

Infections Related to Medical Care

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Annotation: The current problems of the prevention of infections related to the provision of medical care (ISMP) that arise at the present stage, in particular, the spread of antibiotic resistance, are discussed. It is noted that currently, in terms of reducing the risk of developing resistance of pathogenic microorganisms, it is necessary to take into account the phenomenon of antibiotic tolerance of bacteria, which is associated with a decrease in the level of metabolism, cessation of cell growth and shutdown of targets for antibiotics. Such persistent forms of microorganisms ensure the survival of the bacterial population, but not reproduction in the presence of lethal doses of antimicrobials. This kind of phenotypic resistance is not inherited, it is associated with such specific forms as growth in biofilms, and its carriers are a reservoir for the spread of resistance genes. Modern possibilities of avoiding the accumulation of persistent forms of ISMP pathogens, including the creation of antibiotic compositions and substances that block the adaptive reactions of the microorganism, are presented. Modern methods for the indication of ISMP pathogens existing in the hospital environment in the form of biofilms, as well as new methodological approaches to the destruction of such biofilms, are proposed.

Keywords: infections related to medical care, antibiotic resistance, persisters, bacteriophages, biofilms.

Despite the tremendous progress in the field of healthcare, the rapid development of the pharmaceutical industry and medical equipment in the context of modern modernization of healthcare, the widespread introduction of the latest technologies for diagnosis and treatment, the prevention of infections associated with the provision of medical care (ISMP) remains one of the most pressing problems. The addition of ISMP to the underlying disease increases the duration of the patient's stay in the hospital by an average of 6 to 8 days. Nosocomial infections negate the most difficult operations on vital organs, negate the efforts spent on nursing newborns, and have an impact on infant mortality. Mortality in various nosological forms of ISMP in the case of generalization of infection ranges from 35 to 60%, reaching the same level as in the pre-antibiotic era.

Multidisciplinary hospitals create conditions conducive to the occurrence of ISMP: a huge concentration of people with reduced immunity in a limited area, the presence of a significant number of sources of infection (patients and carriers) among patients and medical personnel, a peculiar microbial landscape, changes in the biocenosis of mucous membranes and skin in patients and medical personnel under the influence of widespread use of antibiotics and cytostatics. Under these conditions, the rate of evolution of microorganisms is significantly accelerated, prerequisites are created for the formation of strains with new properties not only from among pathogenic and conditionally pathogenic microorganisms, but also from representatives of normal microflora. The process of formation of multidrug-resistant pathogens is underway [3].

As a result of the above reasons, as well as the irrational use of antimicrobial drugs, resistant hospital strains are increasingly taking the leading place among the pathogens of ISMP. The main reasons for the spread of resistance of microorganisms and harmful organisms of plants are, among other things, the formation of nosocomial strains of microorganisms that are resistant to medicines, chemical and biological agents; and one of the main directions of the implementation of measures aimed at improving measures to prevent and limit the spread and circulation of pathogens with antimicrobial resistance is the introduction of modern methods of prevention, diagnosis and treatment of infectious diseases that prevent the formation and spread of antimicrobial resistance, including etiological diagnostics and determination of resistance of pathogens of infectious diseases to antimicrobial drugs,

optimization of treatment regimens, ensuring a reduction in the risk of developing resistance of pathogenic microorganisms to antimicrobial drugs [2].

Currently, two fundamentally different concepts of bacterial antibiotic resistance are being considered. The first is antibiotic resistance (AR), which is associated with structural changes in the genome, inherited, leading to changes in targets for antibiotics, their release from the cell or destruction. The second direction (apparently more ancient) is antibiotic tolerance (AT), which is associated with phenotypic changes (leading to a decrease in the level of metabolism, cessation of cell growth and shutdown of targets for antibiotics), which ensures the survival, but not the reproduction of bacteria in the presence of lethal doses of medicinal agents. Phenotypic resistance is not inherited and is associated with such specific forms as growth in biofilms, the formation of a small number (0.01-1%) of persistent forms in a developing population [1, 3, 4].

Persistent forms of bacteria (persisters): 1) have multiple drug tolerance; 2) are formed, including in populations of AR bacteria resistant to any particular antibiotic (cam); 3) are formed regardless of the presence of an antibiotic (stressor) as an evolutionarily developed constitutive form of survival of a population (species); 4) are found in the composition of biofilms [5].

In this regard, the appearance of persistent forms resistant to any medicinal agents in the developing microbial population reflects a higher-level phenomenon - the heterogeneity of the isogenic microbial population [2,8], which ensures its resistance to various stressors, where antibiotic tolerance is only a special case.

In recent years, similar studies have been conducted quite intensively in the world, and there are already specific medicines. American scientists have shown that the use of special peptides that block the adaptive capabilities of microorganisms significantly increases the bactericidal activity of AB. There is a French drug that also blocks adaptation processes, which was confirmed when it was used in combination with antibiotics. Although at the moment such drugs have just begun to appear in the world, so to speak, the first sprouts, in the very near future we will witness the rapid growth of such drugs, as happened to AB after the discovery of penicillin.

Scientists are also currently expanding exploratory research aimed at identifying specific molecules involved in bacterial adaptation processes; expanding the range of AAD and verifying their epidemiological and clinical role. We see great practical prospects in creating test systems of various formats to determine the size of the surviving, in other words, adapted, population of microbes.

A technology has already been developed for the production of new binary drugs that reduce metabolic activity in pathogenic bacteria in order to suppress the mechanisms of AR. Such binary compositions (AB+AAD) represent a new type of domestic antimicrobial drugs that carry clear potential for the global pharmaceutical market.

It has been reliably proven that multi-species biofilms of bacteria and fungi play a major role in the emergence and spread of ISMP, in the formation of hospital strains [1, 3]. The ability of bacteria to form biofilms (BP) is currently considered as one of the factors of their virulence, while different types of opportunistic microorganisms have different abilities to form BP, and this phenotypic trait can be considered as a virulence factor of this particular strain [4,7]. The bacteria that form BP exhibit significantly higher resistance in the environment, including to antimicrobial agents (up to 1,000 times compared to planktonic cells), disinfectants, and physico-chemical environmental factors, which makes it extremely difficult to combat the pathogens of ISMP and negates infection prevention measures. Existing in the form of PD, ISMP pathogens persist in the hospital environment, being a reservoir of infectious agents for several weeks and even months. Various objects of the hospital environment (surfaces of beds, bedside tables, trolleys, chairs, telephones, call buttons and others; medical diagnostic equipment and devices) can be "populated" by BP, since it is known that smooth surfaces colonize as easily as rough ones, and the physical features of the surface have very little effect on the adhesion of microorganisms, as well as the presence of moisture on objects [5,6,7].

The ability to intensively biofilm formation on abiotic objects is one of the main manifestations of the adaptive mechanisms of ISMP pathogens, allowing them to survive and persist in an aggressive (for microorganisms) MO environment, which is constantly changing, moreover, improving based on the needs of the microorganisms that create it. In this regard, understanding the patterns of PD formation will allow us to find a way to uncover the mechanisms of formation of hospital strains of microorganisms, which will serve to improve the system of epidemiological surveillance of ISMP.

Conclusion. The main scientific and practical directions of studying ISMP at the present stage are studies in the field of adaptive capabilities of microorganisms in the hospital environment (antibiotic tolerant forms of microorganisms, biofilm formation), contributing to the formation of ISMP pathogens resistant to a wide range of antimicrobial agents.

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