Microbiological Aspects Concerning the Etiology of Acute Odontogenic Inflammatory Diseases in the Soft Tissues of the Head and Neck Region

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Abstract
Odontogenic purulent inflammatory diseases (OPIDs) make up about 20% of cases in the structure of general surgical pathology and are among the frequent diseases of the head and neck region with a high (10–40%) mortality rate. Insufficient information about the source state of acute odontogenic inflammation of the peri-mandibular soft tissues significantly reduces the effectiveness of diagnostic measures of OPID in head and neck region, as evidenced by almost 50% of the diagnostic error rate. Statistically, OPID in soft tissue of head and neck region most often occurs due to dissemination of pathogens of the necrotized pulp, periodontal pockets in periodontitis, or pericoronitis during the difficult eruption of retained teeth. Previously, the quantitative dominance (about 70%) of Staphylococcus spp. among the microorganisms isolated from the odontogenic foci of inflammation was determined. However, in recent years, with the expansion of microbiological diagnostic capabilities, the presence of non-fermenting Gram-negative bacteria and anaerobes with a significant proportional proportion of the total microbiota of OPID in soft tissue of head and neck region has been increasingly indicated. Recently, there has been a rapid acquisition of resistance of pathogens of odontogenic purulent inflammatory diseases of the maxillofacial region to various groups of antibiotics, which leads to ineffectiveness of their treatment and prompts the revision of existing protocols and treatment regimens in surgical dentistry.

Introduction
Odontogenic purulent inflammatory diseases (OPID) make up about 20% of cases in the structure of general surgical pathology and are among the frequent diseases of the maxillofacial region with a high (10–40%) mortality rate [1], [2]. Despite the rapid development of surgical dentistry, the past decade has seen an increase in the number of patients with OPID in maxillofacial region along with a significant aggravation of their course and treatment [3], [4]. They are characterized by a rapid aggressive course against the background of a sharp deterioration of the general condition of the patient with subsequent spread of inflammation from one anatomical part to another. In more than half of patients with OPID in maxillofacial region, there is a need for multistage surgical interventions, powerful complexes of antibiotic therapy, and often-resuscitative treatment [5]. The complex anatomical characteristics of the cicatrical spaces of maxillofacial region associated with each other cause the development of life-threatening complications: contact mediastinitis, cavernous sinus thrombosis, cerebral abscess, damage to ENT organs, sepsis, etc. This makes it evident that the issue of quality diagnosis of OPID can often go beyond the competence of the maxillofacial surgeon and require the involvement of allied professionals [1], [6], [7]. Along with this, insufficient information about the source state of acute odontogenic inflammation of the peri-mandibular soft tissues significantly reduces the effectiveness of diagnostic measures of OPID in maxillofacial region, as evidenced by almost 50% of the diagnostic error rate [1].

Undoubtedly, the increase in the number of patients with OPID in head and neck region is due to a number of factors, both on the part of patients and physicians, and a set of socioeconomic factors. It is natural that the decline in the quality of life of the
population of the country, the worsening of nutrition, the decline in material and living conditions leads to the deterioration of oral hygiene, the development of dental and mucous membrane diseases, the lack of routine sanitation, and untimely detection and treatment of chronic infection foci. In its turn, the irrational therapy of the causal teeth with limited use of paraclinical diagnostic methods and control of periapical tissues during endodontic treatment, the prescription of drug therapy when surgical intervention is necessary or its delaying is the dominant factor in the further development of OPID in MFR [1], [8], [9], [10], [11].

Current Understanding of the Etiology of OPID in Soft Tissue of Head and Neck Region

It is known that the cause of OPID in soft tissue of head and neck region can be a number of pathological processes in the oral cavity through the spread of microorganisms through the destroyed tooth tissue or marginal periodontium into the underlying tissues, as well as during surgical manipulations and trauma [5], [12].

Statistically, OPID in soft tissue of head and neck region most often occurs due to dissemination of pathogens of the necrotized pulp, periodontal pockets in periodontitis, or pericoronitis during the difficult eruption of retained teeth [12], [13]. Previously, the authors identified the contact pathway (by extension) of infection accumulation as the fundamental in the development of OPID in soft tissues. At the same time, the pathway of local spread can be predicted depending on the mutual location of the attachment points of the adjacent muscles and the causal tooth [12]. However, on the time being, the timing of these diseases indicates the prevalence of lympho- and hematogenous pathways of spread. Moreover, the local blood flow plays a key role in this [5], [14], [15]. In fact, abundant blood supply to the head and neck is characterized by a powerful network of anastomoses, potentially playing a role in the spread of infection [1].

In addition to the unique anotomopographic features of head and neck region, the key factor in the development of odontogenic purulent soft-tissue infection of the head and neck is the pathogenic and opportunistic oral microbiota [16]. According to the data, the oral cavity is a powerful biotope inhabited by about 700 species of microorganisms that form a local normicrobiocenosis and perform a number of important functions [17]. It is the resident microbiota that provides colonization resistance in the oral cavity, preventing colonization of mucosal and hard dental tissues from pathogenic transient flora [18]. However, along with this, when both cellular and humoral parts of immunity are reduced, representatives of normobiotota can serve as a “reservoir” of odontogenic infection, thus acquiring pathogenic properties [16], [19].

The literature recently traced the changes in the qualitative composition of the microbiota of OPID in soft tissue, depending on the year of publication and the microbiological research methods used by the authors [20]. Previously, the quantitative dominance (about 70%) of Staphylococcus spp. among the microorganisms isolated from the odontogenic foci of inflammation was determined. However, in recent years, with the expansion of microbiological diagnostic capabilities, the presence of non-fermenting Gram-negative bacteria and anaerobes with a significant proportional proportion of the total microbiota of OPID in soft tissue of head and neck region has been increasingly indicated [20], [21], [22].

At present, the frequency of isolation of staphylococci as a causative agent of inflammatory processes does not exceed 30%, and this figure for Staphylococcus aureus varies from 0.7 to 15.0%. The fact, that the so-called coagulazonegative staphylococci (predominantly Staphylococcus epidermidis) are found in the microbiota of OPID in soft tissue of head and neck region significantly more frequently, is interesting [23], [24]. This microorganism is known to be a permanent representative of skin and mucous membrane norms. It is the ability of S. epidermidis to form biofilms on various surfaces, combined with its widespread acquisition of antibiotic resistance that contributes to its increased role in the development of infectious and inflammatory diseases of soft tissues of various parts of the human body, including head and neck region [25].

It should be noted that, up to now, scientists are divided in their opinions on the dominant role of certain pathogens in the development of OPID in head and neck region. Therefore, recent studies by German scientists indicate a significant prevalence of Streptococcus spp. in the etiological structure of odontogenic processes, and about 30% of cases are caused by the so-called alpha-hemolytic streptococci viridans group [26], [27]. A similar trend was traced by scientists from India, according to whose data streptococci, Staphylococcus aureus and Enterococcus faecalis were most often isolated from foci of purulent odontogenic infections in the head and neck region [28].

At the same time, recent publications of researchers at Justus-Liebig University Giessen note a significant dominance of anaerobic microorganisms in the pus microbiota in the OPID of head and neck region, while the Streptococcus genus is found only in association, playing an auxiliary role. The genera Prevotella, Fusobacterium, Porphyromonas, and Parvimonas are the most numerous among anaerobic bacteria that play a key role in the development of odontogenic infectious diseases [29]. Analyzing the research data of recent years, it can be assumed that both facultatively anaerobic and anaerobic microorganisms are likely...
to be the dominant pathogens of OPID in soft tissues of head and neck region in the alveolar cavity of a patient [30].

*Klebsiella pneumoniae, Eikenella corrodens, Pseudomonas aeruginosa, Acinetobacter baumanii, Candida* spp., and *Actinomyces* are quite often experimentally confirmed the therapy of oral and palatal diseases, which prioritize the monotherapy as a first-line antibiotic. At the same time, and the United States recommend the use of penicillin for acute odontogenic diseases in the United Kingdom [31]. This gave the reason to assume the involvement of chemotherapeutic drugs. This often leads to a number of negative consequences, such as hypersensitivity, dysbiosis, and hematological disorders, but more often, contributes to the development of antibiotic resistance among microorganisms [32], [34], [35]. This indicates the importance of continuous monitoring of antibiotic sensitivity of the dominant OPID pathogens, because the situation is constantly changing.

Recommendations for the therapeutic use of antibiotics in dental practice vary widely around the world. For example, protocols for the treatment of acute odontogenic diseases in the United Kingdom and the United States recommend the use of penicillin monotherapy as a first-line antibiotic. At the same time, in 2019, Australia published updated guidelines for the therapy of oral and palatal diseases, which prioritize the use of a broader spectrum of antibacterial therapy: the combination of penicillin with metronidazole [36].

Analyzing recent studies, it has been established that the most widely used antibiotics in dental practice are penicillin, amoxicillin, followed by amoxicillin clavunate, clindamycin, metronidazole, and azithromycin [34]. However, data from studies at the State University of New York Medical School demonstrate the adaptation of the dominant pathogens of odontogenic infections to these antibiotics. About 10% of the *Staphylococcus* spp. Strains, they obtained show resistance to clindamycin, oxacillin, and penicillin. In turn, some *Streptococcus* spp. isolated from foci of odontogenic infections was resistant to clindamycin in 33.3% of cases [37]. The situation in Europe is no different: German scientists at Justus Liebig University Giessen have almost exactly repeated the results of American researchers. It was found that streptococci were resistant to penicillin in 11% and amoxicillin in 8% of cases, with resistance to metronidazole reaching 100%. However, according to studies by German scientists, *Staphylococcus* genus resistance to clindamycin exceeded 33% [29], [38].

The fact of rapid acquisition of resistance of microorganisms causing OPID in soft tissues of head and neck region to commonly used antibiotics in dentistry is also confirmed by the data obtained in Japan. A very low sensitivity of major oral *Streptococcus* species to penicillin, a first-line drug in the treatment of odontogenic infections has been found [39]. This study demonstrates low efficacy to β-lactams, macrolides, quinolones, and clindamycin among anaerobic microbiota in OPID of head and neck region [39].

Tomas et al. experimentally confirmed the acquisition of resistance among enterococci colonizing the oral cavity in normal and infectious conditions to vancomycin [40]. Moreover, a significant violation of oral mucosal colonization resistance was revealed when this antibiotic was administered orally [40], [41], [42]. In turn, this contributes to the development of infections caused by strains of *Clostridium difficile* in 20–30% of patients in the United States, whose treatment included vancomycin, metronidazole, or their combination [40].

“Frontiers in Microbiology” recently published a comparison of the level of resistance of microorganisms isolated from foci of odontogenic head and neck region infections and from patients with general surgical pathology. Thus, OPID pathogens exceed pathogens of other nosologies in resistance to macrolides, clindamycin, and cephalosporins of the II generation by almost 10%. According to the results presented, the sensitivity of dominant microorganisms in infectious odontogenic diseases to penicillins, III generation cephalosporins, and fluoroquinolones remains lower compared to the level of pathogen sensitivity in general surgery. However, the group of researchers who took part in this study notes disappointing trends: although the resistance of microbiota in OPID of head and neck
region to certain groups of antibiotics remains lower to date, the rate of its development indicates a possible change in the near future [26].

Conclusions

Odontogenic purulent inflammatory diseases of the head and neck region comprise about 20% of cases in the structure of the general surgical pathology; pathogenic and opportunistic microorganisms play an important role in their etiology. The most frequent causative agents of odontogenic infections are *Staphylococcus* spp., *Streptococcus* spp., *Enterococcus* spp., *Prevotella*, *Fusobacterium*, *Porphyromonas*, *Klebsiella pneumonia*, *Eikenella corrodens*, *Pseudomonas aeruginosa*, *Acinetobacter baumanii*, *Candida* spp., *Actinomycetes*, etc.

Recently, there has been a rapid acquisition of resistance of pathogens of odontogenic purulent inflammatory diseases of the head and neck region to various groups of antibiotics, which leads to ineffectiveness of their treatment and prompts the revision of existing protocols and treatment regimens in surgical dentistry.

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