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CONCURRENCE OF EMPIRICAL ANTIBIOTIC THERAPY WITH THE RESULTS OF BACTERIOLOGICAL ANALYSIS IN THE TREATMENT OF ODONTOGENIC PURULENT-NECROTIC PROCESSES OF THE MAXILLOFACIAL REGION

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In connection with the constant development of the spectrum of sensitivity of infectious agents, the dynamic development of antimicrobial resistance and the view of modern medicine on rational antibacterial therapy, we consider it appropriate to study the current state of antibacterial resistance of the microbial composition of odontogenic purulent-necrotic foci of the maxillofacial region. The mismatch of microflora sensitivity to the prescribed antibiotic occurred in 66.7 % of cases. Most often, in postoperative surgical wounds due to the opening of purulent-necrotic foci of the maxillofacial region, colonization of Str. mitis, S. pyogenes, S. epidermidis, and also Pseudomonas spp. Antibacterial drugs of the Access group, to which the microbiota of the studied wounds is likely sensitive, were found: clindamycin, ampicillin, gentamicin. The use of clindamycin as a starting antibacterial drug for the treatment of purulent-necrotic lesions of the maxillofacial region may be appropriate not only in cases where the patient is allergic to beta-lactams.

Key words: treatment, antibiotic therapy, clinical study, clinical cases, inflammation, analysis.

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ЗБІГ ЕМПІРИЧНОЇ АНТИБІОТИКОТЕРАПІЇ З РЕЗУЛЬТАТАМИ БАКТЕРІАЛОГІЧНОГО АНАЛІЗУ ПРИ ЛІКУВАННІ ОДОНТОГЕННИХ ГНІЙНО-НЕКРОТИЧНИХ ПРОЦЕСІВ ЩЕЛЕПНО-ЛИЦЕВОЇ ДІЛЯНКИ

У зв’язку з постійним розвитком спектру чутливості інфекційних агентів, динамічним розвитком антимікробної резистентності та поглядом сучасної медицини на раціональну антибактеріальну терапію, ми вважаємо доцільним оновити дані про мікробний склад одонтогенних гнійно-некротичних вогнищ щелепно-лицевої ділянки та його антибактеріальну резистентність. Не збігання чутливості мікрофлори до призначеного антибіотику склало 66,7 % випадків. Найчастіше у хірургічних ранах з приводу розкриття гнійно-некротичних вогнищ щелепно-лицевої ділянки визначається колонізація Str. mitis, S. pyogenes, S. epidermidis, а також Pseudomonas spp. Антибактеріальними препаратами групи Access, до яких вірогідно чутлива мікробіота досліджуваних ран виявлені: кліндаміцин, ампіцилін, гентаміцин. Призначення кліндаміцину в якості стартового антибактеріального препарату для лікування гнійно-некротичних уражень щелепно-лицевої ділянки може бути доцільним не тільки у випадках наявності у пацієнта алергії на бета-лактами.

Ключові слова: лікування, антибіотикотерапія, клінічне дослідження, клінічні випадки, запалення, аналіз.

The study is a fragment of the research project “Improvement of diagnostics, therapeutic, orthopedic and surgical treatment of the most common dental diseases and their complications in the population affected by military actions”, state registration No. 0124U004521.

A crucial issue in the treatment of infectious diseases is the ongoing need to enhance methods for identifying pathogens [3]. One of the reasons for changes in the etiological factors and features of the epidemiology of infectious diseases is chronic concomitant systemic diseases, as well as excessive and irrational use of antibiotics [8]. Antibiotic resistance is now recognized as one of the main problems for humanity [6].

Antimicrobial resistance – the resistance of pathogens to antimicrobial drugs, often called a “silent pandemic”, contributes to the proliferation of pathogens of purulent infections and their spread, creating increased healthcare costs, a significant threat to public health, and increased mortality [10].

Odontogenic infections differ from other suppurative facial soft tissue infections in the diversity of bacterial agents, acute development and depth of the lesion [4]. In 2022, the WHO book “The WHO AWaRe (Access, Watch, Reserve) antibiotic book” was published, aimed at rationalizing the prescription of antibacterial drugs and reducing the development of resistance [9]. According to this book, antibiotics are divided into four groups – Access, Watch, Reserve, Not-recommended. Access antibiotics have a narrow spectrum of action, lower cost, a good safety profile and generally low potential for resistance. They are often recommended as empirical first- or second-line drugs for the treatment of common infections. Watch antibiotics are broad-spectrum antibiotics, usually with a higher cost, which are recommended only as first-line drugs for patients with more severe clinical manifestations or for infections where pathogens are likely to be resistant to Access antibiotics, such as upper urinary tract infections. Reserve antibiotics are last-line antibiotics used to treat infections with multidrug resistance.

According to the Decree of the Ministry of Health of Ukraine No. 1513 dated 23.08.2023, the Medical Care Standard "Rational Use of Antibacterial and Antifungal Drugs for Therapeutic and Prophylactic Purposes" [1] was approved. Several provisions of this standard indicate mandatory points when using antibacterial and antifungal drugs for therapeutic and prophylactic purposes, including the need to obtain a sample of biological material for bacteriological examination to identify the causative agent of an infectious disease before administering an antibacterial drug to a patient in all cases of prescribing empirical antibiotic therapy in healthcare institutions providing specialized (inpatient) medical care. The choice of a drug for empirical antibiotic therapy is based on the expected therapeutic effect against the most likely infectious agent (depending on the anatomical localization of the focus of inflammation) and its possible resistance to the selected antibacterial drug (data from local / regional / national AMR monitoring). It is also necessary to take into account the conditions of occurrence of a disease of bacterial etiology (hospital / community-acquired) and the risk of the patient having MDR (multidrug resistance), in accordance with Appendix 1 to this Standard.

Due to with the constant development of the spectrum of sensitivity of infectious agents, the dynamic development of antimicrobial resistance and the view of modern medicine on rational antibacterial therapy, we consider it appropriate to investigate the frequency of coincidence between the sensitivity of the microbial composition of odontogenic purulent-necrotic foci of the maxillofacial region (OPNFMFR) and empirically prescribed antibacterial agents.

The purpose of the study was to establish the empirical antibiotic therapy drugs with sensitivity indicators for the microbial flora of postoperative wounds to antibiotics in the treatment of odontogenic purulent-necrotic foci in the maxillofacial region.

Materials and methods. The study used the retrospective analysis method. The study material was the medical record of an inpatient (MROI) of the Department of Maxillofacial Surgery and Otolaryngology of the Municipal Emergency and Ambulatory Hospital of the Zaporizhzhia City Council for the period from 2022 to 2024. 199 (100 %) MROIs were analyzed, randomly selected: 17 (8.5 %) MROIs – for 2022, 52 (26.1 %) MROIs – for 2023, 130 (65.3 %) MROIs – for 2024. Out of the 199 (100.0 %) MROIs, the results of the bacteriological examination were available in 164 (82.4 %). 35 (17.6 %) MROIs, in which there were no results of the bacteriological examination, were excluded from the study.

The distribution of 164 (100.0 %) MROIs by year was as follows: 14 (8.5 %) MROIs were in 2022; 38 (23.2 %) – in 2023, 112 (68.3 %) – in 2024.

The distribution of 164 (100.0 %) MROIs by localization of the purulent process of the maxillofacial region was as follows:

– in the submandibular region – 92 (56.0 %) cases,

– in the intermuscular adiposus tissue spaces of the floor of the mouth unilaterally – 17 (10.3 %),

– in the intermuscular adiposus tissue spaces of the floor of the mouth bilaterally – 14 (8.5 %),

– in the intermuscular adiposus tissue spaces of the face unilaterally (diffuse phlegmon (cellulitis) of the face) – 12 (7.4 %),

– in the adiposus tissue of the pterygoid space – 10 (6.1 %),

– in the submasseteric adiposus tissue – 9 (5.5 %),

– in the adiposus tissue of the submental region – 5 (3.1 %),

– in the adiposus tissue of the peripharynx space – 2 (1.2 %),

– in the adiposus tissue of the parotid-masticatory region – 2 (1.2 %),

– in the adiposus tissue of the orbital tissue – 1 (0.6 %).

Among the archival material included in the analysis, 71.0 % (n=116) of the MROIs were men, 29.0 % (n=48) were women; the average age of the patients was 41±1.7 years (median age – 45.5); the youngest patient was 18 years old, the oldest – 83 years old.

Statistical analysis was performed using the methods of comparing percentages (proportions) using the Student's t test, risk analysis, and comparing frequencies using the $\chi 2$ test.

Results of the study and their discussion. According to 164 (100.0 %) MROIs, all patients with purulent-necrotic processes of the cellular spaces of the maxillofacial region were hospitalized urgently for emergency indications. During hospitalization, a clinical examination was performed. After establishing a clinical diagnosis, the patient underwent preoperative preparation, including antibacterial prophylaxis: intravenous administration of cefazolin 2.0 g 30 min before surgery.

Material collection for bacteriological examination.

Surgery was performed within 2 hours from the moment of the patient's hospitalization. All interventions were performed, depending on the volume and depth of the revision of the anatomical spaces,

under endotracheal anesthesia with mechanical ventilation, or under intravenous anesthesia. According to the surgical protocol of the studied MKSh, after opening and draining the purulent focus, swabs were taken from different areas of the wound with a sterile turunda in a special transport tube after washing the wound with a stream of saline solution.

Antibacterial therapy and bacteriological examination results

In the postoperative period, patients were prescribed intravenous antibiotics until sufficient recovery of swallowing function; all patients were switched to oral antibiotics in the early postoperative period.

According to the medical prescription sheets of the 2022 MROIs, most often in the postoperative period, patients with odontogenic phlegmons of the cellular spaces of the maxillofacial region were prescribed ceftriaxone 1.0x2 per day intravenously: 12 cases out of 14, which amounted to 85.7 % of the analyzed MROIs for 2022. In 2 (14.3 %) cases, cefixime and ciprofloxacin were prescribed, due to the intake of these drugs prior to hospitalization. Out of the 12 (100.0 %) MROIs, where ceftriaxone was prescribed, the sensitivity of the microflora to the antibiotic concurred in 4 cases, which amounted to 33.3 %. Thus, the mismatch of the sensitivity of the microflora to the prescribed antibiotic amounted to 66.7 % (p=0.09) cases. Sensitivity of the flora was also detected to ampicillin in 4 (33.3 %) cases, gentamicin in 5 (35.7 %) and clindamycin in 12 (85.7 %), p=0.02.

Out of the 14 (100.0 %) examined MROIs for 2022, the growth of staphylococcal flora was determined in 50.0 % (n=7) of patients: in 85.7 % (n=6) of them, the growth of Staphylococcus epidermidis (p=0.01) was obtained, which accounted for 42.8 % of the microflora described in the ICRCs for 2022, and in 14.3 % (n=1) – Staphylococcus haemoliticus, which accounted for 7.1 % of the microflora described in the MROIs for 2022.

The growth of streptococci was detected in 42.8 % (n=6) of the MROIs: Streptococcus mitis – in 83.3 % (n=5), p<0.01, Streptococcus pyogenes – in 16.7 % (n=1), which respectively accounted for 35.7 % and 7.1 % of the identified flora in the MROIs for 2022. In 85.7 % of cases of staphylococcal flora growth, methicillin resistance (MRSE+) was detected, which may be triggered by inappropriate antibiotic therapy.

According to the data obtained from the analysis of 38 (100.0 %) MROIs in 2023, amoxicillin+clavulanic acid was prescribed as a “starting antibiotic” in 60.5 % (n=23) cases (p=0.01), ceftriaxone – in 36.8 % (n=14), clarithromycin – 2.6 % (n=1); metronidazole was prescribed as a combined antibacterial therapy in 57.9 % (n=22) MROIs.

Growth of streptococcal flora was obtained in 65.7 % (n=25) cases (p=0.005): in 80.0 % (n=20) of them Streptococcus mitis was detected (p<0.01), in 8.0 % (n=2) – Streptococcus pyogenes, in 12.0 % (n=3) – Streptococcus pneumoniae.

The growth of Staphylococcae was determined in the results presented in 7.9 % (n=3) of the 2023 ICSA: the Staphylococcaceae family were represented by Staphylococcus epidermidis strains. In addition, the following microorganisms were isolated: Enterococcus durans – in 5.3 % (n=2), Delftia acidovorans, Klebsiella pneumoniae, Enterococcus faecalis, Acinetobacter lwoffii, Burkholderia cenocepacia, Pseudomonas putida – in 2.6 % (n=1) of each strain.

According to the MROIs, flora sensitivity was detected to ampicillin in 34.2 % (n=13) cases, to gentamicin in 10.5 % (n=4), and to clindamycin in 55.2 % (n=21), p=0.06.

Analysis of 112 (100.0 %) MROIs in 2024 showed that amoxicillin + clavulanic acid was prescribed as the “starting antibiotic” in 96.4 % (n=108) of MROIs (p<0.01), lincomycin, spiramycin and cefazolin in 0.8 % (n=1) each. After determining the antibacterial sensitivity, the antibiotic was changed to azithromycin in 1.8 % (n=2) of MROIs, to lincomycin, cefepime, linezolid, cefotaxime, meropenem, cefixime, levofloxacin in 0.9 % (n=1) of MROIs. Metronidazole as a combined antibacterial therapy was prescribed in 75.9 % (n=85) of MROIs (p<0.01).

Microbial flora identified in 112 (100.0 %) MROIs in 2024 was represented by the following strains: Streptococcus mitis – in 20.5 % (n=23) MROIs, Streptococcus pyogenes – in 8.0 % (n=9), Staphylococcus epidermidis – in 21.4 % (n=24), Staphylococcus haemoliticus – 0.9 % (n=1), Staphylococcus aureus – in 1.8 % (n=2), Enterobacter durans – 2.7 % (n=3), Enterobacter cloacae – 1.8 % (n=2), Enterobacter faecalis – 3.6 % (n=4), Klebsiella pneumoniae – 1.8 % (n=2), Moraxella osloensis and Candida albicans – in 0.9 % (n=1) each. In 20.5 % (n=23) of the results of the bacteriological study identified contamination with Pseudomonas substrains, half of which (10.3 %) were Pseudomonas aeruginosa.

The sensitivity of the flora was detected to *ampicillin – in 34.8 % (n=39) cases, to ¥gentamicin – in 16.0 % (n=4), *p=0.013, to clindamycin – in 57.1 %21 (n=64), (*p=0.013, ¥p<0.01).

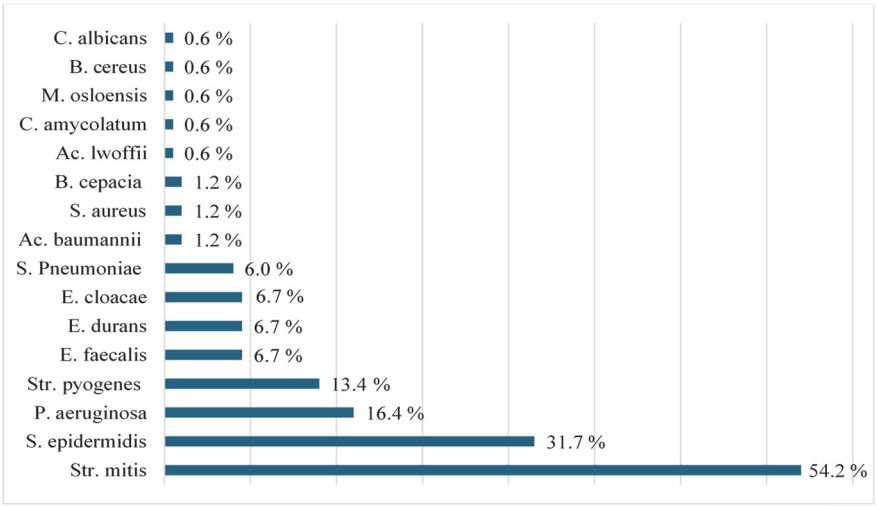

Fig. 1. Frequency of detection of strains of microorganisms from surgical wounds of patients with OPNFMFR.

Statistical analysis of the obtained data.

Microbial strains and the frequency of their detection in 164 (100.0 %) studied MKSA are presented in Fig. 1.

Analysis of the data presented in Figure 1 showed statistical significance ($p<0.05$) of the greater presence of strains of Streptococcus mitis (54.2 %) and Staphilococcus epidermis (31.7 %) in surgical wounds after opening purulent foci of the maxillofacial region. The antibiotics to which the sensitivity of the cultured flora was determined and the frequency of their determination in 164 (100.0 %) MROIs are shown in Fig. 2.

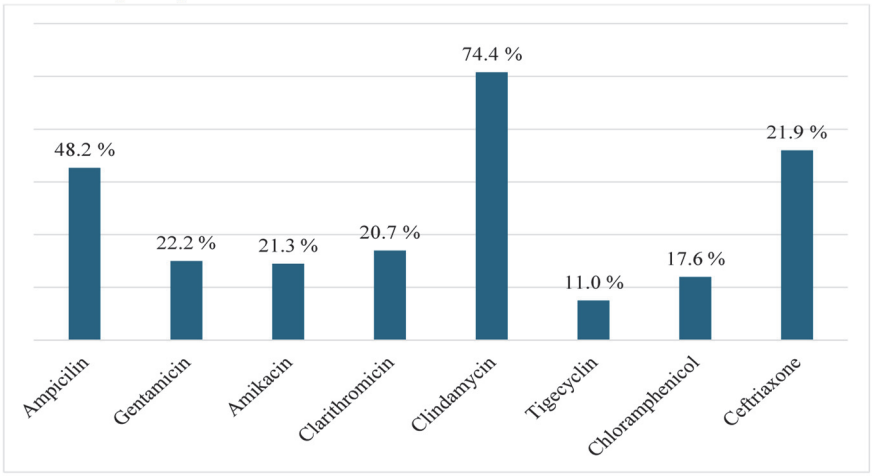

Fig. 2. Frequency of susceptibility testing to some antibacterial agents.

Statistical analysis of the data showed that out of all identified antibacterial drugs ($p<0.01$) the sensitivity of the isolated strains was determined the most tims to Clindamycin 74.4 % (n=122) and Ampicillin 48.2 % (n=79); among them, Clindamycin was determined as an effective agent significantly more often than Ampicillin ($p<0.01$). Ceftriaxone was ranked third – 21.9 % (n=36).

According to the medical prescription sheets in the MROIs from 2022-2024, in the postoperative period, patients with odontogenic phlegmons of the cellular spaces of the maxillofacial region were most often prescribed amoxicillin + clavulanic acid – 79.9 % (n=131) $p < 0.05$, metronidazole (in combination with other antibacterial drugs) – in 65.2 % (n=107), ceftriaxone – in 15.8 % (n=26) cases. Such drugs as cefixime and ciprofloxacin – in 1.2 % (n=2) cases, clarithromycin, lincomycin, spiramycin, cefazolin, levofloxacin – in 0.6 % (n=1) each.

Thus, amoxicillin+clavulanic acid (79.9 %) and ceftriaxone (15.8 %) were prescribed as the main empirical antibacterial agent; metronidazole (65.2 %) was always used as the second antibiotic. Therefore, we calculated the probability of no coincidence between the empirically prescribed antibiotic and the laboratory data on the sensitivity of microflora for amoxicillin+clavulanic acid (there is symmetrical sensitivity with ampicillin) and ceftriaxone.

For ceftriaxone, the probability index (p) was 0.3, indicating the probability that every third patient who was determined to be sensitive to ceftriaxone received another antibiotic. With amoxicillin + clavulanic acid (calculated by sensitivity to ampicillin), on the contrary, in every 4 (p=0.4) patients who received amoxicillin + clavulanic acid, the microflora was not sensitive to it.

According to 164 (100.0 %) prescription sheets, the coincidence of the sensitivity of the cultured flora with the prescription of amoxicillin + clavulanic acid (amoxicillin) was found in 26.8 % (n=44) patients, ceftriaxone – 6.7 % (n=11).

Amoxicillin is the most commonly used antibiotic in dental practice, probably due to its safety and broad spectrum of activity. Data from O. Camps-Font and H. Sábado-Bundó showed that postoperative use of amoxicillin may be the most effective strategy for reducing surgical site infection after extraction of mandibular third molars, followed by preoperative metronidazole and a combination of amoxicillin and clavulanic acid administered both preoperatively and postoperatively [2]. The most effective antibiotic in reducing the risk of post-operative inflammation was preoperative clindamycin, followed by preoperative

azithromycin, while preoperative amoxicillin ranked third and amoxicillin and clavulanic acid administered both preoperatively and postoperatively ranked fourth [5].

Although penicillin remains the antibiotic of choice for mild to moderate odontogenic infections in immunocompetent patients, several authors recommend against its use as initial therapy for more serious infections possibly associated with penicillin-resistant oral anaerobes [7].

According to the 2023 Standard of Care for the Rational Use of Antibacterial and Antifungal Drugs for Therapeutic and Prophylactic Purposes, the combination of metronidazole with protected penicillins or lincosamides is not recommended [1].

The choice of drug for empirical antibiotic therapy is based on the expected therapeutic effect against the most likely infectious agent (depending on the anatomical localization of the focus of inflammation) and its possible resistance to the selected antibacterial drug (data from local/regional/national AMR monitoring). It is also necessary to take into account the conditions of occurrence of the disease of bacterial etiology (hospital/community-acquired) and the risk of the patient having MDR.

According to the data obtained in our study, most often in surgical wounds due to the drainage of purulent-necrotic foci of the maxillofacial area, colonization with Str. mitis, S. pyogenes, S. epidermidis, and also Pseudomonas spp. is determined. The antibacterial drugs of the Access group, to which the microbiota of the studied wounds is likely sensitive, were found to be: clindamycin, ampicillin, gentamicin.

In our opinion, the appointment of clindamycin as a starting antibacterial drug for the treatment of purulent-necrotic lesions of the adipose tissue of the maxillofacial region may be appropriate not only in cases where the patient is allergic to beta-lactams, given its availability, spectrum of action, and osteotropic properties (close etiological relationship of these diseases with inflammatory conditions of the jaws).

Conclusions

1. Most often in the postoperative period, patients with odontogenic purulent-necrotic foci of the cellular spaces of the maxillofacial region were prescribed amoxicillin + clavulanic acid (79.9 %) $p < 0.05$, metronidazole (65.2 %), ceftriaxone (15.8 %).

2. Statistically, the sensitivity of the isolated strains was determined to clindamycin (74.4 %), $p < 0.01$, ampicillin (48.2 %) and ceftriaxone (21.9 %).

3. Statistical analysis showed that every third patient who was determined to be sensitive to ceftriaxone probably received another antibiotic ($p=0.3$), and the microflora of every fourth ($p=0.4$) patient who received amoxicillin + clavulanic acid was probably not sensitive to it.

In the future, we plan to conduct studies on anaerobic microorganisms in postoperative wounds as microbial factors that may have resistance to the indicated antibacterial drugs and change the pattern of antibacterial sensitivity and the course of the studied infections. We also plan to study the quantitative and qualitative composition of the microflora of purulent-necrotic foci of the maxillofacial region and treatment methods during the studied years.

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