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Review Article

Evolution of the treatment of severe odontogenic infections over 50 years: A comprehensive review

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الملخص

أهداف البحث: لا تزال الالتهابات السنية الحادة تشكل تحديا لجراحي الوجه والفكين. الهدف من هذا العمل هو مراجعة الأدبيات حول هذا الموضوع وتحديث المعرفة حول هذا الموضوع.

طرق البحث: تم إجراء مراجعة شاملة بواسطة : "بب ميد" / "ميدلاين" و "شبكة العلوم" و "المجلة الأفريقية على الانترنت" باستخدام الاستراتيجية (الالتهابات السنية الشديدة). لم تطبق قيود لغوية. تم استرداد خيارات العلاج فقط. تم تضمين مقالات من السنوات الخمسين الماضية.

النتائج: تم تضمين ما مجموعه 84 مقالة من 39 دولة مختلفة حول العالم. الإصابات الحادة ذات المنشأ السني ليست فريدة من نوعها في البلدان المنخفضة والمتوسطة الدخل. حتى في البلدان المتقدمة، هذا وضع صعب. تمت مناقشة الإدارة الجراحية والعلاج بالمضادات الحيوية لهذا النوع من العدوى. بعض المرضى الذين يعانون من نقص المناعة لديهم مخاطر أعلى للإصابة بمضاعفات ومعدل وفيات أعلى. تم إنشاء خريطة العالم للمنشورات حول هذا الموضوع.

الاستنتاجات: تمت مناقشة العديد من الجوانب الهامة لإدارة الالتهابات السنية الحادة. تمت مناقشة بعض تنبؤات الشدة بالإضافة إلى اختيار المضادات الحيوية الموصى بها. داء السكري هو مؤشر تنبؤي ضعيف للعدوى ذات المنشأ السني.

الكلمات المفتاحية: خثار الجيب الكهفي؛ نزح؛ مقاومة الدواء؛ جرثومي؛ التهاب اللفافة؛ ناخر؛ عداوى؛ ذبحة لودفيغ.

Abstract

Objectives: Severe odontogenic infections remain a challenge for maxillofacial surgeons. The aim of this work is to review the literature to provide an update of knowledge on the topic.

Methods: A comprehensive review of articles in PubMed, Web of Science and Africa Journals Online was performed through searching for "severe odontogenic infections." No language restrictions were applied. Only articles pertaining to treatment options were retrieved. Articles from the past 50 years were included.

Results: A total of 84 articles from 39 countries worldwide were included. Severe odontogenic infections are not unique to low- and middle-income countries but also pose challenges in developed countries. Surgical management and antibiotic therapy for this type of infection is discussed. Some immunocompromised patients have high risks of complications and mortality rates. A world map of publications on the topic is provided.

Conclusions: Several important aspects of managing severe odontogenic infections are discussed. Predictors of severity in addition to recommended antibiotic choice

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have been debated. Diabetes mellitus is a poor predictor of the prognosis of odontogenic infections.

Keywords: Cavernous sinus thrombosis; Drainage; Fasciitis; Infections; Ludwig's angina; Necrotizing

Introduction

Severe odontogenic infections have plagued humanity for centuries. The first suspected death of a hominid from odontogenic infection is estimated to have occurred more than 2 million years ago.[1] Although these infections are currently rarely lethal, they were the fifth or sixth most frequent cause of death in the 17th century in London.[2] Since the beginning of the 19th century, when Gerhard Domagk discovered sulfonamide, and the Fleming-Florey-Chain trio discovered penicillin, the era of antibiotics has considerably mitigated these death statistics.[3]

Despite the discovery of antibiotics, odontogenic infections remain a cause for concern for many. Contrary to popular belief, they affect not only low- and middle-income countries, but also developed countries.[4] The rapid spread of these infections to high-risk anatomical areas is concerning to maxillofacial surgeons. In addition, bacterial resistance, immunocompromise, untreated metabolic disorders, and poor oral hygiene together can aggravate odontogenic infections.

A wide variety of odontogenic infections exist, ranging from mild to severe. A controlled odontogenic abscess can become potentially lethal within several days. Dental caries, depending on whether they are located in the upper or lower teeth, can cause Ludwig's angina[5] or cavernous sinus septic thrombosis.[6] Other potentially fatal odontogenic infections include necrotizing fasciitis and odontogenic mediastinitis.[7,8] Because of infection severity, the rapid deterioration of patient condition and the high mortality rate, healthcare professionals treating patients with odontogenic infections require up-to-date knowledge on this topic.[9] Delayed diagnosis and treatment could be fatal in most cases.

The aim of this work is to discuss the evolution of knowledge of severe odontogenic infections, describe the debates regarding their epidemiology worldwide, and highlight new findings and limitations that must be overcome regarding this topic.

Materials and Methods

The data in this article were derived from a comprehensive literature review based on PRISMA guidelines. PubMed, Web of Science (WS) and African Journals Online (AJOL) databases were evaluated for any type of study except reviews. Articles on severe odontogenic infections in any language were considered. The search covered the period from the inception of each database to April 22, 2022. Articles published from the past 50 years were included. The following database search strategy was used: ((severe odontogenic infections) NOT review).

The titles and summaries of the records found in the main hits were read, full texts of records selected in this phase were evaluated, and relevant data were extracted. Studies were selected for inclusion if they reflected the research questions in this literature review. Only articles on severe odontogenic infections providing new knowledge on the topic were included. No restrictions were placed on the type of article, country of origin or language. The exclusion criteria were as follows: (1) articles published before 1970, (2) commentaries not providing new knowledge on the topic, (3) odontogenic infections treated in outpatient or dental practices, and (4) endodontic discussion.

We aimed to answer the following focused questions: Is there any new knowledge regarding the diagnosis or treatment of severe odontogenic infections? Where is published research on severe odontogenic infections being conducted worldwide?

Results

The main hits comprised 586 records from the databases. We retrieved 304 articles from PubMed, 171 from WS and 111 from AJOL. After removal of duplicates and off-topic articles, a total of 84 articles were included. A flowchart of the included articles was created (Figure 1). A chart of the published articles on the topic indicated a clear increasing trend in the number of publications (Figure 2).

Some laboratory tests, such as C-reactive protein and white blood cell (WBC) counts, have been used to assess infection severity at patient admission, as a measure of treatment success for severe odontogenic infections.[4,10,19–21,11–18] Although few published articles have addressed this topic, the theme is increasingly being discussed. Four articles on tomographic examinations for diagnosis and therapy monitoring were evaluated.[22–25] Although tomographic studies are considered mandatory for accurate localization of infection and allow for more efficient drainage, they are not available in some low-and middle-income countries.[26]

Thirty authors have discussed the complications of serious odontogenic infections in the context of health problems. The high number of articles underscores the importance of this topic.

The management of severe odontogenic infections was assessed in 41 articles, including 7 focusing on surgical drainage and 27 focusing on antibiotic therapy. Additional measures to achieve successful outcomes were discussed in six articles.

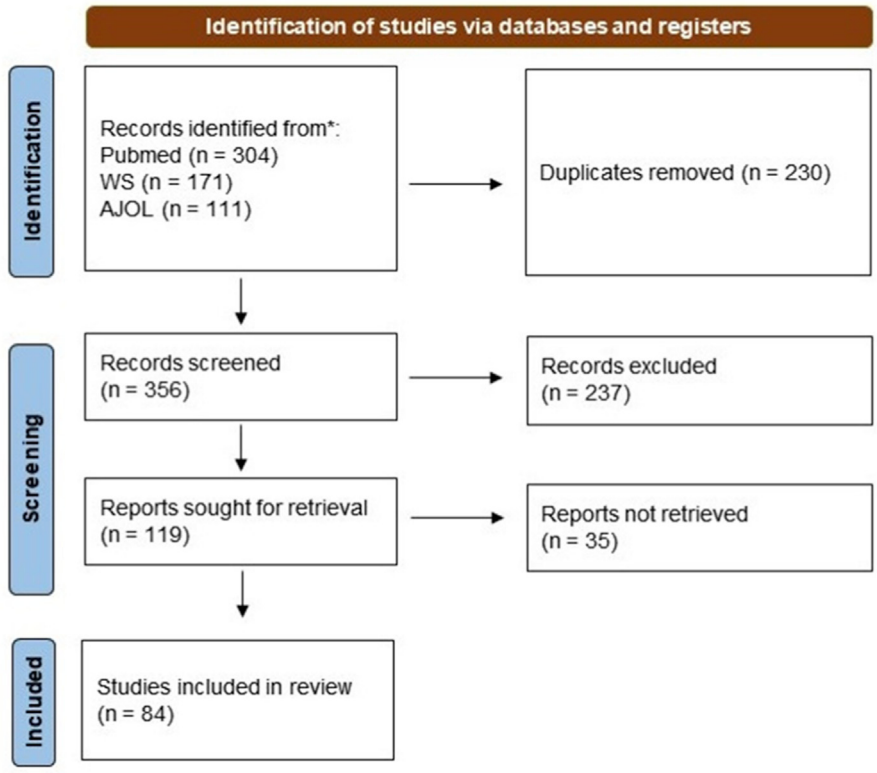

Figure 1: Flowchart of included articles.

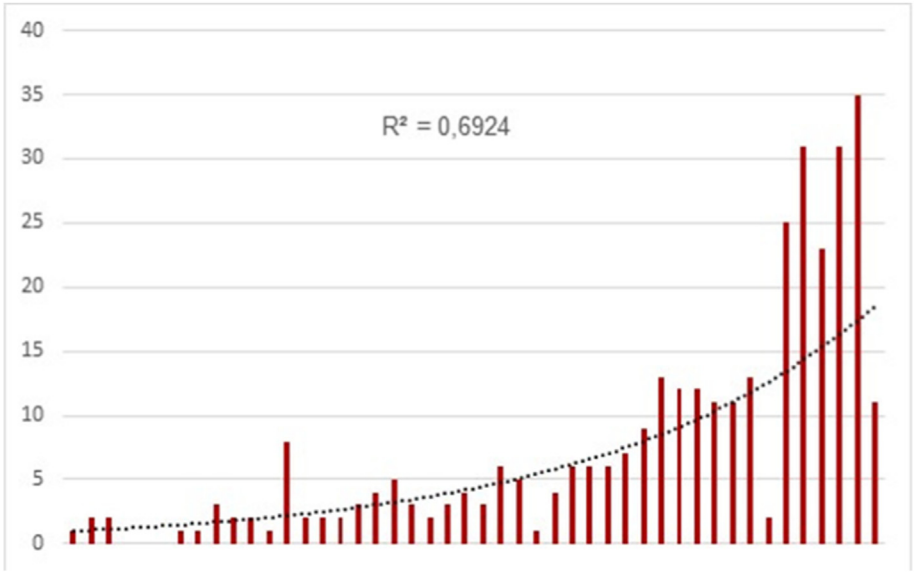

Figure 2: Number of publications on severe odontogenic infections over the past 50 years. An exponential trendline shows a clear uptrend.

Each epidemiological study in which sex and mean age could be determined was assessed to assess the most affected sex and age ranges. A slight predominance of males to females has occurred over decades, in a ratio of approximately 1.33:1. The most affected age group varied between 31–40 and 41–50 years of age, and no clear trend worldwide was apparent over decades.

Table 1 summarizes the countries of origin of the included articles. A world map was created for each included case of severe odontogenic infection (Figure 3). Although Germany had the highest number of publications, the Unites States had the most cases. This difference may be explained by the Unites States having the third largest population worldwide, thus providing researchers with

Table 1: Number of severe odontogenic infections included in articles according to country of origin and number of publications.

Germany	13	Spain	2	Thailand	1
United States	8	Brazil	2	Lithuania	1
Australia	5	Romania	2	Sudan	1
Nigeria	4	Serbia	1	Morocco	1
Finland	3	Angola	1	Pakistan	1
India	3	Rwanda	1	Philippines	1
France	3	Turkey	1	Greece	1
China	3	Egypt	1	Mexico	1
South Korea	3	Israel	1	Poland	1
Austria	3	Ghana	1	Czech Republic	1
Italy	3	Iran	1	Togo	1
Japan	2	Denmark	1	Argentina	1
United Kingdom	2	Kenya	1	Belgium	1

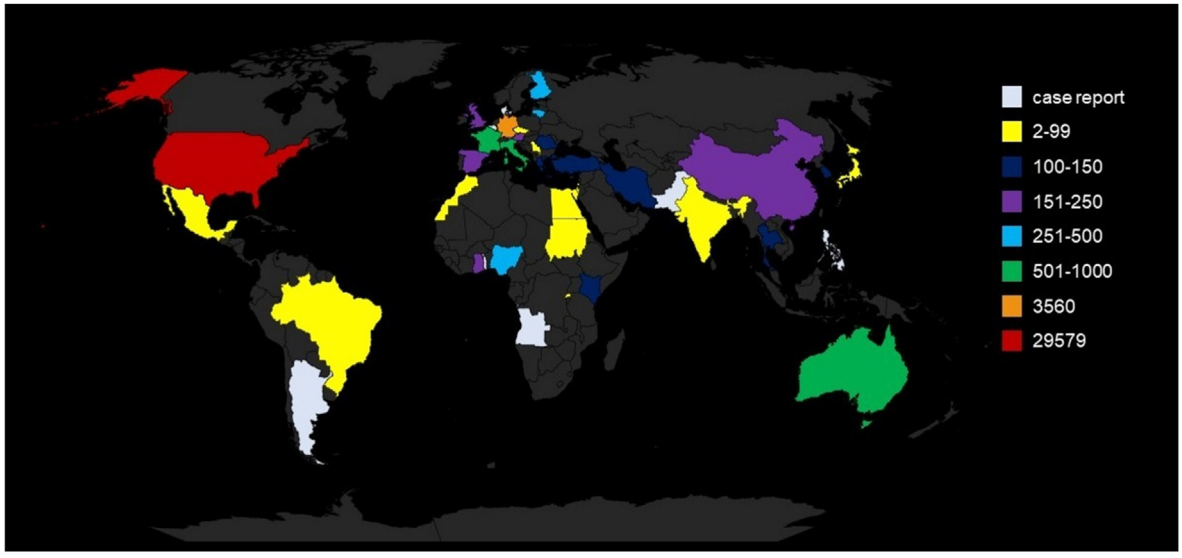

Figure 3: Case number by country of origin for the included articles.

Figure 4: Patient with Ludwig's angina. Concerns regarding trismus, dysphagia and dyspnea. Source: Own authorship.

Figure 5: Vacuum-assisted closure in a patient with necrotizing fasciitis. Source: Own authorship.

extensive epidemiological data. For example, one article analyzed 29,228 cases.[27]

Discussion

Severe odontogenic infections are high-risk situations that may be lethal.[25,27,28] Any delay in diagnosis and treatment can be fatal,[29–31] most commonly because of airway compromise[32] or multiple organ failure.[33] A substantial number of cases may require intensive care.[4,17,34] The incidence of these infections in Africa is very high,[32,35] but even in developed countries, odontogenic infections are increasing and becoming more severe.[4,30,36–38]

Clinical signs are highly important in predicting the risk of odontogenic infections. These signs include severe trismus and dysphagia[20,39,40] (Figure 4). Complications and infections that are difficult to control tend to increase with age,[27,31,41] particularly with comorbidities such as diabetes mellitus (DM).[18,34] DM plays an important role in outcomes,[42–44] because it predisposes individuals to odontogenic infections with more complications due to neutrophil suppression.[45] People with than without DM have more extensive infections, longer hospital stays and higher mortality rates,[46–48] and those with a DM history of more than 10 years have poorer prognosis.[47] Beyond DM, immunosuppression, a history of alcohol and nicotine use, chronic steroid use, mental disorders and human immunodeficiency virus seropositivity are also associated with a higher risk of complications[20,42,43,49–51] in pregnant patients, particularly in a context of poor hygiene maintenance.[52–56] Improper education regarding dental care in these patients and a lack of hygiene programs can lead to severe consequences.[54,55,57]

Other variables of interest include body mass index, which is not usually considered relevant but is in fact important. Both low and high body mass index play important roles in the success of outcomes of severe odontogenic infections.[16,42,58,59] Lower molars are the most affected teeth,[18,36,48,60] particularly the third molars.[40,54,61] The median length of hospitalization stay ranges from 5 to 11 days,[62] and may be as long as 60 days.[25]

The literature has considered Ludwig's angina, descending mediastinitis, septic cavernous sinus thrombosis and necrotizing fasciitis to be serious odontogenic infections. Most articles indicated have treated these infections as severe odontogenic infections without differentiating them. Although each infection has some unique characteristics, prompt incision and aggressive drainage, together with high-dose antibiotic therapy and rehydration, are fundamental in the management of odontogenic infections.[28,36,37,39,42] Surgical drainage is considered the most effective step in treatment.[32,33,48,63–65] Elimination of odontogenic foci is an important part of treatment.[42,64] Surgical debridement may be required in some cases.[37]

WBC count and serum glucose are useful prognostic indicators of infection severity and must be determined upon admission for odontogenic infections.[10–12] A WBC count greater than 11,000/ml may be considered to indicate high risk[11] and is suitable for predicting infections in multiple sites.[13] The neutrophil/lymphocyte ratio is also valuable as a prognostic marker: a ratio greater than 5.19 is indicative of higher antibiotic doses and longer hospitalization.[14] Serum glucose is useful in patients without DM and is essential for monitoring infections in patients with DM.[45,66]

Body temperature and mean platelet volume are not considered adequate prognostic indicators.[10,14] Whereas one article has stated that serum C-reactive protein (CRP) is not a good prognostic indicator,[10] several others have indicated that serum CRP is a good predictor of length of hospital stay and can be used to determine the severity of infection.[4,12,13,15–21] Therefore, CRP may be considered a useful tool for monitoring the effectiveness of applied therapy and decision-making regarding surgical management.[12,15,17,67] Although they are not typically determined, proinflammatory cytokines, prealbumin and procalcitonin levels may also be useful as laboratory tests.[68–71]

CT scans can help maxillofacial surgeons determine the exact location and extent of infection,[22,23] and they are mandatory for surgical revisions.[25] Parapharyngeal, submandibular and masticatory spaces are more likely to be associated with odontogenic infections than with other causes in CT scans,[22,24] because of the proximity of the lower teeth to adjacent deep neck spaces. A lack of proper complementary imaging investigation underscores the importance of assessing clinical signs and laboratory tests in diagnosing and monitoring these infections.

Common bacteria involved in severe odontogenic infections are *Streptococcus viridans* and *Staphylococcus aureus*[42,72]. However, the bacteria normally found in odontogenic infections are a microflora composed of staphylococci, *Prevotella, Peptostreptococcus* and *Bacteroides*. Anaerobic bacteria are commonly found in severe odontogenic infections.[73,74] Unfortunately, the microflora shows variation worldwide, and antibiotic therapy must be adapted to each region.[60,75] Rising global bacterial resistance is an obstacle to treating serious infections. The high resistance rate is approximately 15%–20% to macrolides and 7%–13% to penicillins.[72,73,76,77] The rate of anaerobic resistance to metronidazole is approximately 6%.[76] Penicillin resistance due to extensive previous use is associated with more severe cases of odontogenic infections and is a major cause of a need for re-drainage and longer hospitalization times.[41,73,78] Genetic analysis could improve upon traditional and molecular methods for routine diagnosis.[74] Despite being unavailable in most countries, genetic analysis may provide a promising alternative enabling adequate diagnosis and better outcomes.

Inadequate drug prescribing and improper self-medication are responsible for poorer prognosis.[79] The combination of penicillin with metronidazole remains indicated as the first line empiric treatment in most cases.[43,80] Because of the high effectiveness of penicillin, some authors have used penicillin allergies to classify severity grade.[20] Some authors have suggested prescribing ampicillin/sulbactam, cephalosporins,[41,81,82] amoxicillin + clavulanic acid,[83] imipenem + cilastatin, and ciprofloxacin with clindamycin[73,84,85] in the event of resistance. Caution should be exercised, because reports have indicated approximately 40% resistance to clindamycin in some

countries where clindamycin use is widespread.[60] Despite high rates of susceptibility, cotrimoxazol and moxifloxacin deserve further investigation as empiric antibiotic therapies.[41,86] Tazobactam and piperacillin have been demonstrated to be a favorable empirical choice.[42,72] Antibiogram can be helpful in case of unclear evidence of a positive outcome.[42,72] Antimicrobial administration must be provided extremely quickly to avoid an infection that is difficult to control.

Irrigation drains are not superior to non-irrigating drains in the treatment of severe odontogenic infections,[87] except in cases of cervico mediastinothoracic drainage.[88] In low- and middle-income regions, the use of vacuum-assisted closure after surgical drainage (Figure 5) is an optimal substitute for hyperbaric oxygen therapy, particularly in cases of necrotizing fasciitis.[89–92]

Many cases of odontogenic infection can be found in low- and middle-income countries, but the number of related publications from these countries is very small.[35] The African continent and some countries in Asia and South America may experience a continual lack of medical professionals and equipment, and may experience poverty, long distances and influences of mysticism.[26,35] Measures such as international cooperation and knowledge sharing could be very helpful for maxillofacial surgeons in those regions. Although humanitarian missions are valuable, for severe infections with rapid evolution, such efforts would not be able to achieve the desired goals sufficiently quickly.

This review has several limitations. Despite some similarities in the numbers of odontogenic infections, we hypothesize that global disparities might not have been identified because of the small number of publications from low-income countries. In addition to the limited availability of imaging and laboratory tests, difficulties exist in establishing a worldwide protocol for the treatment of severe odontogenic infections resulting from antibiotic overuse. Future research directions include the use and dissemination of less expensive, more effective diagnostic and localization methods. The effectiveness of contemporary antibiotic therapy, the need for broad-spectrum drugs, and bacterial resistance are also a focus for future studies. Surgical methods or drugs are required to mitigate the severity of these infections.

Conclusions

Clinical signs are fundamental to diagnosis and prompt treatment of odontogenic infections. Aggressive surgical drainage remains an important step in treating serious odontogenic infections. Although penicillin has broad bacterial resistance, it is nevertheless an empirically recommended antibiotic therapy. Combination treatment with metronidazole is a good option for anaerobic bacteria. Other options are amoxicillin + clavulanic acid, and piperacillin + tazobactam. C-reactive protein and WBC count are optimal monitoring tools for management. DM is the highest-risk prognostic complication associated with odontogenic infections. Despite being described in few studies, vacuum-assisted closure appears to be a good option as a dressing. Future studies are needed to assess the effectiveness of laboratory tests such as prealbumin and procalcitonin levels.

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Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

Not applicable.

Consent

Written consent was obtained from patients included in this study.

Authors contributions

The authors testify that all persons designated as authors qualify for authorship and have verified the article for absence of plagiarism. Conceptualization and study design: RG and AMB. Data collection: AMB, MB, SMB, YSS. Analysis and data interpretation: RG, AMB, MB, SMB, YSS, MGNH. Drafting: RG, AMB, SMB, MB, MGNH. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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