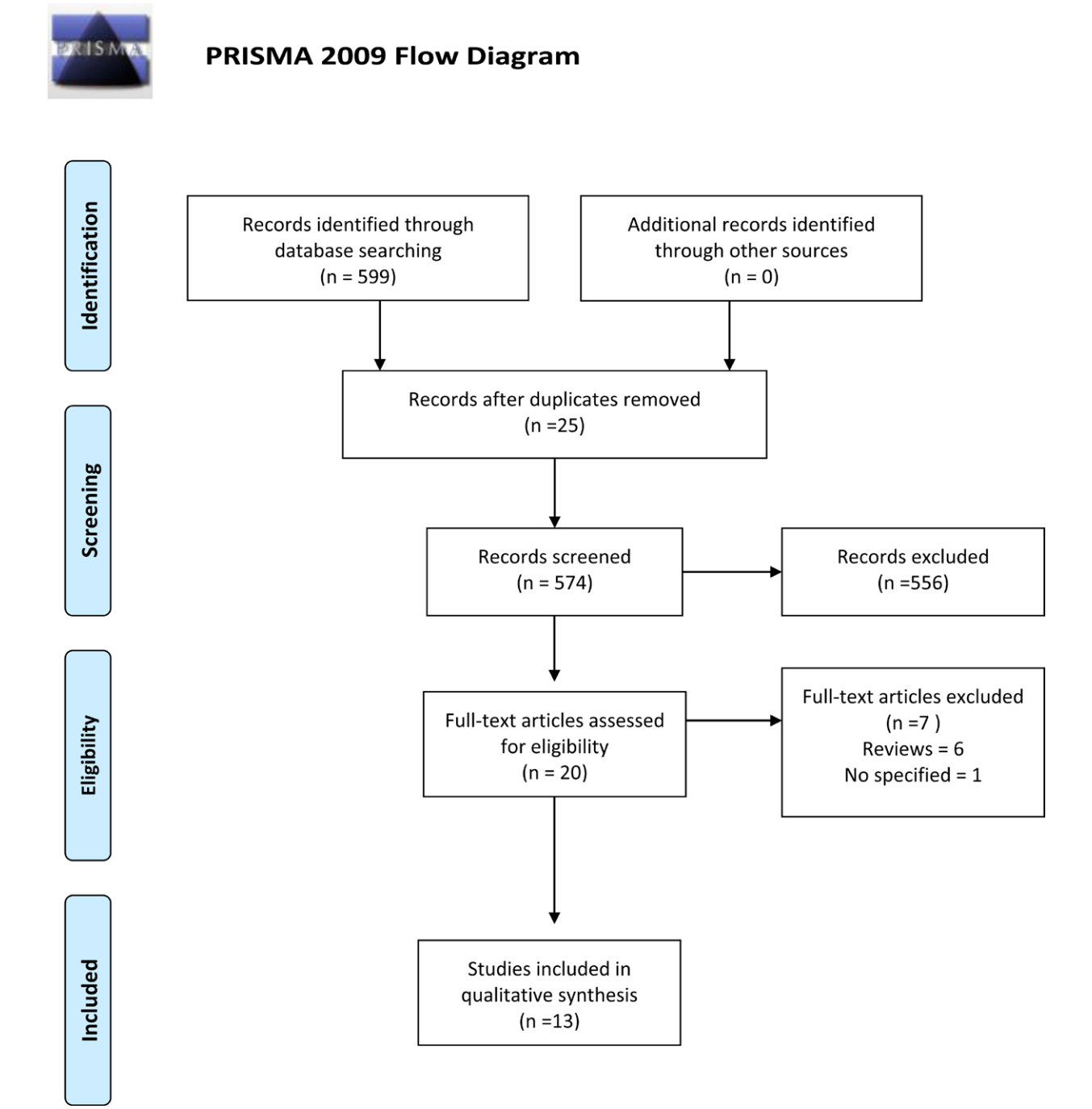

Figure 1. PRISMA flow diagram.

- Studies that did not clearly mention the treatment used.
- Studies conducted on subjects under 18 years of age.
- Studies carried out on animals or in vitro.

2.4. Search strategy

For the search strategy, three databases were used: PubMed, ScienceDirect, and Scopus. The keywords "odontogenic infection", "pharmacological treatment", and "microbial resistance" were used with the Boolean operators "AND" and "OR", and the search was performed with the terms independently and jointly.

2.5. Selection of studies

For the selection of studies, a first filtering by title and abstract was carried out to identify articles that included odontogenic infections and their treatment. Subsequently, the selected studies were placed in a bibliographic manager (Mendeley) to identify repeated studies; then, an extensive review was carried out to identify all the studies that met the established selection criteria. The search was carried out by 2 evaluators independently (Gabriela Anaid Mungarro Cornejo and María Verónica Cuevas González). In case of discrepancy, a 3rd evaluator intervened (Juan Carlos Cuevas González).

2.6. Data extraction

The data obtained from each of the selected studies were author, year, type of study, objective, number of study subjects, age in years, diagnosis, location of the infection, identification of bacteria, main bacteria identified, type of drug and complementary non-antibiotic treatment, antibiotic resistance, and conclusion of the study. All the information was placed in a statistical program for later analysis.

2.7. Analysis of results

Because of the study objective, the data were analyzed only in a descriptive way; for the quantitative variables, measures of central tendency and dispersion were reported; for the qualitative variables, frequencies were reported. The SPSS.25 (IBM SPSS Statistics for Windows, Version 25.0, IBM Corp, Armonk, NY) program was used.

2.8. Risk of bias

Risk of bias was determined using the Joanna Briggs Institute Checklist for Analytical Cross-Sectional Studies.[8] The evaluation was carried out by 2 evaluators independently (Gabriela Anaid Mungarro Cornejo and María Verónica Cuevas González). In case of discrepancy a 3rd evaluator intervened (Juan Carlos Cuevas González),

3. Results

3.1. Search strategy

According to the search strategy, 599 studies were identified. When analyzing the initial filtering by title and abstract, 18 studies were selected. Finally, when evaluating the full text, 13 studies were selected that met the established criteria. (Fig. 1: PRISMA flow chart).

3.2. Data description

When analyzing the extensive studies, the sample size per study was highly variable: from 10 to 1077 study subjects. The mean age was 39.6 years, and the dental pieces responsible for the etiology of these infections were mostly the mandibular molars. When describing the location of the infection in the study subjects, the most common location reported were the submandibular and vestibular spaces. The periodontal, periapical, and dentoalveolar lesions were more prevalent.

Infections of odontogenic origin are polymicrobial, so it is not surprising that a considerable variety of microorganisms were detected in the included studies. The most frequent were bacteria from these groups: *Streptococcus, Staphylococcus, Prevotella, Peptostreptococcus, Clostridium*, and *Klebsiella*. In all the studies, antibiotic resistance tests were carried out on the isolated microorganisms. Ceftriaxone, penicillin, clindamycin, amoxicillin, erythromycin, metronidazole, cotrimoxazole, and clarithromycin were among the drugs that showed resistance.

3.3. Risk of bias

A risk of bias assessment was performed using the Joanna Briggs Institute Checklist for Analytical Cross-Sectional Studies, which consists of eight questions directed towards the identification of basic methodological elements such as inclusion criteria, description of the study subjects, and the description of the strategies used for the analysis of the subjects. According to the evaluation carried out, 100% of the studies had a low risk of bias (Table 1).

4. Discussion

Currently, bacterial resistance to antibiotics has increased. The main reason why a dental professional will recommend antimicrobial therapy is the presence of odontogenic infections. Shakya et al,[9] reported that males are more affected than females in a 2.45:1.00 ratio, and the most affected age group is from 21 to 30 years old. In contrast, Blankson et al,[10] in their 5-year study, reported that both sexes have the same involvement in a 1:1 ratio with a mean age of 42.9 years. In our study, the mean age of patients with odontogenic infections was 39.6 years. These data show that although odontogenic infections can affect either sex indistinctly, the main age of presentation in adults is between the 3rd and 4th decade of life.

When the infectious process develops, it is vitally important that adequate treatment is in place to avoid dissemination to deep maxillofacial spaces. The dispersal of the infection has multiple etiological factors, 2 of which are: (1) resistance of the host due to the presence of systemic diseases; and (2) bacterial resistance to the administered treatment. The main complications include respiratory obstruction,

Table 1

Risk of bias.

Author	Q1	Q2	Q3	Q4	Q7	Q8	Risk bias
Aneesh	*	*	*	*	*	*	Low
Farmahan S	*	*	*	*	*	*	Low
Nils Heim	*	*	*	*	*	*	Low
Inderdeep Singh Walia	*	*	*	*	*	*	Low
López - González E	*	*	*	*	*	*	Low
Mamta Singh	*	*	*	*	*	*	Low
Narita M	*	*	*	*	*	*	Low
Heim N.	*	*	*	*	*	*	Low
Adamson OO	*	*	*	*	*	*	Low
Plum A.	*	*	*	*	*	*	Low
Sánchez R	*	*	*	*	*	*	Low
Rasteniene R.	*	*	*	*	*	*	Low
Kityamuwesi R.	*	*	*	*	*	*	Low

Scientific papers included in the study.

Table 2

Variables included in the study.

	Metodology						Main Bacteria Identified		Treatment			
Autor	**Study type**	**Objective**	**Patients number study**	**Main age patients' study (years)**	**Diagnosis**	**Zone of infection**	**Identify microorganism**	**Aerobe**	**Anaerobe**	**Type drug**	**Adyuvant treatment**	**Type antibiotic resistance**	**Conclusion**
Aneesh (2019)	In vitro	Identify the causative aerobic and anaerobic micro- organisms responsible for head and neck facial space infections and to evaluate the resistance against empirical antibiotics used in the treatment of space infections.	142		Odontogenic infections	Vestibular space	Yes	*Strepto-coccus Viridans*	*Peptostrepto-coccus*	NS	NS	Amoxicillin	There should be substitution of miscellaneous group of antibiotics such as linezolid, clindamycin, third generation cephalosporins such as cefixime, cefotaxime, and fluroqunolones such as ofloxacin and levofloxacin for amoxicillin in the empirical management of odontogenic space infections
Farmahan S (2014)	Retrospec-tive study	Investigate whether the microbi-ological picture and antibiotic sensitivity of space infections in the head and neck have changed over the last 30–40 years.	150	39	Odontogenic infections	Periapical	Yes	*Streptoc-cossus viridans*	*Prevotella*	Co-amoxi-clav	Tooth ex-traction	Penicillin	Penicillin (amoxicillin) still remains the drug of choice for odontogenic space infections in the head and neck because it is effective and has minimal side effects
Nils Heim (2020)	Retrospec-tive study	Precisely categorize the identified microbial flora and the suscepti-bility to antibiotics	206	50.6	Odontogenic infections	Peri-man-dibular/ buccal	Yes	*Strepto-coccus*	*Prevotella*	NS	NS	Cephadroxil and clin-damycin	Streptococcus species were the most frequently identified bacteria in our study presenting antibiotic resistance in more than 50%.
Inderdeep Singh Walia (2014)	Descriptive study	Assess the anatomical spaces and causative microorganisms responsible for deep fascial space head and neck infections, to evaluate the resistance of antibiotics used in treatment of these infection	42	38	Odontogenic infections	Sub-man-dibular	Yes	*Klebsiella*	Staph aureus	NS	NS	Penicillin and erythro-mycin	The key issue here, which needs to be remembered, is that antibiotics alone cannot resolve odontogenic infection satisfactorily
López - González E (2019)	Descriptive study	Evaluate the susceptibility to diferent groups of antibiotics of aerobic and anaerobic microorganisms isolated from purulent exudates of hospitalized patients with severe odontogenic infections	14	37.5	Odontogenic infections	Submaxil-lary	Yes	*Strepto-coccus*	*Clostridium*	Clinda-mycin/ ceftriax-one	Exodontia/ Surgical drainage	Ceftriaxone	The causal microorganisms of odontogenic infections show high resistance to standard antibiotic therapy regimes and cause serious health problems
Mamta Singh (2014)	Descriptive study	Emphasize the detection of pathogenic microorganisms by microbiological examination and culture of specimens representative of the infection, importance of early and correct diagnosis of infections, prompt treatment and supportive care	30	32.4	Odontogenic infections	Mandibular tooth	Yes	*Alpha hem-olityc strepto-cocci*	*Peptostrepto-coccus*	NS	NS	Erythromycin	Importance of thorough drainage of the infected site cannot be overlooked and this should be supported by proper antibiotic therapy based on culture and sensitivity reports.

(*Continued*)

Table 2
(*Continued*)

Metodology								Main Bacteria Identified		Treatment			
Autor	**Study type**	**Objective**	**Patients number study**	**Main age patients' study (years)**	**Diagnosis**	**Zone of infection**	**Identify microorganism**	**Aerobe**	**Anaerobe**	**Type drug**	**Adyuvant treatment**	**Type antibiotic resistance**	**Conclusion**
Narita M (2016)	Descriptive study	Investigate the effectiveness of commonly use antimicrobial agents in the treatment of orofacial odontogenic infections	10		Odontogenic infections	Periodontal lesions	Yes	NS	*NE*	NS	NS	Amoxicilin	Amoxicilin, Cefmetazole and clindamycin are still likely to be effective in the treatment of periapical periodontitis. However these microbial agents, and amozicilin in particular, carry the considerable risk of clinical treatment failure dua to increase in the nubres of resistante strains
Heim N. (2017)	Retrospective study	Evaluate whether susceptibility and resistances of bacteria to antibiotics have an influence on how patients have to be treated (inpatient or outpatient management) or not.	107	48.3	Odontogenic infections	NS	Yes	*Staphylococcus/ S. viridans group*	*Prevotella*	Ampicillin/ sulbactam	Surgical incision and drainage	Clindamycin	Penicillin continues to be a highly effective antibiotic against viridans Streptococci, group C Streptococci and Prevotella, whereas clindamycin could not be shown to be effective as an empirical drug of choice for a large number of odontogenic infections.
Adamson OO (2019)	Retrospective study	Isolate organisms involved in odontogenic infections and compare the sensitivity of the organisms to Ceftriax- one and Amoxicillin-Clavulanate.	55	39	Odontogenic infections	Dentoalveolar	Yes	*Staphylococcus aureus*	*Klebsiella pneumoniae*	NS	NS	Amoxicillin/ clavulanate	Organisms involved in severe odontogenic infections are more resistant to amoxicillin-clavulanate than to ceftriaxone according to our foundings. Thus, ceftriaxone should be considered as an empirical antibiotic for severe odontogenic infections.
Plum A. (2018)	Retrospective study	Characterize the current microbial ora and associated antibiotic resistances observed in Upstate New York.	131	35.1	Odontogenic infections	NS	Yes	Staphylococcus	*Streptococcus/ prevotella*	NS	Surgical incision and drainage	Clindamycin and erythromycin	The most common antibiotics to which resistance was observed were clindamycin and erythromycin, which should be considered when choosing initial antibiotic therapy, especially in adult patients
Sánchez R (2011)	Retrospective study	A retrospective analysis of the odontogenic infections treated in La Paz University Hospital (Madrid, Spain) during the years 2007 and 2008	151	49.3	Odontogenic infections	NS	Yes	*Streptococcus viridians*	*Prevotella*	Clindamycin/ Gentamycin	Drainage or extraction	Erythromycin/ Clarithromycin	the use of antibiotics in head and neck infections requires updated protocols based on the existing scienti c evidence relating to pathogen pro le and resistances

(*Continued*)

Table 2
(*Continued*)

	Metodology						Main Bacteria Identified		Treatment			
Autor	**Study type**	**Objective**	**Patients number study**	**Main age patients' study (years)**	**Diagnosis**	**Zone of infection**	**Identify microorganism**	**Aerobe**	**Anaerobe**	**Type drug**	**Adyuvant treatment**	**Type antibiotic resistance**	**Conclusion**
Rasteniene r. (2015)	Retrospective study	Analyze treatment modalities and results in patients with severe odontogenic maxillofacial infections during a 10-y period.	1077	37	Odontogenic infections	Sub-mandibular	Yes	Streptococcus haemolyticus	*Gamma-hemolytic Streptococcus*	Gentamicin or metronidazole	NS	Metronidazole.	The sensitivity of a microorganism to penicillin remains high, therefore, penicillin can be the drug of first choice for treatment of odontogenic maxillofacial infections
Kityamuwesi R. (2015)	Descriptive study	Determine the microbiology of pyogenic odonto- genic infection and perform antibiotic susceptibility tests in patients attending Mulago Hospital, Uganda	136	29.5	Odontogenic infections	Mandibular	Yes	*Viridans Streptococci*	*Anaerobic bacilli*	NS	NS	Cotrimoxazole/ ampicilli	Dental caries was the most common predisposing factor for pyogenic odontogenic infection, which requires community oral health education. Overall, there was high bacterial resistance to tetracycline, penicillin G, ceftazidime, ampicillin and cotrimoxazole, suggesting the need for susceptibility tests of isolates and rational use of antibiotic in the management of these infections.

NS = Not specified.

sepsis, endocarditis, and pericarditis.[2,3] 1 of the most common examples related to the spread of odontogenic infection is periapical infection. The microorganisms begin invading the root canal and spread towards the periradicular tissues through the apical foramen, causing an inflammatory process that can trigger the formation of an abscess.[2] In this study, we identified that the main localization of the odontogenic infection was in the mandibular region, which, due to the lack of adequate treatment, was able to advance and invade the submaxillary spaces.[3]

One of the main challenges when establishing pharmacological treatment is the polymicrobial characteristic of the odontogenic infections in which aerobic and anaerobic microorganisms have been described. According to the study carried out by Sebastian et al,[11] the most frequent aerobic microorganism in odontogenic infections was *Streptococcus viridians* in 34.9% of cases, and the most frequent anaerobic microorganism was *Peptostreptococci* in 61.1%. They reported that amoxicillin with metronidazole is the standard treatment for this type of infection; however, they observed a resistance of 95% in aerobic microorganisms and 86% resistance for anaerobic microorganisms. In contrast, López-González et al[12] reported that anaerobic microorganisms have the greatest presence in odontogenic infections - mainly gram-positive bacilli - which showed resistance to clindamycin in 33.3% of cases. In the present study, the aerobic microorganism with the highest frequency was *Streptococcus*; within the anaerobic microorganism it was *Prevotella*. The main antibiotics related to bacterial resistance are ceftriaxone, penicillin, clindamycin, and amoxicillin, among others (Table 2).

There are multiple methods by which bacteria generate resistance to drugs. Among the most prominent mechanisms is intrinsic resistance, which is characterized by the presence of enzymes that destroy the drug and prevent intracellular drug binding. The presence of mutations located in the 23S ribosomal gene modifies the binding site of antibiotics (inhibiting transcription and translation); however, resistance is due to the biofilm. The biofilm formation is carried out naturally by quorum sensing, which is when increased cell density increases antibiotic resistance because molecules have a reduced ability to diffuse through the matrix of the biofilm and finally the efflux pump. The block membrane channels are characterized by their ability to alter the entry of the antibiotic into cells and to prevent multicomponent pumps.[13,14]

Bacterial infections previously treated successfully with antibiotics have lost sensitivity as a result of their indiscriminate use.[15,16] In the United States, 10% of the antibiotics prescribed are authorized by dentists - 50% of which could be considered an inappropriate or unnecessary prescription.[17] It is essential that dentists keep up to date on the diagnosis of dental infections in order to achieve early detection of bacterial infections and proper management of the antibiotics. Access to recent information is vital for the practitioners to be aware of the most effective current antibiotic schemes based on the etiology of the infection.

5. Limitations

One of the main limitations of the study is that scientific literature on this topic is sparse. Therefore, it is essential that bacterial resistance to antibiotics is regarded as a health priority to avoid further complications.

6. Conclusions

Antibiotic resistance - an increasing health problem - has highlighted an urgent need for the implementation of strategies by the World Health Organization focused on reducing the progression of antimicrobial resistance. However, it is the health professional's responsibility and obligation to update his/her knowledge to avoid such antibiotic resistance and thus provide better patient care.

Author contributions

Conceptualization: Maria Verónica Cuevas-Gonzalez, Dalia Abril Guzmán-Gastelum.
Data curation: Rosa Alicia Saucedo Acuña, Gabriela Anaid Mungarro-Cornejo.
Formal analysis: León Francisco Espinosa-Cristóbal. Graciela Zambrano-Galván.
Investigation: Alma Graciela García-Calderón.
Methodology: Alejandro Donohue-Cornejo.
Writing – original draft: Karla Lizette Tovar Carrillo, Juan Carlos Cuevas-Gonzalez.

References

[1] Weise H, Naros A, Weise C, et al. Severe odontogenic infections with septic progress – a constant and increasing challenge: a retrospective analysis. BMC Oral Health. 2019;19:1–6.
[2] Ogle OE. Odontogenic infections. Dent Clin. 2017;61:235–52.
[3] Bali R, Sharma P, Gaba S, et al. A review of complications of odontogenic infections. Natl J Maxillofac Surg. 2015;6:136.
[4] Opitz D, Camerer C, Camerer DM, et al. Incidence and management of severe odontogenic infections - a retrospective analysis from 2004 to 2011. J Craniomaxillofac Surg. 2015;43:285–9.
[5] Igoumenakis D, Gkinis G, Kostakis G, et al. Severe odontogenic infections: causes of spread and their management . Surg Infect. 2014;15:64–8.
[6] Smith RD, Coast J. Antimicrobial resistance: a global response. Bull World Health Org. 2002;80:126–33.
[7] Martins JR, Chagas OL, Velasques BD, et al. The use of antibiotics in odontogenic infections: what is the best choice? a systematic review. J Oral Maxillofac Surg. 2017;75:2606.1–2606.e11.
[8] Institute TJB. Reviewers' manual. Methodology for JBI umbrella reviews. Adelaide, Australia: The Joanna Briggs Institute; 2014:1–27.
[9] Shakya N, Sharma D, Newaskar V, et al. Epidemiology, microbiology and antibiotic sensitivity of odontogenic space infections in Central India. J Maxillofac Oral Surg. 2018;17:324–31.
[10] Blankson PK, Parkins G, Boamah MO, et al. Severe odontogenic infections: a 5-year review of a major referral hospital in Ghana. Pan Afr Med J. 2019;32:71.
[11] Sebastian A, Antony PG, Jose M, et al. Institutional microbial analysis of odontogenic infections and their empirical antibiotic sensitivity. J Oral Biol Craniofac Res. 2019;9:133–8.
[12] López-González E, Vitales-Noyola M, González-Amaro AM, et al. Aerobic and anaerobic microorganisms and antibiotic sensitivity of odontogenic maxillofacial infections. Odontology. 2019;107:409–17.
[13] Ali J, Rafiq QA, Ratcliffe E. Antimicrobial resistance mechanisms and potential synthetic treatments. Future Sci OA. 2018;4:FSO290.
[14] Kapoor G, Saigal S, Elongavan A. Action and resistance mechanisms of antibiotics: a guide for clinicians. J Anaesthesiol Clin Pharmacol. 2017;33:300–5.
[15] Rajendra Santosh AB, Ogle OE, Williams D, et al. Epidemiology of oral and maxillofacial infections. Dent Clin. 2017;61:217–33.
[16] Haque M, Sartelli M, Haque SZ. Dental infection and resistance-global health consequences. Dent J (Basel). 2019;7:22.
[17] Montero M. Antimicrobial resistance: what should dentists be doing? Odovtos-Int J Dent Sc. 2016;18:10–4.