

Summary

EPIGALLOCATECHIN-3-GALLATE ALLEVIATES METABOLIC DISORDERS IN RATS SIMULTANEOUSLY EXPOSED TO ROUND-THE-CLOCK LIGHTING AND KEPT ON HIGH-CALORIE CARBOHYDRATE-LIPID DIET

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Key words: bioflavonoids, epigallocatechin-3-gallate, carbohydrate and lipid metabolism, insulin resistance, round-the-clock lighting, high-calorie carbohydrate-lipid diet, blood, rats.

The aim of the study is to investigate the effect of epigallocatechin-3-gallate (EGCG) on the parameters of carbohydrate and lipid metabolism in the blood serum of rats exposed to round-the-clock lighting (RCL) and kept on high-calorie carbohydrate-lipid diet (HCCLD). The experiments were performed on 21 white Wistar rats weighing 210-250 g, divided into 3 groups. Animals in the first group (control) received a standard diet (energy value 2720 kcal/kg) and were exposed to an equally altered light and darkness periods. The rats of the second and third groups were under the constant round-the-clock light exposure and received HCCLD (4477 kcal/kg). In addition to the conditions in the second group, the test animals of the third group were administered EGCG daily through intragastric gavage in a dose of 40 mg/kg. An enzyme-linked immunosorbent assay kit for rat serum was used to assess insulin concentration. The concentration of serum glucose, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and triacylglycerols (TAG) was determined by enzymatic methods using photometric equipment. Insulin resistance was assessed by the HOMA-IR (Homeostatic Model Assessment) index. With the administration of EGCG, the concentration of glucose and insulin in the blood serum decreased by 34.7% and 59.1%, respectively, compared to group 2, and the HOMA-IR was 61.5% lower than in the comparison group. The HDL content increased with the administration of EGCG in the experiment and was 91.3% higher compared to the findings in the group 2. Under these circumstances, the concentrations of VLDL and TAG in the blood serum were significantly lower by 37.5 and 37.1% than the respective values in the group 2. It can be suggested that the administration of the bioflavonoid epigallocatechin-3-gallate significantly alleviates metabolic disorders in rats simultaneously exposed to RCL and kept on HCCLD.

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SENSITIVITY OF CAUSATIVE AGENTS OF INFECTIOUS-INFLAMMATORY DISEASES IN MAXILLOFACIAL SOFT TISSUES TO ANTIBIOTICS

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The aim of this study is to investigate the sensitivity of pathogens causing infectious and inflammatory diseases in soft tissues within the maxillofacial region to antibiotics. The study was performed on 282 clinical isolates collected from patients. The sensitivity of the microorganisms to antibiotics was evaluated based on the EUCAST committee quality control standards. The variability in the sensitivity of microorganisms isolated from patients with infectious and inflammatory diseases of the maxillofacial soft tissues to antibiotics has been determined. Representatives of the genus Staphylococcus exhibit high sensitivity to vancomycin, fluoroquinolones and lincosamides. At the same time, they are characterized by the lowest sensitivity to aminoglycosides and penicillins. Enterococcus spp. has high sensitivity to tetracyclines and fluoroquinolones, showing the lowest results with penicillins and carbapenems. Streptococcus spp. viridans-group show low sensitivity to penicillins, carbapenems, fluoroquinolones, and lincosamides, while maintaining high sensitivity to glycopeptides. Low sensitivity of Acinetobacter spp. isolated from patients with infectious and inflammatory diseases of maxillofacial soft tissues to antibacterial drugs of different groups has been revealed. The study has shown a significant variation in the sensitivity of isolates to antibiotics commonly used in clinical practice and recommended by the EUCAST quality committee, suggesting the prospects for their use.

Key words: antibiotics, sensitivity, maxillofacial localization, resistance, antimicrobial resistance, odontogenic abscess.

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Introduction

Infectious and inflammatory diseases constitute approximately 20% of the cases in the field of general surgical pathology and are quite prevalent in the maxillofacial area (MFA) with mortality rates ranging from 10-40% [1, 2]. Over half of patients having such diseases require an interdisciplinary approach to diagnosis and treatment involving allied specialists, multistage surgical interventions,

and the use of powerful antibiotic therapy complexes [3 – 5].

Until recently, the use of antibiotics in dentistry worldwide has not been dealt with in depth. However, dentists are currently ranked among the top 5 physicians in terms of the frequency of prescribing antibiotics in hospitals and outpatient treatment of patients [6, 7]. This has led to the revision of guidelines for the use of antibiotics in dental patients, aiming to limit the indications for prescription. In-

deed, the proposition that dental procedures lead to the onset of systemic infections is being disproven more and more, particularly due to the dangers of antibiotic prescription side effects [8-10].

The problem of microorganisms acquiring resistance to antibacterial drugs, specially after COVID-19 pandemic, is well recognized and has already reached global scale, as it has serious consequences for public health and dentistry in particular. Scientists have proved a direct correlation between the frequency of antibiotic prescriptions and the spread of antibiotic resistance among microorganisms [11, 12]. Therefore, continuous monitoring of the sensitivity of dental pathogens to antibiotics is an important component of overcoming antibiotic resistance and predicting the development of resistance among clinically relevant microorganisms.

The issue of microorganisms developing resistance to antibacterial drugs, particularly after the COVID-19 pandemic, is widely acknowledged as a global problem, with significant implications for public health and, in particular, dentistry. Research has shown a clear connection between the rate of antibiotic prescriptions and the dissemination of antibiotic resistance among microorganisms [11, 12]. Hence, an important aspect of tackling antibiotic resistance and anticipating potential resistance in clinically significant microorganisms is through objective, continuous monitoring of dental pathogens' antibiotic sensitivity.

Our study **aims** to examine the sensitivity of pathogens causing infectious and inflammatory diseases of soft tissue in the maxillofacial area to antibiotics.

Materials and Methods

The study involved 280 patients of the middle age group according to WHO (average age 47 ± 5.0 years). They took the course of treatment for infectious and inflammatory diseases of the soft tissues in the maxillofacial region at the Department of Maxillofacial Surgery of M.V. Sklifosovskiy Poltava Regional Clinical Hospital during 2019 - 2021.

In order to study aerobic and facultative anaerobic microflora before the beginning of antibiotic therapy, material was collected from the focus of infection using a sterile cotton swabs with Amies transport medium for further cultivation and identification. The study was approved by the bioethics committee of the Poltava State Medical University (#12 from 10.12.2021), and all study participants had signed an informed consent beforehand.

The 282 clinical isolates obtained from patients with infectious and inflammatory diseases of soft tissue in the maxillofacial region were the objects of the study. The isolates were cultured on nutrient media according to the type of microorganism for 24-48 hours at 37°C. Final identification was performed using a Vitec - 2compact bioMérieux automatic bacteriological analyzer (France) according to the manufacturer's instructions.

The sensitivity of the studied microorganisms to antibiotics was determined according to the EUCAST committee quality control standards (Version 12.0, valid from 2022-01-01) using the standard disc diffusion method (DDM) and microdilution if necessary [13]. In order to determine the sensitivity of clinical isolates to antibacterial agents using the above-mentioned methods, Mueller-Hinton agar and broth were used, as appropriate. The results were interpreted according to the EUCAST Clinical Breakpoint tables, whereby microorganisms were divided into sensitive and resistant, and in some cases, if possible, into sensitive at increased exposure.

The results were statistically processed using the Microsoft Excel 2016 program.

Results

282 clinical isolates of aerobes and facultative anaerobes were obtained from patients with infectious and inflammatory diseases of the soft tissues of the maxillofacial area and identified. Gram-positive cocci were found as prevalent, accounting for 93.6% of the isolates (Table 1).

Table 1
Characteristics of microbiota composition obtained from patients with infectious and inflammatory diseases of soft tissues of maxillofacial region

Microorganism	Abs.	%
<i>S. aureus</i>	126	44,7
<i>S. epidermidis</i>	11	3,9
<i>S. saprophyticus</i>	4	1,4
<i>S. haemolyticus</i>	5	1,8
<i>S. hominis</i>	4	1,4
<i>S. warneri</i>	3	1,1
<i>Enterococcus spp.</i>	58	20,6
<i>Streptococcus viridans</i>	33	11,7
<i>Kocuria spp.</i>	20	7,0
<i>Acinetobacter baumannii</i>	18	6,4

Representatives of the genera *Staphylococcus* (54.3%) and *Enterococcus* (20.6%) were the dominant pathogens, which were found both in associations and in monoculture.

The studies yielded insights into the variability of sensitivity in *Staphylococcus aureus* (*S. aureus*)

isolates to antibiotics commonly prescribed in clinical settings and recommended by the EUCAST quality committee.

Out of the 126 isolates of *S. aureus* studied, 68 (54.0%) demonstrated sensitivity to benzylpenicillin. Moreover, the microorganisms studied exhibited

greater sensitivity (69.0%) to the cephalosporin II generation cefoxitin. It is worth noting that only 60 (47.6%) clinical isolates were sensitive to both benzylpenicillin and cefoxitin, therefore, respectively, they can be considered sensitive to all penicillin-type antibiotics.

The proportion of *S. aureus* that showed resistance to benzylpenicillin (58, 46.0%) and cefoxitin (39, 31.0%) indicated a significant increase in resistance to these antibacterial agents. These screening tests enabled us to characterise the resistance of *S. aureus* isolates to penicillins in general. Thus, 19 clinical isolates (15.0%) were resistant to benzylpenicillin while retaining sensitivity to cefoxitin, indicating their sensitivity to β -lactamases, β -lactamase inhibitors, and isoxazolinepenicillins (oxacillin, cloxacillin). Moreover, the absolute number of *S. aureus* resistant to both benzylpenicillin and cefoxitin (31, 24.6%) concurrently highlights their resistance to all penicillins. Additionally, further examination of their sensitivity to oxacillin indicated a minimum inhibitory concentration (MIC) value of the antibiotic >2 (with an average of 3.94 ± 2.22 mg/L), signifying the genetic determination of methicillin resistance among the isolates.

To determine the sensitivity of *S. aureus* to fluoroquinolones, a screening test was conducted using norfloxacin. Results indicate higher sensitivity of coagulase-positive staphylococci to this antibiotic group compared to β -lactams. Out of 126 test subjects, 98 clinical isolates (77.8%) were found to be sensitive to norfloxacin. Causal connections between statements create a logical flow of information. In accordance with EUCAST quality committee guidelines, staphylococci that displayed sensitivity to norfloxacin were automatically classified as sensitive to moxifloxacin. However, susceptibility to ciprofloxacin and levofloxacin increased with exposure. For the 28 *S. aureus* that were resistant to norfloxacin, further testing was necessary to determine their sensitivity to all fluoroquinolones individually. Fourteen clinical isolates, accounting for 11.1% of the total *S. aureus*, demonstrated resistance to norfloxacin, ciprofloxacin, levofloxacin, and moxifloxacin, indicating resistance to this group of antibacterial agents. It is noteworthy that among the norfloxacin-resistant *S. aureus*, 5 (4.0%), 7 (5.6%), and 14 (11.1%) isolates exhibited sensitivity to ciprofloxacin, levofloxacin, and moxifloxacin, respectively.

S. aureus isolated from patients with infectious and inflammatory soft tissue diseases of MFR showed low sensitivity to aminoglycosides. Thus, 47.6% of the studied isolates were resistant to amikacin. In addition, among the amikacin-resistant *S. aureus* there was not a single one sensitive to gentamicin. At the same time, the results of determining the sensitivity of *S. aureus* to gentamicin indicated an even lower result: the proportion of resistant isolates was 57.1% of the total number of studied microorganisms of this species.

Undoubtedly, glycopeptides are currently the

drug of choice for the treatment of infections caused by resistant strains of microorganisms. The tested *S. aureus* isolates demonstrated high sensitivity to vancomycin (abs. 117, 92.9%). On average, the MIC of vancomycin for sensitive staphylococci was 1.14 ± 0.64 mg/L. Moreover, according to the EUCAST committee quality control tables, all vancomycin-sensitive clinical isolates were automatically considered sensitive to dalbavancin and oritavancin.

To determine the sensitivity of *S. aureus* isolated from patients, a screening test with erythromycin was performed. 73 (57.9%) of the clinical isolates tested demonstrated sensitivity to erythromycin and were therefore considered sensitive to azithromycin and clindamycin. Erythromycin-resistant isolates were additionally tested for sensitivity to each macrolide separately. The study revealed a similar trend: among 53 *S. aureus* isolates that were resistant to erythromycin, 51 and 48 continued to show resistance to azithromycin and clarithromycin, respectively. Only 2 clinical isolates exhibited sensitivity to the above antibiotics and 3 *S. aureus* studied were susceptible to clarithromycin.

As a result of the DDM, we found that *S. aureus* was sensitive to the lincosamide representative clindamycin in 61.9% cases. However, for erythromycin-resistant and clindamycin-sensitive clinical isolates we additionally performed a D-test for detection of latent inducible clindamycin resistance. The D-test was positive for 29 clinical isolates, thus, giving the reason to classify these microorganisms as clindamycin-resistant *S. aureus*. Considering the above, the proportion of clindamycin-resistant *S. aureus* increased by 23% reaching 61.1%.

The sensitivity of coagulase-positive staphylococci to tetracycline was assessed by tetracycline screening: microorganisms sensitive to tetracycline were automatically recognized as sensitive to doxycycline and minocycline. Only 73 (57.9%) tetracycline-sensitive *S. aureus* were identified as a result of the test.

Unlike coagulase-positive staphylococci, coagulase-negative representatives of this genus are less frequently subjected to screening tests to determine their sensitivity to antibacterial drugs. Consequently, the studied isolates were primarily tested for each antibiotic individually.

Resistance to benzylpenicillin was detected in 44.4% of clinical isolates of coagulase-negative *Staphylococcus* spp. originating from patients with infectious and inflammatory conditions of the soft tissues of the MFR. Although benzylpenicillin-resistant isolates were found amongst all coagulase-negative species of the genus, the largest proportion (18.5%) was accounted for by *Staphylococcus epidermidis*. Microorganisms exhibited low sensitivity to ampicillin, with over half (51.9%) of clinical isolates proving resistant to the antibacterial agent. The presence of the *mecA* gene in strains of *Staphylococcus saprophyticus* was determined to

be based on ampicillin sensitivity. It should be noted that among the studied *S. saprophyticus* only one isolate maintained sensitivity to ampicillin and, accordingly, was automatically considered sensitive to amoxicillin and piperacillin. Oxacillin MICs against coagulase-negative staphylococci indicated the presence of methicillin resistance in 17 (63.0%) of 27 clinical isolates.

The sensitivity to cephalosporins and carbapenems among coagulase-negative species of *Staphylococcus* spp. was evaluated by the cefoxitin sensitivity screening test, which revealed resistance to antibiotics of these groups in (59.3%) of clinical isolates.

Coagulase-negative staphylococci demonstrated lower sensitivity to fluoroquinolones compared to coagulase-positive *S. aureus*. Only 59.3% of the isolates studied were sensitive to norfloxacin and respectively sensitive to moxifloxacin and sensitive with increased exposure to ciprofloxacin and levofloxacin. It should be noted that an additional study of norfloxacin-resistant strains regarding sensitivity to ciprofloxacin and levofloxacin did not identify a single sensitive isolate. It was found that 63.0% of the coagulase-negative *Staphylococcus* spp. studied were sensitive to aminoglycosides: kanamycin and amikacin. At the same time, the sensitivity of the studied isolates to gentamicin was almost the same: the proportion of sensitive *Staphylococcus* spp. was 66.7%.

Coagulase-negative *Staphylococcus* spp. showed the highest sensitivity to vancomycin. Thus, (abs. 25) 92.6% of the studied clinical isolates retained sensitivity to glycopeptide.

The sensitivity of *Staphylococcus* spp. to macrolides was determined by sensitivity to erythromycin according to the recommendations of the EUCAST committee. Those studied showed that (abs. 15) 55.6% coagulase-negative *Staphylococcus* spp. were sensitive to erythromycin, which simultaneously indicated sensitivity to azithromycin, clarithromycin, and roxithromycin. An additional study found 44.4% erythromycin-resistant isolates and 29.6% resistant to azithromycin and clarithromycin. It should be noted that during the study 11.1% coagulase-negative staphylococci were classified as sensitive with increased clarithromycin exposure.

On average, DDM resulted in sensitivity to clindamycin among coagulase-negative staphylococci of 59.3%. However, an additional D-test revealed latent inducible resistance to lincosamide in (abs. 7) 25.9% sensitive isolates, reducing the rate of clindamycin-sensitive coagulase-negative *Staphylococcus* spp. to 33.3%.

The results of the studies demonstrated 59.3% of clinical isolates of coagulase-negative staphylococci developed antibiotic resistance to tetracyclines. This finding allows for the suggestion of the sensitivity of these microorganisms to antibacterial agents within this group.

Clinical isolates of the *Enterococcus* genus, ob-

tained from patients diagnosed with infectious and inflammatory soft tissue diseases of MFR, have demonstrated a resistance to antibiotics from diverse pharmacological groups. Sensitivity of *Enterococcus* spp. to ampicillin, amoxicillin, and piperacillin was determined via testing for ampicillin sensitivity. Resistance to penicillins was found to have developed in 27.6% of clinical isolates (abs. 16), with 8.6% (abs. 5) of microorganisms being classified as susceptible after increased exposure to antibiotics. Generally, the sensitivity of enterococci to penicillins was within the range of 63.8%. Biased or subjective evaluations have been excluded from the text.

According to the EUCAST tables, imipenem was found to be reasonably effective for determining the sensitivity of *Enterococcus* spp. among carbapenems. Growth inhibition of 41.4% of the *Enterococcus* bacteria under examination was observed following administration of the antibacterial drug. Exposure to imipenem yielded sensitivity in only 13.8% of the clinical isolates.

A screening test using norfloxacin was conducted to assess the sensitivity of *Enterococcus* genus to fluoroquinolones. The tested isolates exhibited superior fluoroquinolone sensitivity as opposed to penicillins. Specifically, 74.1% of microorganisms were sensitive to norfloxacin, signifying sensitivity to both ciprofloxacin and levofloxacin.

Representatives of the genus *Enterococcus* retained sensitivity to the glycopeptide of greatest clinical importance, vancomycin, in 62.1% cases. *Enterococcus* spp. is often naturally resistant to aminoglycosides and therefore is not used as a monotherapy for enterococcal infections. However, synergism between aminoglycosides and penicillins or glycopeptides has been proven with respect to members of this genus without the resulting high level of resistance to aminoglycosides. Thus, the screening test with gentamicin was aimed at distinguishing between natural resistance and acquired high level of resistance. Consequently, we found 48.3% members of the genus *Enterococcus* that did not have an acquired high level of resistance to aminoglycosides, and therefore predicted possible synergism with penicillins and glycopeptides in antibiotic sensitivity. The screening of *Enterococcus* spp. without acquired high levels of resistance to aminoglycosides identified 27.6% clinical *Enterococcus* isolates with potential synergism with penicillins and 29.3% isolates with the same potential for combination.

Among tetracyclines it is recommended to determine the sensitivity of *Enterococcus* spp. only to tigecycline; as a result, high sensitivity of the studied microorganisms to this antibiotic was established. The percentage of sensitive isolates was 91.4%.

It should be noted that the results of sensitivity of enterococci to linezolid were equally divided. Therefore, the proportion of sensitive clinical isolates to this antibacterial agent was 50.0%.

Streptococcus spp. *viridans*-group isolated from patients with infectious and inflammatory soft tissue diseases of the MFR showed varying sensitivity to the antibacterial agents recommended for use. Sensitivity among *viridans* streptococci to benzylpenicillin, for which β -lactam resistance was detected, was low (abs. 11; 33.3%). This result, in accordance with the recommendations of the EUCAST committee, indicated the same sensitivity of the studied microorganisms to all penicillins, cephalosporins, and carbapenems.

In order to identify mechanisms of resistance to fluoroquinolones for *Streptococcus* spp. *viridans*-group, screening with moxifloxacin was performed, which revealed 78.8% resistant clinical isolates and only 21.2% of streptococci with no mechanisms of resistance to fluoroquinolones.

Assessing the sensitivity of *viridans Streptococcus* spp. to glycopeptides, as well as among other Gram-positive cocci, a high sensitivity of microorganisms to this group of chemotherapeutic drugs was established. We found 78.8% vancomycin-sensitive *Streptococcus* spp.

Similar to *Enterococcus* spp., *viridans* streptococci often have natural resistance to aminoglycosides. However, in the absence of an acquired high level of resistance to this group of antibiotics, their synergistic combination with penicillins and glycopeptides is possible. A study of *Streptococcus* spp. *viridans*-group indicated their low sensitivity to gentamicin: 33.3% clinical isolates retained sensitivity to it, indicating acquired low-level resistance to aminoglycosides. In turn, among susceptible *Streptococcus* spp. 12.1% and 24.2% showed potential synergism with penicillins and glycopeptides, respectively.

Viridans streptococci were sensitive to clindamycin in 42.4% cases. However, when investigating the sensitivity of *Streptococcus* spp. to lincosamide, the possibility of acquiring induced clindamycin resistance was taken into account. Thus, the D-test was positive in (abs. 8) 24.2% of the studied isolates considered sensitive to clindamycin by the DDM results. This indicated the presence of latent induced resistance and increased the proportion of clindamycin-resistant streptococci in 84.8%.

Due to the lack of screening tests to determine sensitivity to chemotherapeutic agents among *Kocuria* spp. the sensitivity of clinical isolates to antibiotics of different groups was determined separately. Among penicillins, representatives of this genus had high sensitivity to benzylpenicillin (abs. 10, 50.0%). It should be noted that 35.0% of benzylpenicillin-resistant *Kocuria* were naturally resistant to amoxicillin as well, but the proportion of sensitive (abs. 9; 45.0%) was lower due to an increased number of isolates (abs. 4; 20.0%) sensitive when exposed to amoxicillin. A similar trend was observed for the sensitivity of *Kocuria* spp. to cephalosporins. The sensitivity of isolates to cefotaxime and ceftazidime did not differ and was 55.0%. The difference was in the sensitivity of one

clinical isolate classified as "sensitive with increased exposure to ceftazidime".

The representatives of the genus *Kocuria* had high sensitivity to meropenem: 60.0% of the microorganisms studied retained sensitivity to the antibiotic.

The sensitivity of *Kocuria* to the fluoroquinolones ciprofloxacin and moxifloxacin did not differ between themselves and constituted exactly half of the studied clinical isolates. Along with this, resistance of *Kocuria* spp. to moxifloxacin occurred in 50.0% isolates, while resistance to ciprofloxacin occurred in 35.0% cases.

The studies revealed a moderate sensitivity of *Kocuria* spp. to gentamicin. In fact, the detection rate of sensitive isolates was 45.0%. That is, the number of aminoglycoside-resistant microorganisms exceeded the number of sensitive ones.

The fact that *Kocuria*, as well as of all other Gram-positive cocci isolated from patients demonstrate the highest sensitivity to vancomycin turned out to be quite natural. In this case, 75.0% representatives of the genus *Kocuria* retained sensitivity to vancomycin.

As a result of the research, the sensitivity of *Acinetobacter* spp. isolated from patients with infectious and inflammatory diseases of soft tissues in the MFR to antibacterial drugs of different groups was quite low. Thus, the level of sensitivity of representatives of this genus to imipenem and meropenem did not exceed 27.8%. At the same time, some of the resistant isolates to the above antibiotics also hardly differed: 50.0% microorganisms were resistant to imipenem and 44.4% to meropenem.

Acinetobacter spp. had low sensitivity to fluoroquinolones. The frequency of detection of ciprofloxacin- and levofloxacin-resistant clinical isolates was 61.1% and 50.0% respectively. While the number of members of this genus, which sensitive to levofloxacin (abs. 4; 22.2%) was at the level of those sensitive to carbapenems, the level of sensitivity of these bacteria (abs. 2; 11.1%) to ciprofloxacin was at an all-time low, although the *Acinetobacter* genus proportion, classified as "susceptible with increased ciprofloxacin/levofloxacin exposure", was in the same range of 27.8%.

High sensitivity of *Acinetobacter* spp. to aminoglycosides was discovered. Initially, we identified that only 44.4% of clinical isolates of this genus were resistant to amikacin and 38.9% were resistant to gentamicin. Furthermore, the increased exposure to antibiotics resulted in a lack of sensitive isolates, which in turn increased the number of *Acinetobacter* spp. that were essentially susceptible to the studied aminoglycosides. The percentage of *Acinetobacter* spp. that exhibited sensitivity to amikacin was 55.6%, with gentamicin-sensitive pathogens recording the highest sensitivity at 61.1% among *Acinetobacter* spp.

Discussion

The microbiota composition under infectious and inflammatory diseases of the soft tissues in the maxillofacial region was analysed. Our research supports the widespread belief that Gram-positive cocci are the predominant aerobic and facultative anaerobic microorganisms that inhabit the human oral cavity, leading to odontogenic infections commonly [14, 15].

Multidrug resistance of *Staphylococcus spp.* has been widely acknowledged for many years. Reports of resistance formation among these microorganisms to penicillins emerged in the 1980s. In the past decade, the sensitivity of *S. aureus* to benzylpenicillin and cefoxitin has decreased to 40% [16]. It is noteworthy that pathogens of this species, which were isolated from patients suffering from odontogenic diseases of the soft tissues of the facial region, were slightly more sensitive to penicillins. According to literature data [16–18], a similar trend can be observed in the sensitivity of *Staphylococcus spp.* to antibiotics of other groups, including vancomycin. Therefore, pathogens of odontogenic infections exhibited a lower resistance level than those of systemic infections. The significant resistance seen in staphylococci is linked directly to the presence of a potent range of resistance mechanisms that include the enzymatic inactivation of antibiotics, alteration of the target with reduced affinity for antibiotics, antibiotic trapping, and efflux pumps [19].

As a representative of the normobiota of the human body, *Enterococcus* come into contact with a large number of antimicrobial drugs that a person uses throughout the life. This explains the rapid development of resistance to antibiotics among these microorganisms recently. It is worth noting that in addition to acquired resistance, enterococci have intrinsic resistance, which is encoded in the genome of all representatives of the genus [20].

In our study, *Streptococcus spp.* demonstrated fairly significant resistance to most antibiotics. In these bacteria, apart from mutations, affecting mostly the 23S rRNA genes, acquisition of such genes as *cfr*, *cfr(B)*, *optrA* and *poxtA*, often associated with mobile genetic elements, plays an important role for resistance [21, 22].

It is known that *Acinetobacter spp.* are among the leading causative agents of nosocomial infections due to multidrug resistance. Recent works prove the low sensitivity of representatives of this genus to almost all groups of antimicrobial drugs. *A. baumannii* have porins, capsular polysaccharides, lipopolysaccharides, phospholipases, outer membrane vesicles, metal acquisition systems, and protein secretion systems to provide high level of stability in presence of drugs. Mechanisms of antibiotic resistance of this organism, including acquirement of β -lactamases, up-regulation of multidrug efflux pumps, modification of aminoglycosides, permeability defects, and alteration of target sites provide their unique properties and make it difficult to treat infections caused by them [23, 24].

Conclusions

Based on the findings obtained, we have determined the varying degrees of sensitivity exhibited by microorganisms isolated from infectious and inflammatory diseases in the soft tissues of the maxillofacial region towards antibiotics.

It has been found that members of the *Staphylococcus* genus exhibit high sensitivity to vancomycin, fluoroquinolones, and lincosamides, while they display the least sensitivity to aminoglycosides and penicillins.

Enterococcus species display high sensitivity towards tetracyclines and fluoroquinolones, with the least effective outcomes observed in the presence of penicillins and carbapenems.

On the other hand, the *Streptococcus viridans*-group species show low sensitivity to penicillins, carbapenems, fluoroquinolones, and lincosamides, while maintaining a high sensitivity towards glycopeptides.

Low sensitivity of *Acinetobacter spp.* isolated from patients with infectious and inflammatory diseases of soft tissues in the maxillofacial region to various antibiotic classes was determined.

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Author Contributions

FMO: Writing, Conceptualization, Methodology; NOA: Conceptualization, Methodology; FMO, ChYuV: Writing – original draft, Conceptualization, Formal Analysis; LGA: Methodology, Formal Analysis; LGA, ADS: Review & Editing, Project administration.

Реферат

ЧУТЛИВІСТЬ ЗБУДНИКІВ ІНФЕКЦІЙНО-ЗАПАЛЬНИХ ЗАХВОРЮВАНЬ М'ЯКИХ ТКАНИН ЩЕЛЕПНО-ЛИЦЕВОЇ ЛОКАЛІЗАЦІЇ ДО АНТИБІОТИКІВ

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Ключові слова: антибіотики, чутливість, щелепно-лицева локалізація, резистентність, протимікробна резистентність, одонтогенний абсцес.

Метою роботи було дослідити чутливість збудників інфекційно-запальних захворювань м'яких тканин щелепно-лицевої локалізації до антибіотиків. Методи. Об'єктами дослідження були 282 клінічні ізоляти, отримані від пацієнтів. Чутливість досліджуваних мікроорганізмів до антибіотиків визначали відповідно до стандартів контролю якості комітету EUCAST. Результати: Встановлено варіабельність чутливості мікроорганізмів, виділених при інфекційно-запальних захворюваннях м'яких тканин щелепно-лицевої області, до антибіотиків. Представники роду *Staphylococcus* виявляють високу чутливість до ванкоміцину, фторхінолонів і лінкозамідів. При цьому вони характеризуються найменшою чутливістю до амінглікозидів і пеніцилінів. *Enterococcus* spp. мали високу чутливість до тетрациклінів і фторхінолонів, демонструючи найнижчі результати з пеніцилінами і карбапенемами. *Streptococcus* spp. групи *viridans* виявляють низьку чутливість до пеніцилінів, карбапенемів, фторхінолонів та лінкозамідів, зберігаючи високу чутливість до глікопептидів. Низька чутливість до антибактеріальних препаратів різних груп виявлена серед *Acinetobacter* spp. ізольованих від хворих на інфекційно-запальні захворювання м'яких тканин щелепно-лицевої локалізації. Висновки. Встановлено варіабельність чутливості ізолятів до антибіотиків, які найчастіше використовуються в клінічній практиці та рекомендовані комітетом з якості EUCAST, що забезпечує перспективність їх використання.