ORIGINAL STUDIES

Scientific Article
UDC 615.281.03: 616-9-022.369: 579.861.2.] 015.8
DOI: 10.17816/pmj4125-10

ANALYSIS OF LONG-TERM DYNAMICS OF ANTIBIOTIC SENSITIVITY OF COAGULASE-NEGATIVE STAPHYLOCOCCI ISOLATED FROM SURGICAL HOSPITAL PATIENTS AT VARIOUS TIMES

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АНАЛИЗ МНОГОЛЕТНЕЙ ДИНАМИКИ АНТИБИОТИКОЧУВСТВИТЕЛЬНОСТИ КОАГУЛАЗООТРИЦАТЕЛЬНЫХ СТАФИЛОКОККОВ, ИЗОЛИРОВАННЫХ В РАЗЛИЧНЫЕ СРОКИ ОТ ПАЦИЕНТОВ ХИРУРГИЧЕСКОГО СТАЦИОНАРА

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Objective. To carry out twenty-year analysis of dynamics of antibiotic sensitivity of coagulase-negative staphylococcal strains isolated from surgical hospital patients.

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Materials and methods. The antibiotic sensitivity of 191 strains of coagulase-negative staphylococci isolated in 2004, 2014, 2023 year from surgical hospital patients was studied with the disk diffusion method.
Results. A significant increase in the proportion of strains resistant to all antibiotics known, especially ciprofloxacin, was found.
Conclusion. A twenty-year analysis of the dynamics of antibiotic sensitivity showed a significant increase of antibiotic resistance of coagulase-negative staphylococcus strains isolated from surgical patients.
Keywords. Antibiotic sensitivity, coagulase-negative staphylococci, antibiotic resistance.

Цель. Многолетний анализ динамики антибиотикочувствительности штаммов коагулазоотрицательных стафилококков, изолированных от пациентов хирургического стационара.
Материалы и методы. Изучена антибиотикочувствительность 191 штамма коагулазоотрицательных стафилококков, изолированных в 2004, 2014, 2023 гг. от пациентов хирургического стационара. Чувствительность изолятов к антибиотикам определяли диско-диффузионным методом.
Результаты. В процессе наблюдения установлено значительное увеличение доли антибиотикорезистентных штаммов, что было характерно по отношению ко всем изученным препаратам, особенно существенно к ципрофлоксацину.
Выводы. Двадцатилетний анализ показал существенный рост антибиотикорезистентности штаммов коагулазоотрицательных стафилококков, изолированных от больных хирургического профиля.
Ключевые слова. Антибиотикочувствительность, коагулазоотрицательные стафилококки, антибиотикорезистентность.

INTRODUCTION

Staphylococci are widespread in nature. They inhabit various biotopes of the human and animal body, can be found in the air, water, and on household items [1]. These microorganisms are characterized by a pronounced species diversity. There are more than 45 species currently known. Traditionally, bacteria of the *Staphylococcus* genus are classified as conditionally pathogenic microorganisms. Meanwhile, they can cause a wide variety of infectious and inflammatory diseases, from the ordinary purulent processes to severe pneumonia and sepsis [1–3]. This diversity of infectious nosology is appreciably explained by the polytropic character of staphylococci. The aetiological role of these microorganisms in the development of healthcare associated infectious (HAIs) and inflammatory diseases is of a particular significance [2; 3].

Previously, the main cause of staphylococcal infections was only considered to be bacteria of one type – *S. aureus*. Representatives of this type of staphylococci have been the main causative agents of various purulent infections of surgical wounds for more than a hundred years [4]. In recent years, coagulase-negative staphylococci (CoNS) have become more and more common as aetiological agents of such diseases. [5]. They cause a significant number of HAIs. Treatment of such diseases is significantly difficult, since CoNS strains circulating in hospitals are usually characterized by high antibiotic resistance [6; 7]. At the moment, the problem of resistance of staphylococci to chemopreparations is becoming increasingly relevant.

Methicillin-resistant CoNS strains are often isolated from patients in surgical hospitals, which is due to the synthesis of penicillin – binding protein (target change mechanism). Strains that are resistant to carbapenems and other modern antibacterial drugs are also frequently isolated [8; 9]. Their source can be both medical personnel and patients undergoing treatment in an inpatient department [10; 11]. At the same time, the number of pandrug-resistant strains of CoNS – pathogens of HAIs – is steadily increasing [5; 6].

The objective of the study was a long-term analysis of the dynamics of antibiotic sensitivity of coagulase-negative staphylococcal strains isolated from surgical hospital patients.

MATERIALS AND METHODS

The antibiotic sensitivity of 191 CoNS strains isolated from the wound effluent of surgical patients with various infectious and inflammatory complications developed after thoracic surgery was studied in a comparative aspect, including: 62 strains in 2004; 48 – in 2014; 81 – in 2023. Pure cultures were isolated and identified using the classical bacteriological method. The sensitivity of isolates to antibiotics was studied using the traditional disk diffusion method on Givental-Vedmina (2004) and Muller-Hinton (2014, 2023) agar. Inoculation, recording of the results obtained, and selection of test preparations were carried out in accordance with methodological guidelines MUK 4.2.1890-04 "Determination of the sensitivity of microorganisms to antibacterial drugs". The main groups of antibiotics used were oxacillin/ceftazidime (β-lactams), erythromycin (macrolides), gentamicin (aminoglycosides), lincomycin (lincosamides), thienam (carbapenems), ciprofloxacin (fluoroquinolones). The proportion of sensitive strains was expressed as a percentage.

RESULTS AND DISCUSSION

CoNS strains isolated from surgical hospital patients at various times were of a fairly wide species diversity: *S. epidermidis, S. varneri, S. saprophyticus, S. cochnii, S. hominis, and S. chromogenes*. However, in the vast majority of cases (from 78 to 90 %), the wound effluent contained cultures of *S. epidermidis*, while representatives of other species were detected in isolated cases. In this regard, we further considered it possible to group all such isolated strains together under the term "CoNS". Since earlier antibiotics were periodically rotated in medical institutions, when studying the antibiotic sensitivity of isolated strains, we only used the drugs that were used at all the specified reference points. The results obtained are shown in the table.

It follows from the received data that the proportion of sensitive strains isolated from patients in 2004 was higher. Further – in 2014 and especially in 2023 – the proportion of resistant strains increased. This trend was characteristic for practically all tested antibiotics.

Results of studying the antibiotic sensitivity of CoNS strains isolated from surgical hospital patients at different periods of observation

Reference points, years	Proportion of antibiotic-resistant CoNS strains, %					
	oxacillin/ ceftazidime	gentamicin	erythromycin	lincomycin	thienam	ciprofloxacin
2004	15.91	7.8	14.3	8.6	1.4	9.8
2014	19.4	35.7	21.2	21.0	7.4	35.7
2023	38.2	36.4	44.1	17.6	21.1	98.0

It was specifically evident in the case of ciprofloxacin (fluoroquinolones). While in 2004, only 9.8 % of bacterial strains were resistant to this antibiotic, by 2023, this number had increased to 98 %.

As for the antibacterial activity of certain drugs, thienam was the most effective in all observation periods. Thus, 1.4 % of strains were resistant to it in 2004, while 7.4 % and 21.1 % appeared to be resistant in 2014 and 2023, respectively.

It should be noted that the antibiotic resistance of the studied CoNS strains increased. Thus, after the first 10 years from the beginning of observation, the proportion of resistant strains increased slightly. This applies essentially to all tested drugs, except gentamicin. Subsequently, from 2014 to 2023, the antibiotic resistance of CoNS strains increased several times over. It can be assumed that the accumulation of antibiotic-resistant strains circulating in the healthcare institutions in recent years is largely due to the widespread use of antibiotics during the COVID-19 pandemic, when they were used for the prevention and treatment of bacterial complications.

The analysis of the resistance of CoNS strains to methicillin in different periods of observation is of certain interest, since, as is known, the resistance of bacteria to this drug indicates their resistance to β-lactam antibiotics. Over time, an increase in the proportion of resistant strains to this drug was also observed. Thus, in 2004 there were 2.8 % of them, while in 2014 their number increased up to 21 %, and up to 38 % – in 2023. At the same time, among methicillin-resistant staphylococci, some multidrug resistant cultures resistant to three or more antibiotic drugs were detected significantly more often.

CONCLUSION

A twenty-year analysis of the dynamics of changes in the antibiotic sensitivity of CoNS strains isolated from patients with infectious and inflammatory complications that occurred after thoracic surgery showed a significant increase in the antibiotic resistance of these bacteria, especially to ciprofloxacin. The number of methicillin-resistant strains also increased significantly. These circumstances should

be taken into account in the treatment of emerging postoperative complications. The administration of certain antibacterial drugs should be preceded by an investigation of the antibiotic sensitivity of isolated aetiopathogens.

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Funding. The study had no external funding.

Conflict of interest. The authors declare no conflict of interest.

Author contributions are equivalent.

Received: 12/03/2023
Revised version received: 12/26/2023
Accepted: 03/15/2024

Please cite this article in English as: Afanasievskaya E.V., Kasatov A.V., Nikolaeva N.V., Pospelova S.V. Analysis of long-term dynamics of antibiotic sensitivity of coagulase-negative staphylococci isolated from surgical hospital patients at various times. *Perm Medical Journal*, 2024, vol. 41, no. 2, pp. 5-10. DOI: 10.17816/pmj4125-10