**Introduction**

Gram-negative non-fermenting microorganisms are the dominant pathogens of nosocomial infections, including those in maxillofacial surgery units [0]. Representatives of the genus *Acinetobacter* and *Pseudomonas* are quite often isolated from foci of infection in the facial area. In addition, they prevail in the development of postoperative complications, delaying the recovery of patients [2, 3]. *Acinetobacter* and *Pseudomonas* infections have been recognized as an emerging problem (one of major cause of nosocomial infections) and appeared to be associated with high mortality rates throughout the world [4].

The main problem in the treatment of infections caused by gram-negative non-fermenting bacteria is a powerful set of pathogenicity factors of pathogens and their rapid development of antibiotic resistance [2, 5]. Representatives of the above-mentioned genera have mobile genetic elements that ensure resistance in the presence of antibiotics of different groups and are responsible for the transfer of information about them between microorganisms [4]. Moreover, pathogens are able to produce hydrolytic enzymes that inactivate beta lactam antibiotics [6].

It becomes obvious that possessing such an arsenal of means for adaptation, *Acinetobacter* and *Pseudomonas* mutate rather quickly and develop multidrug resistance. The annual reports of EUCAST show that the therapeutic doses of antibiotics for these microorganisms are progressively decreasing [7].

Considering the above, timely monitoring of the sensitivity of gram-negative non-fermenting bacteria taken from various site of the human body to antibiotics is extremely important to cut off and overcome their significant resistance.

The aim of the study is to determine the sensitivity of gram-negative causative agents of infectious inflammatory diseases of soft tissues in the face area to antibiotics.

**Materials and methods**

The study included 25 clinical isolates of the genus *Acinetobacter* and 22 clinical isolates of the genus *Pseudomonas*. The microorganisms were isolated from patients with infectious and inflammatory diseases of the soft tissues of the face who took treated at Poltava Regional Centre of Dentistry - Dental Clinical Polyclinic for 2019 – 2022. The material was collected before the beginning of antibiotic therapy after the patient had signed an informed consent giving the permission to take the material for research. Cultivation of microorganisms was carried out according to generally accepted methods, final identification was performed by using morphological, tinctorial and
biochemical properties of pathogens.

Determination of the sensitivity of microorganisms was evaluated by using the disc diffusion method and the method of double serial dilutions in a liquid nutrient medium, in accordance with the recommendations EUCAST (Version 12.0, valid from 2022-01-01) [7]. Mueller Hinton agar and broth were used to determine the sensitivity of microorganisms. The list of antibiotics used in the study was determined according to the EUCAST recommendations for each genus of microorganisms separately. Interpretation of the results was performed based on the EUCAST Clinical Breakpoint tables, according to which microorganisms were divided into sensitive and resistant, in some cases, if possible, into sensitive to the antibiotic under increased exposure.

Descriptive statistical methods with determining the arithmetic mean and percentage of the total number were used to process the findings obtained. We used the start-up packages of the Microsoft Excel 2019 and Prisma Pad programs.

Results and discussion

The study has shown that Acinetobacter spp., isolated from patients with infectious and inflammatory diseases of the soft tissues of the face, have a low sensitivity to antibacterial drugs of various groups (Pic. 1). The level of sensitivity of representatives of this genus to imipenem and meropenem did not exceed 29.6%. At the same time, the proportion of isolates resistant to the above-mentioned antibiotics was also almost unchanged: 51.9% of microorganisms resistant to imipenem vs. 48.2% of microorganisms resistant to meropenem.

The lowest sensitivity of Acinetobacter spp. demonstrated to fluoroquinolones. The frequencies of detection of clinical isolates resistant to ciprofloxacin and levofloxacin were 63.0% and 55.6%, respectively. When the number of acinetobacteria sensitive to levofloxacin was at the level of those sensitive to carbapenems, the level of sensitivity of these bacteria (11.1%) to ciprofloxacin was record as low. Although the shares of representatives of the genus Acinetobacter that were classified as "susceptible to increased exposure to ciprofloxacin and levofloxacin were within 25.9% and 6% 22.2%, respectively.

The study revealed the highest sensitivity of Acinetobacter spp. to aminoglycosides: there were 44.4% of resistant clinical isolates of this genus to amikacin and 37.0% resistant microorganisms to gentamicin. In addition, the absence of sensitive isolates under increased exposure to the antibiotic increased the number of sensitive Acinetobacter spp. to the investigated aminoglycosides. Thus, the proportion of acinetobacter sensitive to amikacin made up 55.6%, pathogens sensitive to gentamicin constituted 63.0% that was recorded as the highest result of sensitivity among Acinetobacter spp.

Among penicillins, the EUCAST committee recommended determining the sensitivity of Pseudomonas spp. only to piperacillin (Pic. 2). The level of resistance found exceeded 50% of cases. In turn, only 18.2% of clinical isolates of the genus Pseudomonas showed sensitivity to the studied penicillin. Pseudomonas spp. showed higher sensitivity to cephalosporins. Thus, the shares of sensitive microorganisms of this genus to cefepime and ceftazidime were 22.7% and 36.4%, respectively, while the number of resistant isolates (45.5%) was the same to both antibiotics.

The similarity of the sensitivity results of Pseudomonas spp. to carbapenems, imipenem and meropenem, was found. The frequency of detection of resistant isolates among them to imipenem was within 40.9%, to meropenem – within 36.4%. Along with this, testing the sensitivity of pseudomonads to protected carbapenems showed a better result. The sensitivity of the studied isolates to imipenem relabactam (51.1%) exceeded the sensitivity to unprotected imipenem twice as much and the sensitivity to meropenem verobactam increased in 1.6 times compared to the sensitivity to unprotected meropenem.

Clinical isolates of Pseudomonas spp. showed high resistance to fluoroquinolones. The level of resistance among representatives of this genus to ciprofloxacin and levofloxacin reached 54.5% and 51.1%, respectively. At the same time 27.3% isolates were assigned to the category of sensitive under increased exposure to both ciprofloxacin and levofloxacin, reducing the proportion of actually sensitive microorganisms.

Among aminoglycosides, Pseudomonas spp. demonstrated sensitivity to amikacin, which was at the level of 45.5%.

Conclusions

Acinetobacter spp. and Pseudomonas spp., isolated from patients with infectious and inflammatory diseases of the soft tissues of the face, have low sensitivity to antibacterial drugs of various groups. Acinetobacter spp. showed the highest sensitivity to gentamicin and amikacin. Pseudomonas possessed the highest sensitivity to cefiderocol, imipenem relabactam and meropenem verobactam.
References

1. Nazarchuk O, Dmyrtriiev D, Babina Y, et al. Research of the activity of local anaesthetics and antiseptics regarding clinical isolates of Acinetobacter baumannii as pathogens of postoperative infectious complications. Acta Biomed. 2022 Mar 14;93(1):e2022003.

2. Meinen A, Reuss A, Willrich N, et al. Antimicrobial resistance and the spectrum of pathogens in dental and oral-maxillofacial infections in hospitals and dental practices in Germany. Front Microbiol. 2021 Jun 2;12:676108.

3. Shaprynskyi V, Nazarchuk O, Faustova M, et al. Some aspects of infectious complications in patients with surgical diseases. Multicent trials. Lek. Obzor. 2020;69(7–8):257–260.

4. Abdar MH, Taheri-Kalani M, Taheri K, et al. Prevalence of extended-spectrum beta-lactamase genes in Acinetobacter baumannii strains isolated from nosocomial infections in Tehran, Iran. GMS Hyg Infect Control. 2019 Jan 25;14:Doc02.
5. Nazarchuk O, Faustova M, Bobyr V et al. The investigation of the relationship between biofilm-forming properties of clinical strains of p.aeruginosa and their sensitivity to antiseptic medicines. Reports of Vinnytsia National Medical University. 2018; 22(3), 403-406.

6. Khoshnood S, Heidary M, Mirnejad R, et al. Drug-resistant gram-negative uropathogens: A review. Biomed Pharmacother. 2017 Oct;94:982-994.

7. European Committee on Antimicrobial Susceptibility Testing. European antimicrobial breakpoints. Basel: EUCAST, 2021. [Internet] Available from: https://eucast.org/clinical_breakpoints/

Реферат

ЧУТЛИВІСТЬ ГРАМНЕГАТИВНИХ ЗБУДНИКІВ ІНФЕКЦІЙНО-ЗАПАЛЬНИХ ЗАХВОРЮВАНЬ М’ЯКИХ ТКАНИН ЛИЦЕВОЇ ДІЛЯНКИ ДО АНТИБІОТИКІВ

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Ключові слова: Acinetobacter, Pseudomonas, антибіотики, резистентність, чутливість до антибіотиків.

Сьогодні надзвичайно важливим є своєчасний моніторинг чутливості грамнегативних неферментуючих бактерій, виділених з різних біотопів організму людини, до антибіотиків задля зупинення та подолання їх значущої резистентності.

Мета дослідження – визначити чутливість грамнегативних збудників інфекційно-запальних захворювань м’яких тканин лицевої ділянки до антибіотиків.

Матеріали та методи. Об’єктами дослідження були 25 клінічних ізолятів роду Acinetobacter та 22 клінічних ізолятів роду Pseudomonas.

Визначення чутливості мікроорганізмів проводили диско-дифузійним методом та методом подвійних серійних розведень у рідкому питому середовищі, згідно з рекомендаціями EUCAST.

Результати. Рівень чутливості представників роду Acinetobacter до іміпенему та меропенему не перевищував 29,6 %. Найнижчу чутливість вони продемонстрували до фторхінолонів, найбільшу – до амінглікіозідів.

Pseudomonas spp. виявляли низьку чутливість до пеницилінів і цефалоспоринів. Подібність результатів чутливості Pseudomonas spp. до карбапенемів: іміпенему та меропенему, зареєстровано. Разом з цим, тестування чутливості Pseudomonas spp. до захищених карбапенемів показало кращий результат. Крім того, клінічні ізоляти Pseudomonas spp. показали високу стійкість до фторхінолонів та амінглікіозідів. Висновки. Acinetobacter spp. та Pseudomonas spp., виділені від хворих на інфекційно-запальні захворювання м’яких тканин лицевої ділянки, мають досить низьку чутливість до антибактеріальних препаратів різних груп.

Acinetobacter spp. виявили найбільшу чутливість до гентаміцину та амікацину. Pseudomonas володіли найвищою чутливістю до цефідероколу, іміпенему релабактаму та меропенему верабактаму.