Progress in antibiotic resistance research

Minghong Li

Abstract

Antibiotics are chemical substances produced by microorganisms that have antibacterial and anti-inflammatory effects. It inhibits or kills infections caused by sensitive bacteria and is mainly used to treat various infectious diseases caused by bacteria. Antibiotics can exert their antimicrobial effects by inhibiting cell wall synthesis, inhibiting protein synthesis, and affecting bacterial DNA synthesis. There are many types of antibiotics, including penicillins, cephalosporins, tetracyclines, macrolides, aminoglycosides, and so on. When using antibiotics, sensitive antibiotics should be selected according to the specific infectious agent and used correctly according to the doctor's advice to avoid the development of drug resistance and reduce the Impact of side effects. With the extensive use of antibiotics, antibiotic resistance has become a key concern in the use process, closely related to the genetic mutation of bacteria, antibiotic abuse, and decreased immunity. This paper provides a way to understand more about antibiotics by expressing the classification of antibiotics, the causes of resistance, and the mechanism of resistance.

Keywords: Antibiotic Antibiotic-resistant Bacteria

Status of antibiotic resistance

Antibiotic resistance has become a growing problem in today's healthcare. The current state of antibiotic resistance encompasses several aspects, including increased bacterial resistance, difficulties in treating infections with resistant bacteria, the spread of hospital-acquired infections, the problem of antibiotic misuse, the spread of resistance genes, insufficient surveillance of resistance globally, and insufficient preventive and control measures for resistance. Antibiotic resistance is very serious, and there is an urgent need to strengthen antibiotic resistance surveillance and preventive and control measures globally. Antibiotic resistance has become a major risk to human health, causing 700,000 deaths worldwide each year, with millions more expected to die by 2050 if the problem is not properly addressed. Only through joint efforts can we effectively reduce the emergence of antibiotic resistance and safeguard human health and social development.

1. Classification of antibiotics

1.1 Beta-lactams

Beta-lactam antibiotics are a class of broad-spectrum antibiotics, including penicillins, cephalosporins, and carbapenems. These antibiotics kill bacteria by inhibiting the synthesis of bacterial cell walls and are highly effective, low toxicity, and broad-spectrum. Recently, it has been found that β-endophthalaminase inhibitors have obvious synergistic effects with ampicillin, and the combination of the two can improve the efficacy of ampicillin and expand the indications. Aminobenzylpenicillin and penicillin sulfone, with a 2:1 composition of compound ampicillin, can make the original ampicillin-resistant bacteria such as Aureobasidium, Escherichia coli, Klebsiella and Aerobacter, etc., to restore the sensitive, clinically, to achieve the corresponding results[1]. The antibacterial spectrum of carboxythiophene penicillin is similar to that of carboxybenzylpenicillin, with stronger antibacterial power against anaerobic bacteria and Pseudomonas aeruginosa, and resistance to Klebsiella pneumoniae, Serratia marcescens and β-propionic acid aminase-producing bacillus influenzae[2].

1.2 Macrolides

Macrolide antibiotics mainly include erythromycin, azithromycin, clarithromycin, and so on. These antibiotics kill bacteria by inhibiting the synthesis of bacterial proteins, which have the characteristics of a narrow antibacterial spectrum and do not easily produce drug resistance. The special position of new macrolides in respiratory out-of-hospital infections The pharmacokinetics of new macrolides have been improved, with a prolonged half-life, further increase in tissue penetration, good oral absorption, as well as a reduction in the occurrence of side-effects and undesirable drug interactions, and improved patient compliance. Azithromycin has good antibacterial activity against Haemophilus influenzae G, a common pathogen of community-acquired pneumonia, and is now considered the drug of choice for community-acquired pneumonia[3]. In recent years, it has been striking that macrolides also have some clinical applications other than anti-infective, such as bronchial asthma has a certain therapeutic effect, diffuse bronchiolitis also has a special therapeutic effect, and the results of animal experiments show that it also

has an inhibitory effect on bleomycin-induced pulmonary fibrosis[4].

1.3 Aminoglycosides

Aminoglycoside antibiotics mainly include streptomycin, gentamicin, kanamycin, and so on. These antibiotics mainly act on the process of bacterial protein synthesis, with a wide antibacterial spectrum, not easy to produce drug resistance and other characteristics. Still, there is a certain degree of nephrotoxicity. Aminoglycoside antibiotics can inhibit protein synthesis by inhibiting protein synthesis to play an antibacterial effect and bacterial ribosomal 30S subunit binding, inhibiting peptide chain extension and protein synthesis. Aminoglycoside antibiotics are less resistant, but bacteria may still develop resistance. Among the major resistance mechanisms are mutations in ribosomal proteins, increased expression of efflux pumps, and enhanced methylase activity. These resistance mechanisms can act individually or in combination, reducing bacterial susceptibility to aminoglycoside antibiotics. Different coping strategies, such as combinations of drugs and replacement with new antibiotics, can be adopted to overcome bacterial resistance to these resistance mechanisms[5].

1.4 Tetracyclines

Tetracycline antibiotics include tetracycline, oxytetracycline, and gentamycin. These antibiotics are mainly used to kill bacteria by inhibiting the synthesis of bacterial proteins and are characterized by a narrow antimicrobial spectrum and susceptibility to drug resistance[6]. The mechanism of action of tetracyclines is that the drug specifically binds to the A position of the 30S subunit of the bacterial ribosome, preventing the linkage of aminoacyl-tRNA at that position, thus inhibiting the growth of peptide chains and affecting bacterial protein synthesis. Some tetracyclines also increase the permeability of the bacterial plasma membrane to allow leakage of important intracellular substances, thus achieving a bacteriostatic effect. With the development and spread of drug resistance, the classical tetracyclines have severely compromised their bacteriostatic and bactericidal effects on bacterial infections.

1.5 Quinolones

Quinolone antibiotics include ofloxacin, ciprofloxacin, moxifloxacin, and so on. These antibiotics are mainly used to kill bacteria by inhibiting the activity of bacterial DNA gyrase and other enzymes, which have the characteristics of a wide antibacterial spectrum and good effect. Still, it is easy to produce drug resistance. Quinolone antibiotics have a good antibacterial effect on many kinds of bacteria, including Gram-negative bacteria and some Gram-positive bacteria. Quinolone antibiotics are widely distributed in the body, can enter the bones and joints, prostate tissue, etc., which most drugs can not enter, and its half-life is relatively long to reduce the number of times of taking the drug to a certain extent, and it is more convenient to use. However, quinolone antibiotics have side effects on epiphyseal development in adolescents and should be considered contraindicated in children and adolescents. In addition, quinolones also have adverse effects on the central nervous system, such as insomnia and headache. Therefore, when using quinolone antibiotics, it is necessary to strictly follow the doctor's instructions, use them reasonably, and pay attention to observing the adverse reactions[7].

2. Causes of antibiotic resistance

2.1 Genetic mutation

Mutations in bacterial genes often cause antibiotic resistance. Some bacterial genes encode enzymes that can break down antibiotics, and these enzymes can destroy the antibiotic, thus making the bacteria resistant to the antibiotic. A few base pair changes may occur during bacterial replication, mainly point mutations that substitute one or a few amino acids in a key target (enzyme, cell wall, or cell structure) to create a new resistant strain. Previously susceptible strains can accumulate resistance from another species. Most antimicrobial resistance genes are carried on plasmids or other types of genetic material that bacteria can transmit to other bacteria of different species, such that resistant bacteria pass on their resistance genetic material to other non-resistant bacteria, thus allowing the non-resistant bacteria to accumulate new resistant DNA and develop resistance[8]. In addition, selective pressure is the environmental condition that allows organisms with new mutations or newly developed characteristics to survive and spread. Bacteria encountering antibiotics are either eliminated or survive due to the presence of drug-resistant genes, and these surviving bacteria continue to multiply, rapidly displacing the non-resistant bacteria and gradually becoming the predominant form of survival for that group of bacteria.

2.2 Misuse of antibiotics

Misuse of antibiotics is one of the major causes of antibiotic resistance. Antibiotics are a double-edged sword, the correct use of which can treat diseases, but overuse or abuse may lead to the emergence of bacterial resistance. Prolonged, excessive, or inappropriate use of antibiotics, especially broad-spectrum antibiotics, can lead to the gradual development of resistance in strains of bacteria. Most reasons for this are public misconceptions about antibiotics, which are mistaken for essential household medicines and commonly used medicines. In addition, the public's limited knowledge of the efficacy and effectiveness of antibiotics is limited to the belief that

antibiotics can quickly cure a variety of diseases and that antibiotics are involved in minor and major illnesses[9].

2.3 Decreased immunity

Decreased immunity is also a factor in the development of antibiotic resistance. When the body's immune system is weakened, pathogenic bacteria can easily invade and colonize the body, and the use of antibiotics may increase, leading to strain resistance. The link between reduced immunity and antibiotic resistance is complex and interactive, with reduced immunity making antibiotic treatments less effective and increasing antibiotic resistance, affecting the functioning of the immune system, which can exacerbate infections and worsen the patient's condition.

2.4 Hospital infections

Hospital infections are an important route to the development of antibiotic resistance. Antibiotics are used frequently in the hospital setting, which can lead to the development of resistant strains of bacteria within the hospital. Some resistant strains can spread within the hospital and lead to infections in other patients. The aggregation of various pathogens in the hospital environment, coupled with the extensive use of medical devices, results in a higher risk of cross-infection, and the degree of cleanliness, implementation of disinfection measures, and the quality of disinfection of the medical devices involved can all affect the development of antibiotic resistance.

3. Antibiotic resistance mechanisms

3.1 Antibiotic passivation enzyme

Antibiotic passivation enzymes are enzymes capable of destroying the structure of an antibiotic by breaking down the chemical bonds of the antibiotic, causing it to lose its antimicrobial activity. For example, β-lactamase is a common antibiotic passivating enzyme that breaks down β-lactam antibiotics, causing them to lose their antimicrobial effect. The production of passivating enzymes is an important mechanism of bacterial resistance to antibiotics, and avoiding the production of antibiotic passivating enzymes is an important direction to improve the efficacy of antibiotics. Blunt enzymes are classified according to their mode of action: hydrolases and oxidoreductases. Hydrolytic enzymes catalyze the hydrolysis of ester, peptide, or glycosidic bonds of antibiotics, such as β-lactamases, which catalyze the hydrolysis of the β-lactam ring, resulting in the inactivation of penicillin and cephalosporins. Oxidoreductases convert antibiotics to inactive forms by oxidation or reduction reactions. For example, aminoglycoside acetyltransferases render aminoglycoside antibiotics inactive by acetylating them so they lose their ability to bind to bacterial ribosomes[10].

3.2 Drug effluent

The drug efflux pump is an important mechanism by which bacteria expel antibiotics that have entered the cell. Bacteria excrete antibiotics out of the cell through drug efflux pumps, thus reducing the concentration of antibiotics in the cell and achieving resistance. In Gram-negative bacteria, the efflux pumps work with the double-layered cell membrane to make them resistant to a wide range of antibiotics. Different efflux pumps do not have the same effect on antibiotics, with some providing a high level of resistance and others providing a low level of resistance. The efflux pumps for the substrate have a certain degree of selectivity [11].

3.3 Altered metabolic pathways

Altered metabolic pathways are an important mechanism in antibiotic resistance. Bacteria reduce the antibacterial effect of antibiotics by altering metabolic pathways to synthesize substances structurally similar to the antibiotic. For example, when sulfonamide antibiotics are used, if the required substrate is missing from the bacterial metabolic pathway, the antibiotic cannot be synthesized, which leads to bacterial resistance. Resistance mechanisms targeting altered metabolic pathways can be addressed by blocking these pathways to enhance the therapeutic effect of antibiotics[12].

3.4 Target change

The targets of antibiotic action are important proteins or enzymes in bacteria. In antibiotic resistance, bacteria reduce antibiotics' binding and action effects by altering their targets. For example, the action target of β-lactam antibiotics is penicillin-binding proteins (PBPs) in the bacterial cell wall. If the PBPs of bacteria are altered, the antibiotics will not be able to bind and thus lose their antibacterial effect. In response to the resistance mechanism of altered targets, better antibiotics can be designed against these targets to be able to overcome resistance[13].

4. Summary and outlook

Antibiotic resistance is a growing threat to human health, and we should fully face up to the enormous benefits that antibiotics bring to our fight against germs and the resistance that arises from the misuse and overuse of antibiotics. Only by deepening our understanding and research can we address the root causes of antibiotic resistance by gradually raising public awareness of antibiotic resistance and by strengthening the regulation of antibiotics by the relevant authorities.