Journal of Pharmaceutical and Medical Research
Print ISSN: 2663-1954
Online ISSN: 2663-1962
DOI: https://doi.org/10.61784/jpmr3075

CURRENT STATUS OF CLINICAL USE OF ANTIBACTERIAL DRUGS AND RESEARCH ON COUNTERMEASURES AGAINST DRUG RESISTANCE

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Abstract: Antimicrobial drugs are the main means of treating bacterial infections in clinical practice and play an important role in protecting human health. However, with the large-scale use and even rampant abuse of antimicrobial drugs in the medical, animal husbandry, and agricultural fields, the problem of bacterial resistance is becoming increasingly intractable and has now evolved into a global public health crisis. This article analyzes the current status and characteristics of the clinical application of antimicrobial drugs, explores the diverse mechanisms and harms of drug resistance, and proposes systematic prevention and control measures from multiple levels, including medical standards, technological innovation, and policy supervision, based on the latest research results and management experience at home and abroad. The aim is to provide theoretical basis and practical reference for preventing the spread of drug resistance and enhancing the level of rational use of antimicrobial drugs.
Keywords: Antibacterial drugs; Clinical application; Drug resistance; Rational use

1 INTRODUCTION

Antimicrobial drugs refer to drugs with bactericidal or bacteriostatic activity, including antibiotics such as β-lactams, macrolides, and aminoglycosides, as well as synthetic antimicrobial drugs such as quinolones, sulfonamides, and nitroimidazoles [1]. They have a strong inhibitory and bactericidal effect on certain substances produced or chemically synthesized by microorganisms such as bacteria, actinomycetes, or fungi through culture [2]. Previous studies have reported that antimicrobial drugs have played an important role in the treatment of various infectious diseases, but with the widespread and irrational use of clinical drugs, the resistance of bacteria to them has been continuously enhanced, which has increased the difficulty of clinical treatment [3]. Drug resistance monitoring is the basis for reducing bacterial resistance rate and guiding the rational use of antimicrobial drugs in clinical practice, and continuous monitoring of drug-resistant bacteria helps to provide dynamic guidance information for clinical practice [4]. According to domestic scholars [5], with the irrational use of clinical antimicrobial drugs, drug-resistant strains such as Enterobacteriaceae producing extended-spectrum β-lactamases (ESBLs) and methicillin-resistant Staphylococcus aureus (MRSA) have been continuously produced, leading to an upward trend in the resistance rate of pathogens to commonly used antimicrobial drugs. In China, the clinical application of antimicrobial drugs has gone through a development process from shortage to popularization and from disorder to standardization. Since the implementation of the "Administrative Measures for the Clinical Application of Antimicrobial Drugs" in 2015, the irrational use rate of antimicrobial drugs in China has dropped from 35% to 20% in 2023, achieving phased results, but the situation of drug resistance prevention and control is still severe [6]. The problems of drug abuse in primary medical institutions, the spread of multidrug-resistant bacteria, and the lag in the research and development of new antimicrobial drugs have not been completely solved. Systematically analyzing the clinical use of antimicrobial drugs, deeply exploring the mechanism of drug resistance formation, and building a scientific and effective prevention and control system are of great practical significance and strategic value for ensuring medical quality and safety and safeguarding public health stability.

2 CURRENT STATUS OF CLINICAL USE OF ANTIMICROBIAL DRUGS

2.1 Wide Range of Use but Uneven Distribution

Clinical application of antimicrobial drugs involves multiple departments such as internal medicine, surgery, obstetrics and gynecology, and emergency medicine. They are commonly used drugs to treat diseases such as respiratory tract infection, urinary tract infection, skin and soft tissue infection. The number of people using antimicrobial drugs worldwide is over 10 billion per year [7]. The amount of antimicrobial drugs used in tertiary hospitals accounts for more than 60% of the total. Given the higher level of diagnosis and treatment and the concentration of patients with difficult and severe illnesses, the intensity and variety of antimicrobial drug use in tertiary hospitals are significantly higher than those in secondary hospitals and primary healthcare organizations [8]. In terms of the types of diseases, respiratory tract infection is the most concentrated area of antimicrobial drug use, accounting for nearly 40% of the total clinical drug use, followed by perioperative prophylactic drugs in surgery and related drugs for the treatment of urinary tract infections.

Antimicrobial use exhibits a clear regional and institutional imbalance. Urban tertiary hospitals have relatively complete antimicrobial management systems and a high level of rational drug use. However, rural areas and community health service centers, due to scarce medical resources and limited professional skills of medical staff, often have problems with no indication for drug use and excessive use of drugs, becoming hotspots for antimicrobial abuse. There are also significant differences in drug use between different departments. Departments such as ICU and surgery use antimicrobial drugs at a significantly higher intensity than general internal medicine and pediatrics departments due to the severity of patients' conditions and the large number of invasive procedures .

2.2 The Problem of Unreasonable Use Still Exists

The efforts of medical institutions , the rational level of clinical application of antimicrobial drugs in China has significantly improved. Measures such as implementing a tiered management system, promoting electronic prescription review, and improving clinical pharmacy services have effectively curbed problems such as off-label use, duplicate medication, and inappropriate dosage. However, problems with irrational use still exist, mainly manifested in three aspects: First, the proportion of empirical drug use is too high. Some physicians blindly use broad-spectrum antimicrobial drugs without obtaining etiological testing results, leading to a lack of targeted medication. Second, the implementation of treatment courses is not standardized, facing the dual challenges of "too long a course" and "too short a course." Too long a course can induce drug resistance, while too short a course may cause infection recurrence. Third, there are inappropriate combinations of drugs. In some clinical situations, unnecessary multi-drug combinations are used, increasing the economic burden and adverse reaction risks for patients, and potentially promoting the emergence of drug-resistant strains. The control of antimicrobial drug use in outpatients still needs to be strengthened. The phenomenon of some primary healthcare institutions illegally using restricted and special-use antimicrobial drugs in outpatient settings is still common.

2.3 The Selection of Drug Types is Concentrated and the Application of New Drugs is Limited

Clinically commonly used antibacterial drugs mainly include β-lactams, macrolides, aminoglycosides, and fluoroquinolones. β-lactams (penicillins and cephalosporins) have a broad antibacterial spectrum and definite therapeutic effects, accounting for over 50% of all drugs used clinically. With the development of drug resistance, the use of high-level antibacterial drugs such as carbapenems has been increasing year by year, becoming a key means of treating multidrug-resistant bacterial infections. However, overuse of these drugs can further exacerbate the risk of drug resistance evolution. From the perspective of drug research and application, the shortage of new antibacterial drugs is very prominent. In the past 20 years, fewer than 10 new antibacterial drugs have been launched globally. The long development cycle, high costs, and limited market returns have dampened the enthusiasm of pharmaceutical companies for research and development. In China's antibacterial drug market, generic drugs dominate, and the number of independently developed new antibacterial drugs is limited. The range of drugs available for clinical treatment of pan-drug-resistant bacterial infections is limited, and some multidrug-resistant bacterial infections face the thorny problem of "no drugs available. "

3 THE FORMATION MECHANISM AND HAZARDS OF ANTIMICROBIAL RESISTANCE

3.1 The Core Mechanism of Drug Resistance Formation

The emergence of antimicrobial resistance is the result of the combined effects of bacterial biological characteristics, drug use behavior, and environmental factors. Its core mechanisms encompass both biological evolution and external driving factors. In terms of biological mechanisms, gene mutation and horizontal gene transfer are the main pathways for bacteria to acquire resistance. Random gene mutations may occur during bacterial reproduction; some mutations can enable bacteria to resist antimicrobial drugs, such as modifying drug targets or generating inactivating enzymes that can degrade drugs. Under the screening pressure of antimicrobial drugs, resistant strains survive and begin to multiply rapidly. Bacteria use vectors such as plasmids and bacteriophages to transfer resistance genes between different strains, achieving rapid spread of resistance. This horizontal transfer mechanism allows resistance to spread to different bacterial populations in a short period, forming multidrug-resistant or even pandrug-resistant bacteria. Among external driving factors, the irrational use of antimicrobial drugs is the primary factor. Approximately 50% of antimicrobial drug use worldwide each year is not in accordance with reasonable requirements. Unindicative use, overuse, and improper control of treatment duration increase the probability of bacterial contact with drugs, accelerating the process of resistance screening.

3.2 Multiple Harms Caused by Drug Resistance

Antimicrobial resistance has had a comprehensive impact on clinical treatment, public health, and the socio-economic landscape, becoming a significant barrier to the development of healthcare. In clinical treatment, resistance significantly increases the difficulty of treating infections. Bacterial infections that were originally easy to cure may become chronic or severe. Infections caused by multidrug-resistant bacteria such as methicillin-resistant Staphylococcus aureus (MRSA) and carbapenem-resistant Enterobacteriaceae require treatment with expensive and potent antibiotics such as vancomycin, and the treatment effect is often unsatisfactory, and may even cause serious adverse reactions such as nephrotoxicity and ototoxicity. Due to drug-resistant infections, patients' treatment cycles are prolonged, with an average hospital stay increasing by 3-5 days, and the mortality rate rises significantly . For example, the mortality rate of multidrug-resistant tuberculosis is three times that of ordinary tuberculosis. From a public health perspective, there is a risk of drug-resistant bacteria spreading across regions and forming a global epidemic. Hospital-acquired infections are the main mode of transmission of drug-resistant bacteria. Key departments such as ICUs and neonatal wards are high-incidence areas for multidrug-resistant bacterial infections, putting enormous pressure on hospital infection control efforts. The spread of drug resistance increases the difficulty of controlling common infectious diseases and may lead to the resurgence of some infectious diseases, weakening the level of public health emergency response.

4 PREVENTION AND CONTROL STRATEGIES FOR ANTIMICROBIAL RESISTANCE

4.1 Improve the Standardization of Antimicrobial Drug Use in the Medical Field

Strengthening the hierarchical management of antimicrobial drugs is a core means of standardizing clinical drug use. Medical institutions must strictly meet the requirements of the three-tiered classification management of unrestricted, restricted, and special-use drugs, and define the indications and approval processes for each level of drug use: general practitioners can immediately prescribe unrestricted drugs directly; if restricted drugs are used, approval from the department head is required; and special-use drugs must be used only after consultation by the antimicrobial drug management working group or expert group. Based on the antimicrobial resistance data monitored by the institution, the antimicrobial drug classification catalog should be adjusted in real time to improve drug combinations.

Implementing etiological testing and promoting precision medicine are key measures to reduce irrational drug use. Medical institutions should increase investment in microbiology laboratories to improve the timeliness and accuracy of bacterial culture and drug sensitivity testing. Drug sensitivity test results should be used as the key basis for selecting antimicrobial drugs, reducing the proportion of empirical drug use. For patients with severe infections, specimens should be collected for etiological testing before medication, and the medication plan should be adjusted in a timely manner according to the test results to achieve "precision diagnosis and treatment." Artificial intelligence-assisted decision-making systems can be introduced, relying on machine learning algorithms to analyze the patient's condition, etiological data, and drug resistance trends to provide reasonable opinions for clinical medication and reduce medication errors.

4.2 Strengthen Drug Resistance Monitoring and Data Sharing

Building a unified national antimicrobial resistance monitoring network is the foundation of prevention and control efforts. The monitoring framework at the national, provincial, and municipal levels should be improved, and the scope of monitoring coverage should be expanded to include secondary and above hospitals, primary healthcare institutions, and key departments. The monitoring content should cover key indicators such as the usage rate, intensity, and rational use rate of antimicrobial drugs, as well as the detection rate of drug-resistant bacteria and changes in the resistance spectrum. A standardized data collection and reporting system should also be established.

We must strengthen the special monitoring and prevention of key drug-resistant bacteria. For key drug-resistant bacteria such as methicillin-resistant Staphylococcus aureus, carbapenem-resistant Enterobacteriaceae, and multidrug-resistant Mycobacterium tuberculosis, we should build a special monitoring system to track the prevalence and transmission routes of these drug-resistant bacteria. Medical institutions should increase the implementation of hospital infection control measures to meet the needs of hand hygiene, environmental disinfection, and isolation protection, and reduce the spread of drug-resistant bacteria in hospitals. In particular, we should strengthen infection control in key departments such as ICU and neonatal departments.

4.3 Promote the Research and Development and Technological Innovation of Antimicrobial Drugs

Increasing investment in the research and development of novel antimicrobial drugs is a key approach to addressing drug resistance. The government should establish a special research and development fund to support innovative research and development of antimicrobial drugs, provide policy support such as tax incentives and expedited approval for the research and development of novel antimicrobial drugs, enhance the enthusiasm of enterprises to invest in research and development, and encourage cooperation between research institutions and enterprises to focus on basic research on targets of multidrug-resistant bacteria, and develop antimicrobial drugs with novel mechanisms of action, such as novel β-lactamase inhibitors, antimicrobial peptides, and phage therapy. Research on the reuse of existing antimicrobial drugs should be strengthened, and the ability of old drugs to combat drug-resistant bacteria should be enhanced by improving dosage forms and optimizing combination drug therapy.

Exploring the development and application of non-pharmaceutical prevention and control technologies, and developing and promoting antimicrobial vaccines can effectively reduce the probability of infection and reduce the demand for antimicrobial drugs. For example, pneumococcal vaccines and Haemophilus influenzae vaccines have played an important role in preventing infection, and the scale of their distribution should be expanded. New prevention and control methods represented by phage therapy, antimicrobial nanomaterials, and gene editing technology have shown good application prospects. We should increase the efforts in clinical verification and translational application, and expand the technical means of drug resistance prevention and control.

5 CONCLUSION AND OUTLOOK

The current status of clinical application of antimicrobial drugs and the prevention and control of drug resistance are major issues concerning public health security and the sustainable development of human health. While the rationality of clinical application of antimicrobial drugs in China is continuously improving, the problem of irrational use has not been completely resolved, and the situation regarding drug resistance remains severe. Challenges such as the spread of multidrug-resistant bacteria and the lagging development of new antimicrobial drugs urgently need to be addressed. To address the problem of antimicrobial resistance, the government, medical institutions, research units, enterprises, and the public must participate together. A multi-dimensional collaborative approach is needed, including improving medical standards, strengthening monitoring and early warning systems, promoting technological innovation, improving regulatory methods, and enhancing health education, to create a scientific and practical prevention and control system, providing a solid foundation for maintaining human health and the sustainable and stable development of the social economy.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

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