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THE MODERN ASPECTS OF ANTIBIOTIC RESISTANCE AND WAYS OF ITS PREVENTION

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Summary. In this work, we present the information about the importance of the problem of antibiotic resistance all over the world. Main reasons and biochemical mechanisms of that dangerous situations are described. Initial ways and measures for prevention of progression of the antibiotic resistance are detected.

Key words: antibiotic resistance, biochemical mechanisms, prevention, global threat, microorganisms.

Since the beginning of the antibiotic era, with the discovery of the first antibiotics the irrational and abuse of antibiotics in human medicine have accelerated the growing worldwide phenomenon of antimicrobial resistance (AMR). Nowadays, the frequency of antibiotic resistance is rapidly increasing and spreading daily across the world, according to the up-to-date data. According to the World Health Organization antibiotic resistance has been described as one of the one of the top 10 global threats of the 21st facing humanity. It causes about 700,000 deaths each year, reaching 10 million worldwide by 2050, unless effective measures are fulfilled. It is becoming actual today because of uncontrolled using of antibiotics while treating SARS-CoV-2 pandemic [1, p 105].

Antimicrobial resistance is the ability of microorganisms, such as bacteria, fungi, viruses or protozoa to invalidate the effects of antimicrobial drugs. As a result, the microorganisms survive, multiply and spread rapidly, being no longer respond to the particular drug. The more drugs are used in this case, the more chance bacteria have to become resistance to them [2, p. 53].

It is known two kinds of AMR, such as natural and acquired [3, p. 14]. Natural resistance can be intrinsic (always expressed in the species), which is easily predictable and remains unchanged for a period of time or induced (the genes are naturally occurring in the bacteria, but are only expressed to resistance levels after exposure to an antibiotic). Moreover, microorganisms with such kind of resistance are insensitive to defined antibiotics a priory, as they do not have the target for specific drugs or their membrane is impenetrable. While the acquired resistance is caused by the main routes by which bacteria acquire any genetic material: transformation, transposition, and conjugation or the bacteria may experience chromosomal DNA mutations [4, p 38].

The mechanisms of ARM have been known for a long time, there are 4 main mechanisms of antibiotic resistance: inactivation, alteration of the target, circumvention of the target pathway or efflux of the antibiotic.

The most common is inactivation of antibiotic molecules. This mechanism function for antibiotics belonging to the most diverse classes of chemical compounds, such as β-lactamase, aminoglycosides, chloramphenicol, erythromycin, lincomycin and related compounds [5, p. 202]. Inactivation occurs due to the synthesis of enzymes capable of specifically reacting with the antibiotic and modifying it, by disrupting its affinity for the target, by irreversibly binding and not allowing it to react with the target, or by completely inactivating or destroying the antibiotic molecule.

The alteration of the target is caused by 2 diffract mechanisms. The first one is associated with the occurrence of spontaneous gene mutations leading to structural changes in the target molecules encoded by it, disrupting antibiotic binding, and the stabilization of such mutations in the presence of antibiotics. The second way of

resistance by this mechanism is caused by the presence of genes that can be transmitted using horizontal transfer. The products of these genes modify the target molecule. In this case, because of modification of the target, the process of binding of the antibiotic to it is either partially or completely disrupted.

The circumvention of the target is carried out in two main ways: (1) active elimination of the antibiotic from the microbial cell and (2) disruption of the permeability of the outer membranes of the microbial cell.

The efflux is based on the work of a specialized set of proteins that form the so-called transmembrane pumps. Such transmembrane pumps are capable of transporting toxic substances, xenobiotics, including antibiotics of most of the currently known classes, except glycopeptides, from the intracellular space into the external environment [6, p. 490].

The WHO has detected high levels of resistance to third-generation cephalosporins in the case of Klebsiella pneumoniae infection throughout the Europe. According to reports from different countries, 60% of Staphylococcus aureus infections show resistance to methicillin (methicillin-resistant Staphylococcus aureus -MRSA) [3, p. 16].

According to the WHO, in order to prevent antibiotic resistance, it is used seven key priorities, such as: optimizing prescribing practices (i.e. antimicrobial stewardship), improving infection prevention and control, raising awareness and changing behavior, improving the evidence base through research, development of new drugs/vaccines/other diagnostics and treatments, improving evidence base through surveillance, strengthening the international collaboration [7, p. 390].

Thus, the problem of antibiotic resistance began to take shape extremely fast and has become a global threat. It is crucial to educate our societies about the danger behind the overuse and misuse of antimicrobial drugs. As there is no single reason of this problem existence, we should prescribe antibiotics very carefully due to the patient`s anamnesis and laboratory tests, accommodate all for and against factors and explain to the patients the consequences of taking antibiotics irrational. Everyone can take simple actions in order to prevent AMR, prevention is better than cure.

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