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Empiric systemic antibiotics for hospitalized patients with severe odontogenic infections

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A B S T R A C T

Introduction: Odontogenic infections may lead to severe head and neck infections with potentially great health risk. Age, location of purulent affected sites and beta-lactam allergy are some mentionable factors regarding patients' in-hospital stay and course of disease. Are there new challenges regarding bacteria' antibiotic resistance for empiric treatment and what influences do they have on patients' clinical course?
Methods: We analyzed in a 4-year retrospective study the medical records of 294 in-hospital patients with severe odontogenic infections. On a routine base bacteria were identified and susceptibility testing was performed. Length of stay in-hospital was evaluated regarding patients' age, beta-lactam allergy profile, affected sites and bacteria susceptibility to empiric antibiotics.
Results: Length of stay in-hospital was detected to be associated with affected space and penicillin allergy as well ($p < 0.05$). Isolates presented large amounts of aerobic gram-positive bacteria (64.2%), followed by facultative anaerobic bacteria (gram+/15.8%, gram−/12.7%). Tested ampicillin in combination with sulbactam (or without) and cephalosporins displayed high susceptibility rates, revealing distinguished results regarding clindamycin ($p < 0.05$). Co-trimoxazol and moxifloxacin showed high overall susceptibility rates (MOX: 94.7%, COTRIM: 92.6%).
Discussion: This study demonstrates ampicillin/sulbactam in addition to surgical intervention is a good standard in treatment of severe odontogenic neck infections. Cephalosporins seem to be a considerable option as well. If beta-lactam allergy is diagnosed co-trimoxazol and moxifloxacin represent relevant alternatives.
Conclusion: Age, allergic profile and bacteria' resistance patterns for empiric antibiotics have an influence on patients in-hospital stay. Ampicillin/sulbactam proves itself to be good for empiric antibiosis in severe odontogenic infections. Furthermore cephalosporins could be considered as another option in treatment. However moxifloxacin and co-trimoxazol deserves further investigation as empiric antibiosis in odontogenic infections if beta-lactam allergy is diagnosed.

1. Introduction

In the field of head and neck surgery, severe odontogenic infections remain potentially life-threatening events (Wang et al., 2003). Initially caused by pericoronitis of an emerging tooth, a cariogenic necrosis of the dental pulp, and subsequent infection of the root canal, odontogenic cysts or an infection of the periodontal tissues by bacteria of the subgingival microflora, these infections evolve to major purulent health risks (Dahlen, 2002; Boscolo-Rizzo and Da Mosto, 2009). Infections spreading in the facial planes through communicating lodges may endanger sensitive tissues such as the patient's orbita or brain (Al-Nawas and Maeurer, 2008; Azenha et al., 2012; Tavakoli et al., 2013). Likewise, a purulent fluid collection may travel the fascial layers deep into the neck (Daramola et al., 2009). This compromises the patient's health by secondary infection or compression of anatomical landmarks, such as the upper airways, major blood vessels, or the mediastinum

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(Garatea-Crelgo and Gay-Escoda, 1991; Biasotto et al., 2004; DeAngelis et al., 2014).

Infection expansion and tissue infection largely depend on the patient's immunological response (Lin et al., 2006; Lee et al., 2007; Tzermpos et al., 2013). Predisposing factors for severe progression of an odontogenic infection are deficiencies of immunological competence, such as human immunodeficiency virus positivity, long-term diabetes mellitus, chronic alcohol abuse, hepatitis and liver cirrhosis, systemic lupus erythematosus, and history of immunosuppression after transplant surgery (Peters et al., 1996; Whitesides et al., 2000; Seppanen et al., 2008; Sandner and Börgermann, 2011).

Patients with severe odontogenic abscesses benefit most from a biphasic treatment, incision, and drainage combined with intravenous antibiotic therapy (Wang et al., 2003; Islam et al., 2008; Walia et al., 2014). Additionally, immediate or secondary removal of the odontogenic focus is inevitable for sufficient therapy (Jundt and Gutta, 2012).

Commonly, intravenous antibiosis is administered using a peripherally inserted venous catheter (Islam et al., 2008), and penicillin derivatives are administered as the empirical drug of choice for odontogenic infections (e.g., Ampicillin plus sulbactam) (Rega et al., 2006). One in 10 patients report a history of a penicillin allergy; however, up to 90% of these patients are able to tolerate penicillin treatment, and consequently, they are falsely considered to be allergic to penicillin (Sogn et al., 1992; Gadde et al., 1993; American Academy of Allergy, 2010). Odontogenic infections are not specific, but usually involve a variety of different bacteria. The infections involve strictly anaerobic Gram-positive cocci and Gram-negative rods, along with facultative and microaerophilic streptococci that are implicated in purulent odontogenic infections (Stefanopoulos and Kolokotronis, 2004). Nevertheless, streptococci seem to be predominant in early stages of infection, corresponding to cellulitis and abscess formation. Streptococci species' susceptibility to β-lactam drugs, including penicillin V, ampicillin, and amoxicillin, largely remains; but an emerging resistance to erythromycin and clindamycin has been reported (Limeres et al., 2005). *Viridans streptococci* have been isolated in vast amounts from purulent odontogenic infections, representing a group of aerobic facultative anaerobic bacteria; likewise, *Prevotella* species (spp) have been frequently detected as anaerobic bacteria (Warnke et al., 2008). Additionally, in severe odontogenic head and neck infections, the involvement of *Fusobacterium* species and *Bacteroides fragilis* must be considered in therapy regimens (Boyanova et al., 2006).

The aim of this study was to evaluate the efficiency of frequently applied empiric antibiosis and to investigate alternatives in antibiotic treatment if needed.

2. Materials and methods

2.1. Patients

A 4-year retrospective study evaluated hospital records of 294 patients with severe odontogenic infections who received medical attention from the Department of Oral and Maxillofacial Plastic Surgery of the University Cologne, Germany. All patients in this study underwent extraoral incision and drainage under general anesthesia. They received intravenous antibiotics and underwent culture and sensitivity testing. Patients' clinical data were reviewed, including sex, age, medical record, involved fascial space, dental focus, bacteria identified, and antibiotic resistance from culture and sensitivity testing performed. All patients included in this study showed trismus or dysphagia, and at least minor respiratory problems due to upper airway compression.

2.2. Procedures

In the operating room, the patient's skin was disinfected with alcohol, an extraoral incision was made, and a swab was inserted into the abscess space; the swab was then retracted and immediately stored in culture medium for aerobic and anaerobic bacteria growth (Sarstedt AG & Co., Nümbrecht, Germany). Once bacteria were harvested, samples were transported to the University Clinic's Department for Microbiology within the first hour after surgery. Culturing of the bacteria started within 24 h after surgery. The testing for resistance was carried out on a routine basis by a trained specialist. Anaerobic bacteria were identified and separately tested. Susceptibility testing was performed according to the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). After testing, the results were reported to the institution's Department for Oral and Maxillofacial Plastic Surgery.

The standard antibiotic therapy consisted of ampicillin/sulbactam administered three times a day in a dose according to patient's weight (2 g < 70 kg < 3 g). Patients were asked if they had a penicillin allergy. If a patient confirmed a penicillin allergy or reported unspecified skin reactions in combination with earlier penicillin therapy, clindamycin (4.8 g/d administered in 3 doses) was administered instead. Children were treated likewise. They received lower daily doses according to their body weight, in such case a pediatrician was consulted as well.

For statistical analysis, the Shapiro–Wilk-test and χ^2 test was used. Descriptive analysis was performed as well.

3. Results

A total of 294 subjects (176 male, 59%, and 118 female, 41%) from 1 to 88 years of age were enrolled in this study. The patients' mean age was 41.1 (±1.17 standard deviation [SD]). Patients were divided into groups according to age (Fig. 1). The distribution was normal according to the Shapiro–Wilk-test ($p < 0.05$). Hospitalized patients were analyzed by their length of stay (LOS), the location of abscess, and microbial resistance regarding the different antibiotics.

Subjects were further sorted by the main affected fascial space regarding their medical report. If different fascial spaces were involved, the most purulent space was determined by the amount of drainage and selected for general diagnosis. Submandibular (n = 83, 28%) and perimandibular/buccal (n = 177, 60%) spaces were mostly affected, followed by the canine fossa (n = 16, 5.4%) or submental space (n = 11, 3.7%). The distribution of abscess locations is illustrated in Fig. 1. The affected site significantly correlated with patients' age in the groups ($p < 0.05$). For instance, canine fossa abscesses with severe clinical courses were seen mostly within the group of patients with first or mixed dentition (<16 years) (Fig. 2).

Of 294 patients, 12 (4.1%) had a confirmed penicillin allergy (Table 1). The majority (n = 234, 79.6%) reported being unsure whether they had a penicillin allergy, and 16.3% denied an allergy to penicillin based on previous experiences. Penicillin allergy was significantly associated with the patient's age, showing a maximum between ages 31 and 60 years.

The mean LOS was 7.2 (±3.1 SD) days. Age groups significantly correlated with LOS ($p < 0.05$) (Fig. 3). Patients in the first or mixed dentition group had their maximum LOS within the first 4 days; none of the 27 patients stayed longer than 10 days and one patient exceeded 7 days of hospitalization. Ten of 65 patients (15.4%) in the 41- to 50-year age group were hospitalized longer than 10 days; similarly, 10 of 29 patients (34.5%) stayed longer than 10 days in the hospital. Throughout all age groups, the maximum LOS was in 5–7 days (50.0%), followed by individuals staying 8–10 days (23.8%). LOS and affected spaces significantly correlated as well ($p < 0.05\%$)