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# Identification of Pathogenic Microflora and Its Sensitivity to Antibiotics in Cases of the Odontogenic Purulent Periostitis and Abscesses in the Oral Cavity

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**Abstract:** Odontogenic infections are the most common infectious and inflammatory diseases of the maxillofacial area and problem of the causative pathogen identification is an actual task, part of a permanent process of updating and modernization of treatment and diagnostic protocols and standards. In presented study a purulent exudate from 13 patients with acute purulent odontogenic intraoral lesions was studied by bacteriological method with detection of sensitivity to antibacterial agents. Bacteriological studies showed that genus *Streptococcus* predominated in 69.23% cases. Pathogenic microorganisms in clinically significant concentrations ($10^5$ per 1 ml and above) (*Streptococcus* and *Staphylococcus*) were resistant to Tetracycline and Doxycycline, had moderate sensitivity to macrolides in 22.22% and resistance in 77.78%. Amoxicillin/clavulanate caused effective growth retardation in 22.22% cases and moderate delay – in 77.78% without cases of resistance. Sensitivity to cephalosporins was detected in 50.00% cases, moderate sensitivity – in 38.89%, resistance – in 11.11%. Fluoroquinolones were the most effective – sensitivity in 72.22% cases, moderate sensitivity – in 22.22%, resistance – in 5.56%. The most effective fluoroquinolones were Moxifloxacin and Ciprofloxacin.

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The highest resistance to antifungal agents was shown by genus *Candida*, antifungal susceptibility was observed only in 20.00% cases. The microbiota of purulent odontogenic inflammation in the oral cavity was identified in clinically significant concentrations in only 61.54% cases with predominance of *Streptococcus*. The most effective antibacterial agents for odontogenic purulent process may be considered among cephalosporins and fluoroquinolones. There is a need to repeat similar studies in other regions of Ukraine and at other times of the year.

## Introduction

Odontogenic infections are the most common infectious diseases of the maxillofacial area affecting the human population for a long time. Their nosological forms include a whole number of diseases ranging from periapical abscesses of the jaws to phlegmons of the deep cervical areas and mediastinitis. The success of treatment of abovementioned diseases depends on the timeliness of care (decompression of foci of bone inflammation, tooth extraction and dissection the foci of purulent inflammation in soft tissues), elimination of etiological factors and administration of a rational antibacterial chemotherapy (Connors et al., 2017; Dave et al., 2021). This problem continues to be studied at many scientific and clinical centers around the world and to date a significant amount of scientific and medical information on infectious and inflammatory complications of dental diseases has been collected (Schmidt et al., 2021).

## Oral microbiome and odontogenic inflammation of maxillofacial area

The rapid spread of odontogenic purulent infection in the maxillofacial area tissues is determined by a range of factors – both anatomical (close location of large blood vessels, venous plexuses and lymphatic ducts) and immunological response, infectious agent's virulence and its resistance to antibiotics (Heim et al., 2017). Even simple damage of the oral mucosa may be a gateway for the penetration of certain genera of bacteria – *Actinomyces*, *Streptococcus mitis*, *Streptococcus mutans* and *Streptococcus sanguinis* (they normally colonize a tooth enamel), *Streptococcus salivarius* and *Veillonella spp.* (they often inhabit oral mucosa and tongue surface), *Porphyromonas*, *Prevotella* and *Spirochetes* colonize gum surface and gingival sulcus.

The problem of pathogen's identification is part of a permanent process of updating and modernization of treatment and diagnostic protocols and standards for the treatment of infectious and inflammatory diseases of the maxillofacial area. Nowadays, different methods of pathogenic microorganisms' identification may be used (Zhang et al., 2020; Böttger et al., 2021b).

The study of Böttger et al. (2021a) showed that odontogenic abscesses of the maxillofacial area are mainly caused by bacteria involved in the oral microbiome. When using the standard cultural method of pathogen's identification, a causative agent may be identified among 85.50% of patients. Associations of microorganisms were determined in 96.00% of cases, monoculture – 4.00%. Moreover, the maximum information may be obtained by using molecular genetic methods of identification, especially for anaerobes. In the cases of standard cultivation only the families *Streptococcus*, *Staphylococcus*, and *Prevotella spp*. were recognized. According to the next work by Böttger et al. (2021b), the oral microbiome among patients with odontogenic maxillofacial area abscesses is quite diverse, even compared to healthy patients. Moreover, healthy people often have enough amount bacteria in the mouth with germs with high pathogenic potential. Mostly such infections were caused by anaerobic microorganisms, aerobes and facultative anaerobes play a smaller role. *Prevotella*, *Porphyromonas* and *Fusobacterium* combined with *Veillonella*, *Parvimonas*, *Streptococcus*, *Mogibacterium* and *Filifactor* were the most commonly identified in the purulent exudate. Pathogenic microorganisms of purulent exudate had a higher pathogenic potential compared to those obtained from saliva. Today, molecular genetic diagnosis has become a more accurate method of identifying pathogens in purulent inflammation given the predominance of anaerobic flora in the etiology of such diseases.

As shown in the work of Kang and Kim (2019), odontogenic inflammatory diseases of the maxillofacial area are also most often caused by bacteria from the residents of the oral cavity. Among such strains are more common *Streptococci* – *S. anginosus*, *S. viridans* and others. The data of Plum et al. (2018) showed that in purulent exudate the different microbial associations were identified in 60.00% cases and monocultures in 34.00%. Among the identified pathogens, the most common were α-hemolytic streptococci – *Streptococcus milleri* (32.10%), *Prevotella* (16.80%), and coagulase-negative staphylococci (14.50%). *Candida* and *Morganella spp.* were more common among pediatric patients. Sweeney et al. (2004) showed that the results of studies of the microbiome of purulent foci emphasize regional, age and geographical differences in the microbiological profile of inflammation, susceptibility of pathogenic microorganisms to antibacterial and antimicrobial agents, which affects the development of national and regional protocols for medical care.

The results of studies performed by Zhang et al. (2020) showed that purulent exudate in periapical abscesses revealed the presence of 125 species of bacteria (mostly anaerobes) among which were *Firmicutes*, *Proteobacteria*, *Fusobacteria*, *Bacteroides*, *Actinobacteria*, *Tenericutes*, *Deinococcus-Thermus* and *Spirochaetes*. The most dominant species were *Streptococcus* (13.30%), *Fusobacterium* (11.80%), *Parvimonas* (7.80%), *Prevotella* (6.70%), *Sphingomonas* (5.80%) and *Hafnia* (5.20%). Among the *Fusobacteriae* the most common was *Fusobacterium nucleatum*.

Studies of Turchina and Pinelis (2016) were performed on purulent exudate from abscesses and phlegmons of maxillofacial area. The results showed that patients were more likely to have hemolytic and non-hemolytic *Streptococcus*, *Staphylococcus aureus*, Gram-negative bacilli, bacteroides, diphtheroides, moderately pathogenic *Staphylococcus*, *Micrococci*, *Peptostreptococcus* and *Candida*. According to literature data the microbial landscape of purulent wounds of patients-residents of different inhabitant areas may differ significantly. Hemolytic *Streptococci* and bacilli or hemolytic *Streptococci* and *Staphylococcus aureus* were more common among urban residents. The microbial flora of rural residents was inferior to urban residents in the number of pathogenic strains. Analysis of microbiota species revealed that purulent secretions from wounds were dominated by pathogenic *streptococci* (α- and β-haemolytic) which had hemolytic activity and *staphylococci* (in particular, *Staphylococcus aureus*) capable of coagulating citrate plasma, also they had anti-lysozyme activity. The study found that leading associations of bacteria include *Staphylococci*, pyogenic *Streptococci*, *Peptostreptococci*, *micrococci*, *Veilonella*, diphtheroides, bacilli, bacteroides, *Escherichia coli* and *Candida*. The study found 100.00% susceptibility of all microorganisms isolated from periostitis (odontogenic subperiosteal abscesses) to cefotaxime, moderate susceptibility of most microorganisms to ampicillin, gentamicin and rifampicin and no susceptibility of most presented microorganisms to Lincomycin and Tetracycline.

According to the analysis of the specialized literature, early detection of pathogens of purulent inflammation and determination of their properties are necessary measures for the successful functioning of health care systems in many countries. This is the basis of infection control and monitoring of the evolution of human pathogens. The constant use of antibacterial agents in outpatient dental practice makes a small contribution to deepening the problem of antibiotic resistance in health care. According to Kabanova (2017), the prevalence of highly pathogenic and resistant to antibacterial drugs microorganisms leads to the development of severe inflammatory processes in maxillofacial area characterized by severe intoxication and impaired immune status. Insufficient effectiveness of treatment of these complications partially may be explained by the presence among microorganisms of some effective protection mechanisms against external damaging factors.

Widespread use of antiseptics and disinfectants in health care facilities, specialized laboratories of biotechnology and food production, as well as in everyday life, provides a pronounced selective effect on populations of microorganisms. This process promotes the selection of resistant strains among microorganisms and requires new tools and approaches to save an antibiotics' curative effect (Kryvtsova et al., 2018; Ivanova et al., 2019). Microorganism resistance to antimicrobial substances may be natural or acquired. The first type of resistance is characterized by the absence of target microorganisms for the action of antimicrobial drugs or its unavailability. Acquired resistance is due to the effects of antimicrobial drugs on microorganisms, especially in low concentrations. In recent decades, the study of the mechanisms of bacterial survival had an especial importance. The widespread of antibiotic resistance among infectious agents poses a serious threat to the health care systems of most countries. The next statements should be minded: clinical strains of *streptococci* are the most commonly identified bacteria resistant to antibiotics, especially to Penicillin and Clindamycin (Heim et al., 2021).

According to Tent et al. (2019), from 7.00 to 10.00% cases of antibiotics usage in clinical practice accounted for cases of infectious lesions of the head and neck. Since the introduction of the first antibiotics into clinical practice in the human population the strains of pathogenic microorganisms that are not sensitive to antibacterial agents have begun to appear and circulate. That is explained by the evolution of microorganisms (genetic mutations, exchange of genetic material, changes in gene expression and metabolic adaptation).

As shown by Sweeney et al. (2004), today, aminopenicillins are one of the most commonly prescribed groups of antibacterial drugs in dental practice. Since the mid-1980s, strains of beta-lactamase-positive pathogenic and opportunistic bacteria that are resistant to semisynthetic penicillins have been periodically isolated. Although beta-lactamase production is not a characteristic of *streptococci*. Some strains of *Streptococcus salivarius*, *Streptococcus oralis* and *Streptococcus mitis* (except *Streptococcus mutans*) have been shown to be resistant. It has been shown that resistance to penicillin antibiotics may be transmitted between bacteria found in the oral cavity – especially between *S. pneumoniae* and other α-hemolytic *streptococci*. Resistance of oral bacteria to tetracyclines is a new phenomenon, especially for *Streptococci*, and this quality is encoded by a mosaic of 27 *tet-* genes. Along with penicillins, α-hemolytic *Streptococci* may have a high resistance to cephalosporins, especially first- and second-generation cephalosporins (especially Cefotaxime). High resistance to cephalosporins was determined among *Enterococcus spp*. obtained from root canals. Bacterial resistance to Erythromycin has been linked to the acquisition of one of the 21 *erm* genes or by inactivation of the substance by enzymes encoded by the *mph-* and *efflux-* genes (among *Staphylococci*). Resistance to Erythromycin in 38.50% cases was described for α-hemolytic *streptococci* of the oral cavity of healthy patients and in 33.50% cases to Clarithromycin. About 50.00% of oral *streptococci* were resistant both to erythromycin and clarithromycin. This situation is considered to be a consequence of the widespread use of macrolides in the treatment of inflammatory periodontal lesions in the world. The problem of increased resistance of microorganisms to the most commonly used antibiotics affects the effectiveness of treatment of major dental diseases (Kryvtsova and Kostenko, 2020).

Thus, according to Hatilo et al. (2016), cases of ineffective drug treatment of acute and exacerbated chronic apical periodontitis may be explained due to the resistance of odontogenic microflora (*Streptococci* and *Staphylococci*) to the antibiotic used and the state of hypersensitivity to that germs. Therefore, measures to prevent complications in the treatment of acute apical periodontitis with antibiotics should include the use of those antibacterial agents to which the odontogenic microbial flora is most sensitive, in parallel with the administration of antiallergic medicines.

Antibiotic resistance of pathogenic microorganisms that cause odontogenic abscesses of the maxillofacial area has distinct regional and age differences. Although protocols for the treatment of odontogenic abscesses and phlegmon of the maxillofacial area contain mostly recommendations for the use of penicillin antibiotics, it seems more rational to use third-generation cephalosporins, Clindamycin or fluoroquinolones (Kang and Kim, 2019).

From the work of Sobottka et al. (2012) it is seen that in odontogenic abscesses of the maxillofacial area the main etiological factors may be considered the group of *S. anginosus* and hemolytic *Streptococci*, and in inflammatory infiltrates of odontogenic origin the group of *S. mitis* and *Neisseria spp*. Also, the identified strains were found to be highly sensitive to Moxifloxacin.

According to the results of studies performed by Kabanova (2008), for patients with periostitis of the jaws in dental clinics, including stepwise antibiotic therapy, may be recommended the penicillins (Amoxicillin), fluoroquinolones (Ofloxacin, Cyprofloxacin, Pefloxacin), lincosamides (Clindasole). Penicillins (Amoxicillin), fluoroquinolones (Ciprofloxacin, Ofloxacin, Pefloxacin) and sulfanilamides (Co-trimaxosol) are used for outpatient treatment of maxillofacial lymphadenitis. Fluoroquinolones Ofloxacin, Norfloxacin and Ciprofloxacin may be used for the treatment of maxillofacial furuncules at outpatient clinics.

Therefore, odontogenic infectious-inflammatory diseases of the maxillofacial area are the most common complications of dental caries which may occur in clinical practice. Problem may develop due to untimely dental treatment, the lack of a system of medical examination of dental patients and changes in the pathogenic properties of the causative agents of odontogenic inflammatory diseases. Control of etiological agents and their properties, especially the sensitivity of pathogenic microorganisms to antibacterial and antimicrobial agents is an urgent task of the health care system which has become the purpose of this study partly.

The aim of this study was to determine the microbiota of the purulent inflammation focus of odontogenic origin using a bacteriological method followed by a study of the sensitivity of detected pathogenic microorganisms to antibacterial agents.

## Material and Methods

The study group included 13 patients who applied for emergency care in the surgical ward of the municipal city dental clinic from March till May of 2021. Patients were aged from 26 to 82 years with average age of 43.54 ± 13.66 (median = 42.00) years. Among the patients there were 8 women (61.54%) and 5 men (38.46%). 11 cases of acute purulent odontogenic periostitis of the jaw (84.62%) and one case of odontogenic abscess of the palate and purulent radicular cyst of the jaw (7.69%, respectively) were identified. All patients were treated with the next standard protocol – conductive and infiltrative local anesthesia with articaine hydrochloride, removal of the causative tooth, hemostasis, dissection and emptying a zone of purulent inflammation, drainage of purulent wound (if possible) for 3–5 days with rinsing with antiseptic solutions, prescribing of general and local anti-inflammatory therapy. Anti-inflammatory therapy included the empirical use of wide-spectrum antibacterial agents, histamine receptor blockers (antiallergic), non-steroid anti-inflammatory drugs (non-selective cyclooxygenase-2 blockers seu pain-killers), local – mouth washing with light alkaline-salt water solutions. Patients were observed daily – until the removal of the draining latex tape. During each examination revision of the purulent wound was performed together with its rinsing (using a solution of decamethoxin or chlorhexidine bigluconate). All patients reported an improvement in general condition from the second day of treatment, while maintaining a slight asymmetry of the face, resulting from swelling of soft tissues around the affected area.

The samples of the purulent exudate were obtained during dissection of abscess (or accidental damage of its capsule). The samples were placed in a sterile transport system (plastic tube with AMIES gel and applicator for biological fluids). All tubes were transported to the bacteriological laboratory within 24 hours without freezing and over-heating. At the laboratory a passage of the material was performed on the different nutrient media: "Sabouraund Dextrose Agar" ("HiMedia") for the cultivation of microscopic fungi of the genus *Candida*; for hemolytic microflora, in particular bacteria of the genus *Streptococcus* and *Neisseria* – bloody agar, *Enterobacteriaceae* – medium Endo and Ploskirev's agar ("HiMedia"), bacterias of the genus *Staphylococcus* were cultivated on "Mannitol Salt Agar" ("Biolif-Italia") bacteria of the genus *Enterococcus* – on "Bile Esculin Agar" ("Biolif-Italia"). Pure culture of microorganisms was isolated by the method of sector seeding by Gold. Identification of microorganisms was performed due to the morphological, tinctorial, cultural and biochemical properties of bacteria using "ENTEROtest 24", "STREPTOtest 16" and "STAPHYLOtest 16" produced by "Erba Lachema" (Czech Republic).

Susceptibility to antibacterial agents was determined using the method of discs due to the diameter of the growth retardation of the culture on a nutrient medium. Susceptibility was determined to the following antibacterial agents – Doxycycline, Tetracycline, Erythromycin, Azithromycin, Amoxicillin/clavulanate, Ceftriaxone, Cefuroxime, Ciprofloxacin, Norfloxacin, Moxifloxacin and Ofloxacin ("HiMedia"). Itraconazole, Fluconazole, Ketoconazole and Nystatin were selected as antifungals. All measurements were performed three times; in the intermediate spreadsheets the average value was entered. The statistical analysis was performed in the software package Microsoft Excel 2016. All stages of bacteriological studies were performed at the bacteriological laboratory of the Department of Genetics, Plant Physiology and Microbiology, Faculty of Biology, Uzhhorod National University, Uzhhorod, Ukraine (Head of bacteriological laboratory – Professor Maryna Kryvtsova, DrBiolSc.).

## Results

Bacteriological studies showed that from the vast majority of patients a monoculture of pathogenic microorganisms was cultivated – 7 out of 13 cases. The following microorganisms were identified in samples of purulent exudate obtained from patients: *Streptococcus agalactiae*, *Streptococcus viridans*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus faecium*, *Enterococcus faecalis*, *Acinetobacter spp.* and *Candida albicans*.

Among the identified genera of microorganisms, the genus of *Streptococcus* (*S. agalactiae*, *S. viridans*, *S. pyogenes*, *S. pneumoniae*) predominated. Such bacteria were detected in 69.23% cases; the most common was *S. agalacticae* – 30.77%, *S. viridans* and *S. pneumoniae* were found in 15.39% cases each. Bacteria of the genus *Enterococcus* were detected in three cases, which was 23.08% of the total. In one case, a monoculture of the genus *Enterococcus* was detected – 15.39% of the total number of patients – one case of *E. faecalis* and *E. faecium*.

Bacteria of the genus *Staphylococcus* were identified in two cases out of thirteen – 15.39% of the total. In both cases, the culture was defined in the association. In one case *S. aureus* was detected and in another – *S. epidermidis* (which can be considered a representative of the transient microflora, not characteristic of the oral microbiota).

The genus *Acinetobacter* was identified in one case (7.69%) in the association, no further species identification was obtained (Figure 1).

In five cases (38.46%) associations of microorganisms were found that did not recur:

1) *S. viridans* and *S. aureus*
2) *S. agalactiae* and *S. epidermidis*
3) *S. viridans* and *C. albicans*
4) *E. faecalis* and *C. albicans*
5) *Acinetobacter spp.* and *C. albicans*

In the most common association of microorganisms *C. albicans* was presented (three cases out of five).

Analysis of the amount of colony-forming units (CFU) in 1 ml of the isolated bacteria showed that pathogenic microorganisms in the clinically significant

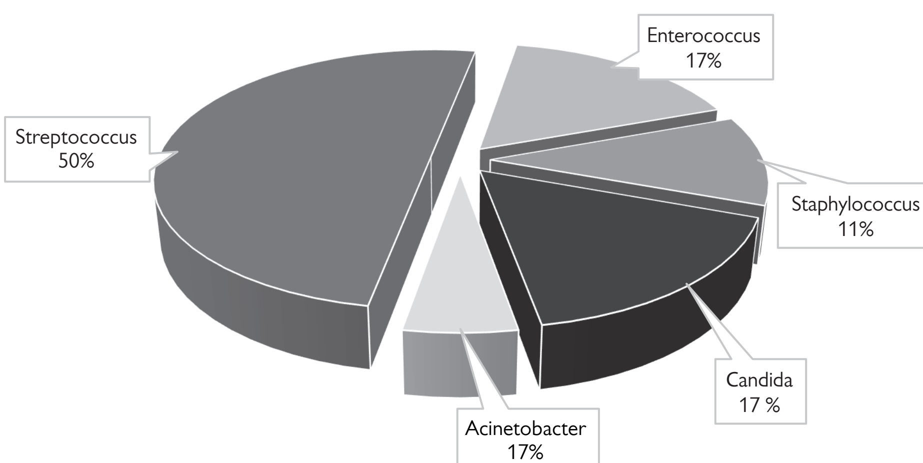


*Figure 1 – Representation of detected microorganisms genuses.*

**Table 1 – Identified microorganisms with the highest resistance to antibacterial agents**

| Zone of growth retardation of the culture around the disc with the antibiotic, mm | Microorganism | |
|---|---|---|
| | *Enterococcus faecalis* | *Acinetobacter spp.* |
| Ofloxacin | 8.00 ± 0.15 | 0.00 |
| Moxifloxacin | 11.00 ± 0.10 | 8.00 ± 0.15 |
| Norfloxacin | 0.00 | 0.00 |
| Ciprofloxacin | 10.00 ± 0.12 | 0.00 |
| Cefuroxime | 0.00 | 0.00 |
| Ceftriaxone | 0.00 | 0.00 |
| Amoxicillin/clavulanate | 0.00 | 0.00 |
| Azithromycin | 0.00 | 0.00 |
| Erythromycin | 0.00 | 0.00 |
| Tetracycline | 0.00 | 0.00 |
| Doxycycline | 0.00 | 0.00 |

concentrations (CFU in the order of $10^5$ per 1 ml and above) were found in 8 cases – 61.54% of the total. In such cases, the predominance of the genus *Streptococcus* was observed – in 8 of 13 (61.54%), including one case of association with *S. aureus* ($2.1\times10^5$ CFU/ml), which was 7.69% of the total number of cases. All cases of detection bacteria of the genus *Enterococcus* were marked by clinically insignificant concentrations of microorganisms. Fungi of the *Candida* genus were also found in associations and in clinically insignificant concentrations ($10^2$–$10^4$ CFU/ml).

The analysis of the sensitivity of isolated microorganisms' cultures to antibacterial agents revealed that the most resistant bacteria were presented in two clinical cases, they were isolated in clinically insignificant concentrations. *E. faecalis* and *Acinetobacter* were resistant to the whole set of antibacterial agents in this study (Table 1).

Analysis of the level of growth retardation of isolated bacterial colonies by groups of antibiotics showed that the use of medicines from the tetracyclines group (Tetracycline and Doxycycline) was ineffective – all detected bacteria were resistant. The results of the macrolide antibiotics (Erythromycin and Azithromycin) usage were also questionable. Only in 3.57% cases this group was effective, in 14.30% the bacteria were moderately sensitive and in 85.71% the resistance of isolates was determined. Only the one culture of *E. faecium* was sensitive to Azithromycin. The cultures of isolated bacteria were sensitive to semi-synthetic penicillins (Amoxicillin/clavulanate) in 28.57% cases, moderately sensitive – in 57.14% cases and resistant – in 14.29% cases. The cephalosporines group caused an effective growth retardation of microorganisms in 42.86% cases, in 35.71% cases there was a moderate growth retardation, and in 25.00% the resistance was determined. The group of fluoroquinolones was the most effective – effective growth retardation of

**Table 2 – Sensitivity of all isolated bacterial isolates to antibiotics, % of cases**

| Group of antibacterial agents | Sensitive | Moderately sensitive | Resistant |
|---|---|---|---|
| Tetracyclines | 0.00 | 0.00 | 100.00 |
| Macrolides | 3.57 | 14.29 | 85.71 |
| Semi-synthetic penicillins | 28.57 | 57.14 | 14.29 |
| Cephalosporins | 42.86 | 35.71 | 25.00 |
| Fluoroquinolones | 53.57 | 21.43 | 25.00 |

**Table 3 – Sensitivity of isolated bacteria of the genus *Streptococcus* to antibiotics, % of cases**

| Group of antibacterial agents | Sensitive | Moderately sensitive | Resistant |
|---|---|---|---|
| Tetracyclines | 0.00 | 0.00 | 100.00 |
| Macrolides | 0.00 | 22.22 | 77.78 |
| Semi-synthetic penicillins | 33.33 | 66.67 | 0.00 |
| Cephalosporins | 38.89 | 50.00 | 11.11 |
| Fluoroquinolones | 66.67 | 22.22 | 11.11 |

microorganisms was found in 53.57% cases; moderate effect – in 21.43% cases and resistance was found in 25.00% cases (Table 2).

Given that the most common pathogenic bacteria isolated from purulent exudate belonged to the genus *Streptococcu*s the results of determining the sensitivity to antibacterial agents for this subgroup of microorganisms were calculated separately. It was found that the group of tetracyclines does not affect the growth of isolated *Streptococci* – there was 100.00% resistance of cultures. Macrolides caused moderate growth retardation in 22.22% cases and resistance was observed in 77.78% cases. No sensitive bacteria were isolated. Amoxicillin/clavulanate caused effective growth retardation in 33.33% cases, in 66.67% moderate growth retardation was observed, but no resistant isolates were detected. Higher sensitivity to cephalosporines was observed – in 38.89% cases sensitivity was determined, in 50.00% there was moderate sensitivity and in 11.11% – resistance. The medicine for parenteral administration (Ceftriaxone) was more effective than oral Cefuroxime. To Ceftriaxone microorganisms were sensitive in 55.56% cases, moderately sensitive – in 33.33% cases and resistant – in 11.11%. Fluoroquinolones were the most effective in influencing on the genus *Streptococcus*. Sensitivity to fluoroquinolones was determined in 66.67% cases, moderate sensitivity – in 22.22% cases and resistance – in 11.11% cases. The highest sensitivity among the isolated bacteria was observed to Moxifloxacin (88.89% cases and no resistant strains

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were detected) and to Ciprofloxacin (77.78% cases and also without the resistant microorganisms). Ofloxacin was found to be the least effective – the amount of sensitive, moderate sensitive and resistant cultures divided equally into three parts (Table 3).

Analysis of properties of the group of pathogenic microorganisms isolated in clinically significant concentrations (CFU of $10^5$ per 1 ml and above) which included bacteria of *Streptococcus* and *Staphylococcus*, showed strengthening of previously identified trends in determining the sensitivity of cultures to antibacterial agents. Thus, all isolated microorganisms were resistant to the group of tetracyclines (Tetracycline and Doxycycline). Only moderate sensitivity to macrolides was determined in 22.22% cases, and resistance in 77.78%. Semi-synthetic penicillins

**Table 4 – Sensitivity of isolated pathogenic bacteria in clinically significant concentrations to antibacterial agent's groups, % of cases**

| Group of antibacterial agents | Sensitive | Moderately sensitive | Resistant |
|---|---|---|---|
| Tetracyclines | 0.00 | 0.00 | 100.00 |
| Macrolides | 0.00 | 22.22 | 77.78 |
| Semi-synthetic penicillins | 22.22 | 77.78 | 0.00 |
| Cephalosporins | 50.00 | 38.89 | 11.11 |
| Fluoroquinolones | 72.22 | 22.22 | 5.56 |

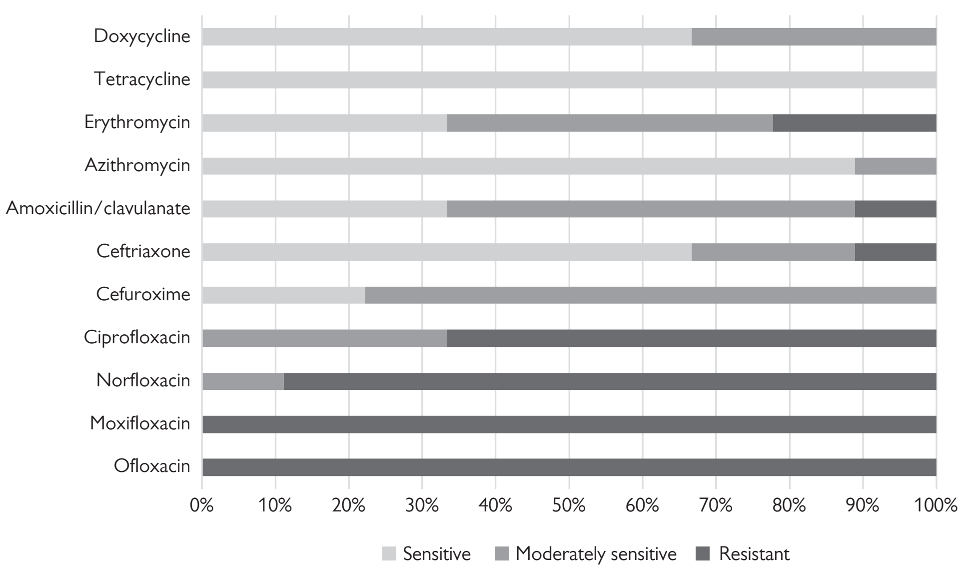


*Figure 2 – Sensitivity of pathogenic microorganisms isolated in clinically significant concentrations to antibacterial agents.*

**Table 5 – Sensitivity of isolated pathogenic bacteria in clinically significant concentrations to Cephalosporins and Fluoroquinolones, % of cases**

| Antibacterial agents | Sensitive | Moderately sensitive | Resistant |
|---|---|---|---|
| Ceftriaxone | 66.67 | 22.22 | 11.11 |
| Cefuroxime | 33.33 | 55.56 | 11.11 |
| Ciprofloxacin | 88.89 | 11.11 | 0.00 |
| Norfloxacin | 33.33 | 44.44 | 22.22 |
| Moxifloxacin | 100.00 | 0.00 | 0.00 |
| Ofloxacin | 66.67 | 33.33 | 0.00 |

(Amoxicillin/clavulanate) caused effective growth retardation in 22.22% cases, and moderate delay – in 77.78% cases, resistant microorganisms were not detected. Sensitivity to cephalosporins was detected in 50.00% cases, moderate sensitivity – in 38.89%, resistance – in 11.11%. Fluoroquinolones were the most effective. Sensitivity to them was noted in 72.22% cases, moderate sensitivity – in 22.22%, resistant bacteria – in 5.56% cases (Table 4).

In the group of fluoroquinolones, the greatest effect on microorganisms was caused by Moxifloxacin – 100.00% susceptibility. Ciprofloxacin caused effective growth retardation in 88.89% cases and moderate delay in 11.11 cases. 66.67% of cultures were sensitive to Ofloxacin, 33.33% were moderately sensitive, and no resistant ones were observed. The least effective among the group of fluoroquinolones was Norfloxacin – 33.33% of cultures were sensitive, 44.44% were moderately sensitive and 22.22% of bacterial cultures were resistant (Figure 2).

It should be noted that isolated in clinically significant concentrations of pathogenic microorganisms were not resistant to four used antibacterial agents – Amoxicillin/clavulanate, Ofloxacin, Ciprofloxacin and Moxifloxacin (Table 5).

A study of susceptibility to antifungal agents in selected from associations of fungi of the genus *Candida* revealed a higher resistance of isolated cultures to specific agents. In one case the selected culture of fungi was not sensitive to any of the selected antifungal agents, there was only moderate sensitivity and resistance. In general, antifungal susceptibility was observed in 20.00% of the study cases, moderate susceptibility was determined in 46.67%, and resistance in 33.33%. There were no cultures sensitive to Itraconazole and Fluconazole, all were either moderately sensitive or resistant.

## Discussion

Despite improved diagnostic and treatment methods in dentistry, the availability of antimicrobial and antibacterial agents the problem of treatment of acute and chronic inflammatory diseases of the maxillofacial area which occur as a complication of dental caries is relevant to the modern health care system in Ukraine. It is generally accepted in maxillofacial surgery and general surgery that there is a significant predominance in the etiology of odontogenic abscesses and phlegmones of the maxillofacial area of bacteria of the genus *Staphylococcus* and their associations (Bali et al., 2015; Bertossi et al., 2017; Dregalkina et al., 2020).

In our study the obtained results indicate the predominance of *Lactobacilli* in the etiology of acute odontogenic purulent diseases that occur in the oral cavity as a complication of dental caries. The revealed fact is the basis for revision and clarification of generally accepted approaches to complex treatment of the abovementioned diseases because in the presence of a significant mass of saprophytic, transient and opportunistic microorganisms of the *Lactobacilli* family in the oral microbiota there are reasonable grounds for potentially high risk of biofilms exchange of genetic information between bacteria of the same family which increases the pathogenicity of associations of microorganisms and increases antibiotic resistance in particular (Siqueira and Rôças, 2017). All the identified facts suggest a special attention to the abovementioned contingent of patients and in the choice of rational therapy in particular.

By the way, the biofilming properties of pathogenic microorganisms' isolates were not studied in the current study. And what types of bacterial cultures were received (planktonic or biofilming) remains as an unknown fact. The study of these properties requires sequencing of the bacterial genome in order to identify biofilm-making genes.

The problem of antibiotic resistance increasing among pathogenic microorganisms is relevant for many countries in the world and Ukraine is not an exception. Given the progressive decline in the availability of dental care for the country's population as the health care reform continues which has been affected by the COVID-19 pandemic, it can be argued that untimely visits to the dentist in Ukraine are becoming more frequent, and quite often such patients are treated urgently, in the presence of either acute pain or already acute inflammatory complications of dental caries – such as acute periostitis of the jaws, periodontal abscesses and purulent radicular cysts of the jaws. At the same time, with the availability of antibacterial medicines in the pharmacy network in some cases such drugs are prescribed independently, uncontrolled without following the accepted recommendations for dosage and duration of the course (Palmer, 2016; Koyuncuoglu et al., 2017). In addition, antibacterial agents are widely used in industry and food production, all this contributes to improper selection of antibiotic-resistant microorganisms and in the absence of new available compounds with antibacterial and antimicrobial properties the risks of malignant duration of infectious diseases and their complications may increase significantly (Jagadish Chandra et al., 2017; Sideris et al., 2022).

With regard to dental practice, antibacterial agents are prescribed to patients regularly and it is common practice to empirically select antibacterial agents without identifying the causative infectious agent and due to their sensitivity to antibiotics and antimicrobials compositions. If you open the current local protocols of dental health institutions which are used to treat acute odontogenic periostitis of the jaws, odontogenic abscesses of maxillofacial soft tissues in an outpatient conditions you can find recommendations for the appointment of complex anti-inflammatory therapy with predominant tetracyclines, macrolides, macrolides, semi-synthetic penicillins and cephalosporins in oral forms. Protocols for the treatment of such diseases in the hospitals contain more recommendations for the use of cephalosporines parenterally and fluoroquinolones for oral administration (Hatilo et al., 2016).

The results obtained in the current study showed that mostly outpatients are patients with dental caries complications where the etiological agent is bacteria of the genus *Streptococcus*. The identified number of cases where the concentration of microorganisms was lower than level of clinical significance may indicate on possible participation in associations of pathogenic bacteria caused the current disease of the other members of the micro-world that were not cultured. They also might include the obligate anaerobes or microorganisms that are difficult to distinguish in standard conditions. Also, such cases may be explained by self-medication of patients and presenting not full information to doctor during visits to the clinic. Therefore, the results obtained on the level of sensitivity of detected pathogens are alarming and are objective prerequisites for qualitative changes in local protocols of empirical antibacterial therapy of acute inflammatory diseases of the maxillofacial area or expanding indications for other antimicrobials of artificial and natural origin.

The obtained results showed that an etiological agent of the inflammatory process was identified in only 61.54% cases with further determination of sensitivity to antibacterial agents. And we can assume that in almost 40.00% cases of odontogenic purulent inflammatory processes in the oral cavity the effect of standard antibacterial therapy remains unknown. That's why detected absence of effective inhibition the pathogenic microorganism's growth by the tetracyclines may not be total. The next hypotheses may be suggested: tetracyclines may be effective in the range from 0.00 to 35.71% cases, moderate sensitivity to this group can also be found in the

**Table 6 – Probable ranges of sensitivity to antibacterial agents of pathogenic bacteria caused purulent inflammatory diseases of the oral cavity, % of cases**

| Group of antibacterial agents | Sensitive | | Moderately sensitive | | Resistant | |
|---|---|---|---|---|---|---|
| | min. | max. | min. | max. | min. | max. |
| Tetracyclines | 0.00 | 35.71 | 0.00 | 35.71 | 64.29 | 100.00 |
| Macrolides | 0.00 | 35.71 | 14.29 | 50.00 | 50.00 | 85.71 |
| Semi-synthetic penicillins | 14.29 | 50.00 | 50.00 | 85.71 | 0.00 | 35.71 |
| Cephalosporins | 37.50 | 67.86 | 25.00 | 60.71 | 7.14 | 42.86 |
| Fluoroquinolones | 46.43 | 82.14 | 14.29 | 50.00 | 3.57 | 39.29 |

range from 0.00 to 35.71% cases, similarly, antibiotic resistance may range from 64.29 to 100.00%.

When using the macrolides, the sensitivity of the microflora may also be in the range from 0.00 to 35.71% cases, moderate sensitivity may be determined in the range from 14.29 to 50.00%, antibiotic resistance – from 50.00 to 85.71% cases. Regarding the sensitivity to semi-synthetic penicillins we can assume that it is in the range from 14.29 to 50.00%, moderate sensitivity – from 50.00 to 85.71%, and resistance to this group – from 0.00 to 35.71%.

As for sensitivity to cephalosporines, it may range from 37.50 to 67.86%, moderate sensitivity may be determined from 25.00 to 60.71%, and resistance to this group of drugs – from 7.14 to 42.86%. Regarding the sensitivity to fluoroquinolones, it can range from 46.43 to 82.14%, moderate sensitivity can be outlined in the range of 14.29–50.00%, and resistance – 3.57–39.29% cases (Table 6).

## Conclusion

Our study of the microbiota in foci of purulent inflammation of odontogenic origin in the oral cavity showed that the pathogenic microflora was identified in clinically significant concentrations in only 61.54% of cases. Bacteria of the genus *Streptococcus* predominated in the studied samples of purulent exudate. The study of the sensitivity of the detected pathogens to the most widely used antibiotics showed a high level of resistance of such microflora to tetracyclines to macrolides. The most effective antibacterial agents for the treatment of purulent inflammatory diseases of the oral cavity which are caused by *Streptococci* and microbial associations with their inclusion may be considered groups of cephalosporins and fluoroquinolones. Given the common approaches to infection control implemented in many countries around the world, there is a need to repeat similar studies in other regions and at other times of the year to offset regional and circadian effects on macro-, microorganisms and their associations.

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